Managing Patients With Psoriasis in the Busy Clinic: Practical Tips for Health Care Practitioners

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Abstract
Psoriasis is a common inflammatory disease with significant comorbidities, whose management can be challenging given the variety of treatment options. It is critical for nurse practitioners, physician assistants, general practitioners, and dermatology trainees to have useful information about the treatment and monitoring of patients with psoriasis. Although certain aspects of care apply to all patients, each therapeutic agent has its own nuances in terms of assessments, dosing, and monitoring. The most appropriate treatment is based not only on disease severity but also on comorbid conditions and concomitant medications. These practitioners are vital in facilitating patient care by thorough understanding of systemic agents, selection criteria, dosing, and recommended monitoring. This article provides high-yield practical pearls on managing patients with moderate to severe psoriasis. It includes case-based discussions illustrating considerations for special populations, such as pregnant women, children, and patients with comorbidities (eg, human immunodeficiency virus infection, hepatitis C, hepatitis B, and history of malignancy).

Keywords
psoriasis, biologics, TNF inhibitor, cyclosporine, methotrexate

Introduction
Psoriasis is a prevalent condition in the United States, estimated to affect 7.4 million adults on the basis of 2013 estimates.¹ Although the prevalence of psoriasis has remained relatively stable among adults (estimated at 3.2%),¹ it is becoming an increasingly common diagnosis in children; from 1970 to 1974, the pediatric incidence rate was 29.6 per 100,000, which increased to 62.7 per 100,000 by 1995 to 1999.²

Appropriate treatment decisions for psoriasis are complex because of the variety of topical and systemic options, each carrying distinct advantages and disadvantages. Evidence-based clinical practice guidelines are available to guide both diagnostic and therapeutic decision making in clinical practice. In the United States, these include a series of guidelines and recommendations from the National Psoriasis Foundation,³-⁷ as well as guidelines from the American Academy of Dermatology Working Group.⁸-¹¹

Given that psoriasis is a chronic condition requiring ongoing treatment and monitoring for both response and tolerability, nurse practitioners, physician assistants, general practitioners, and dermatology trainees (in later practice) can play a key role in influencing outcomes. As part of the patient care team, all practitioners can assist in establishing realistic treatment goals for a given patient, which need to be reassessed and tailored over time. Goals for psoriasis treatment, as defined by a European consensus program, are outlined in Table 1.¹² Health care practitioners should also ensure that patients provide comprehensive medical histories before treatment options are discussed, which is particularly important in the setting of systemic therapy, whether it be with older agents such as methotrexate or cyclosporine or with biologics. The importance of assessing overall health status before and during systemic treatment of psoriasis cannot be overstated, because comorbidities such as...
for topical therapies, as well as suboptimal adherence to events and a lack of long-term efficacy and safety data, they have limitations, including cutaneous adverse effects. Vitamin D analogs, retinoids, coal tar preparations, and keratolytic agents are common first-line treatments, yet systemic therapies have become more rigorous in recent years. Although topical therapies (such as corticosteroids, vitamin D analogs, retinoids, coal tar preparations, and keratolytic agents) and phototherapy are common first-line treatments, they have limitations, including cutaneous adverse events and a lack of long-term efficacy and safety data for topical therapies, as well as suboptimal adherence to phototherapy (only 11% of patients received the recommended regimen of at least 3 sessions weekly). Nonetheless, surveys have shown that a large proportion of patients with moderate to severe disease receive topical medications alone, indicating a pattern of undertreatment in this population. Because of difficulties in accurately quantifying the frequency and amount of topical medication use and its relationship to clinical practice guidelines. Future studies in this area will greatly inform clinicians and researchers of the patterns of topical medication use, which is a cornerstone of treating patients with psoriasis of varying severity. In contrast, more rigorous evidence is available for the use of systemic treatments, on which the rest of this article is focused.

Currently, commonly used and approved systemic agents in the United States include methotrexate (with folate supplementation), cyclosporine, oral retinoids (acitretin), and apremilast, and 4 biologic agents, namely, etanercept, infliximab, adalimumab, and ustekinumab. Other types of therapies are on the horizon, including biologic agents that inhibit interleukin-17A (ixekizumab and brodalumab) or interleukin-23 (tildrakizumab and guselkumab), as well as oral molecules that inhibit the Janus kinase pathway (tofacitinib and baricitinib). The first interleukin-17A inhibitor, secukinumab, received approval in the United States for the treatment of moderate to severe plaque psoriasis in January 2015.

Methotrexate
Methotrexate was the first drug approved by the US Food and Drug Administration for the treatment of psoriasis, at a time (1972) when there were no well-designed studies of this agent. Weekly dosing for methotrexate typically ranges from 7.5 to 25 mg, with a suggested maximal dose of 30 mg/wk (Table 3). Patients should be screened for preexisting renal or liver disease because methotrexate elimination is reduced with impaired renal function, and careful monitoring for toxicity and altered dosing may be required in these patients. Various specific adjustments have been suggested, such as reducing the dose of methotrexate to 50% for a creatinine clearance of 10 to 50 mL/min and avoiding methotrexate altogether when creatinine clearance is <10 mL/min. This is particularly important for patients with reduced glomerular filtration rates or other significant risk factors for hematologic toxicity, such as advanced age, hypoalbuminemia, or alcohol intake exceeding moderate levels. Patients should be advised that it can take up to 4 weeks for a clinical response to occur. Supplementation with folate 1 to 5 mg/d is generally recommended and is especially important for patients who develop adverse gastrointestinal effects (most commonly nausea, vomiting, and anorexia, as well as stomatitis) and early bone marrow toxicity; in these patients, an increase in the initial dose of folate is warranted. Additional strategies for reducing the gastrointestinal effects of methotrexate include

### General Guidelines for Dosing and Monitoring Medications in Clinical Practice

The armamentarium of medications used to treat patients with moderate to severe psoriasis has grown continually in recent years. Although topical therapies (such as corticosteroids, vitamin D analogs, retinoids, coal tar preparations, and keratolytic agents) and phototherapy are common first-line treatments, they have limitations, including cutaneous adverse events and a lack of long-term efficacy and safety data for topical therapies, as well as suboptimal adherence to

### Table 1. Treatment Goals for Moderate to Severe Psoriasis

| Goal Description                                                                 | Percentage of Baseline |
|----------------------------------------------------------------------------------|------------------------|
| ≥75% reduction in PASI score from baseline                                        | ≥50% to <75% reduction in PASI score from baseline and DLQI score ≤5 |
| Modification of treatment*                                                        | <50% reduction in PASI score from baseline and DLQI score > 5 |

*DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index.

In this review we focus on providing practical monitoring tips during systemic therapy for psoriasis, which may be implemented by practitioners in routine clinical practice. Detailed information regarding pathophysiology, diagnosis, and the mechanism of action of each drug is not covered. Recommendations provided herein are consistent with the most current approved product labeling for each agent and the aforementioned published clinical practice guidelines.

### Table 2. Comorbidities Associated With Psoriasis

| Comorbidities                          |
|----------------------------------------|
| Cardiovascular disease                 |
| Metabolic syndrome                     |
| Obesity                                |
| Depression                             |
| Increased risk for infection (most clearly in patients with erythrodermic psoriasis) |
| Malignancies                           |
| Psoriatic arthritis                    |
| Other immune-mediated inflammatory diseases (Crohn’s disease) |

Cardiovascular, obesity, malignancy, infection, and depression are of high relevance in this population (Table 2). Ongoing assessments for psoriatic arthritis and other immune-mediated inflammatory diseases are also fundamental components of care. Although a discussion of monitoring and management principles for psoriatic arthritis (which may include referral to a rheumatologist) is beyond the scope of this review, interested readers may consult published guidelines.

In this review we focus on providing practical monitoring tips during systemic therapy for psoriasis, which may be implemented by practitioners in routine clinical practice. Detailed information regarding pathophysiology, diagnosis, and the mechanism of action of each drug is not covered. Recommendations provided herein are consistent with the most current approved product labeling for each agent and the aforementioned published clinical practice guidelines.
Table 3. Highlights of Approved Conventional Agents for Psoriasis.

| Agent          | Pregnancy Category | Starting Dose and Baseline Assessments                                                                 | Maintenance Dose and Follow-Up Assessments                                                                 | Response Rate in Clinical Trial(s) |
|----------------|--------------------|--------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|----------------------------------|
| Methotrexate   | X                  | Dose: 7.5-25 mg/wk PO, IM, SC, or IV; Laboratory assessments: LFT, CBC, BUN, Cr, pregnancy test if appropriate; Tb may be considered | Dose: 7.5-30 mg/wk PO, IM, SC, or IV on the basis of patient response and tolerability; Laboratory assessments: periodic CBC, BUN, Cr, LFT, pregnancy test if appropriate; Other assessments: consider liver biopsy in patients with increased hepatotoxicity risks or in all patients with accumulated doses of >3.5-4 g methotrexate reached PASI75 at 16 wk, 36% with individualized doses up to 25 mg/wk¹ | PASI75 at 16 wk, 36% with individualized doses up to 25 mg/wk¹ |
| Cyclosporine   | C                  | Dose: 2.5-5 mg/kg/d PO in 2 divided doses; Laboratory assessments: LFT, CBC, BUN, Cr, urinalysis, uric acid, lipid profile, electrolytes (K, Mg), pregnancy test if appropriate; Tb may be considered | Dose: 2.5-5 mg/kg/d PO in 2 divided doses, tapered downward in 0.5- to 1.0-mg increments on the basis of response and tolerability; Laboratory assessments: periodic LFT, CBC, BUN, Cr, uric acid, lipid profile, electrolytes (K, Mg), pregnancy test if appropriate | PASI75 at 8 and 16 wk, 50%-70% with 3 mg/kg/d |
| Acitretin      | X                  | Dose: 10-25 mg/d PO; Laboratory assessments: LFT, CBC, renal function, lipid profile, pregnancy test if appropriate | Dose: 25-50 mg/d PO; ≤25 mg/d in combination with UV may increase efficacy response and minimize side effects; Laboratory assessments: periodic LFT, CBC, renal function, lipid profile, pregnancy test if appropriate | PASI75 at 8 wk, 23% with 50 mg/d |
| Apremilast     | C                  | Dose: day 1, 10 mg AM; day 2, 10 mg AM and PM; day 3, 10 mg AM and 20 mg PM; day 4, 20 mg AM and PM; day 5, 20 mg AM and 30 mg PM; day 6 and thereafter, 30 mg PO bid; Laboratory testing: none | Dose: 30 mg PO bid; Laboratory assessments: none; Other assessments: monitor for weight loss and depression | PASI75 at 16 wk, 29%-33% with 30 mg bid |

bid, twice daily; BP, blood pressure; BUN, blood urea nitrogen; CBC, complete blood cell count; Cr, creatinine; IM, intramuscular; IV, intravenous; K, potassium; LFT, liver function test; Mg, magnesium; PASI75, 75% improvement in the Psoriasis Area and Severity Index score; PO, by mouth; SC, subcutaneous; Tb, tuberculosis; UV, ultraviolet.

¹Tb testing can be done using either QuantiFERON-TB Gold or purified protein derivative.

⁴The approved maximal dose is 4 mg/kg/d, but a maximal 5 mg/kg/d dose is often used in clinical practice.

¹²The approved initial dosing is 25 to 50 mg/d; however, because side effects are related to dose, individualization of the dosing regimen on the basis of tolerability and response is suggested.
administration via intramuscular or subcutaneous injection, dividing the dose, and having the patient take it in conjunction with food or at bedtime. Oral ulcers can also occur with methotrexate. Less common but serious and potentially fatal adverse events include myelosuppression, pulmonary fibrosis, and hepatotoxicity; patients with diabetes and nonalcoholic steatohepatitis have an elevated risk for liver impairment. Cases of hepatitis, reactivation of tuberculosis, and lymphoma have all been reported. It is recommended that patients be screened for latent tuberculosis infection before starting methotrexate. Monitoring guidelines for patients lacking risk factors for hepatotoxicity are outlined in Table 4. In patients with risk factors for hepatotoxicity, a different systemic agent may be considered, whereas liver biopsies are warranted in high-risk patients who ultimately initiate methotrexate therapy. Methotrexate is a teratogen and abortifacient, necessitating effective contraceptive methods in both men and women who receive this therapy. Methotrexate use may be associated with oligospermia in men; although the studies are limited and not conclusive, it is recommended that men wait 3 months after methotrexate discontinuation before attempting to father a child.

**Cyclosporine**

Cyclosporine has demonstrated high efficacy, with a short onset of action, against psoriasis in clinical trials. Recommended maximal dosing is 4 to 5 mg/kg/d in 2 divided doses for 4 weeks to achieve initial disease control. Once initial disease control is achieved, stepwise decreases are recommended. Different formulations are available, with the microemulsion formulation offering a better pharmacokinetic profile relative to the regular preparation. Patients need to be advised of the importance of taking cyclosporine at the same time each day and that solutions should be mixed with milk or orange juice but not grapefruit juice because of its cytochrome P450 inhibitory effects. Practitioners must ensure comprehensive, up-to-date knowledge of all concomitant medications, given the high drug-drug interaction potential. Nephrotoxicity (acute or chronic) is a primary concern and is correlated with the length of therapy. Therefore, renal function testing should be done at baseline and at frequent intervals (every 2 weeks during the first 3 months and then monthly if stable) after initiation of therapy. Other noteworthy adverse effects include hypertension, which often occurs in conjunction with renal toxicity, and an increased risk for the development of lymphomas and other cancers. As with methotrexate, it is recommended that patients be screened for latent tuberculosis infection before starting cyclosporine. Because the risks for renal toxicity and skin cancer increase with longer use, and the vasoconstrictive effects on renal arterioles associated with long-term therapy exceeding 2 years frequently lead to permanent scarring and loss of renal function, cyclosporine may be best reserved for intermittent short-term (<12 weeks) disease flares and then replaced with another therapy for ongoing use.

**Oral Retinoids (Acitretin)**

Oral retinoid therapy with acitretin has produced mixed efficacy results in clinical studies of its use in plaque psoriasis and may be less effective than other systemic agents. It has a slow onset of action, taking as long as 3 to 6 months for maximal responses, and has modest efficacy. Particular advantages of acitretin include its suitability for patients with pustular psoriasis and its lack of immunosuppression. Acitretin can be useful to treat flares of pustular psoriasis, such as may occasionally occur on the distal extremities as a paradoxical reaction to biologic therapy. Characteristic adverse effects include mucocutaneous dryness and other dermatologic abnormalities, as well as triglyceride elevations; laboratory monitoring should comprise liver function tests (LFTs), fasting lipids, complete blood cell count (CBC), and renal function tests. The high teratogenicity of retinoids and associated pregnancy category X rating limit their use in women of childbearing potential, who must be thoroughly counseled on the importance of contraception and the need for routine pregnancy testing. Donation of blood while on acitretin and for 3 years following therapy is not recommended, because of the risk for teratogenicity.

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**Table 4. Monitoring for Methotrexate Hepatotoxicity in Patients With No Risk Factors for Hepatotoxicity.**

- No baseline liver biopsy
- Monitor LFT results monthly for the first 6 mo and then every 1-3 mo thereafter
  - For elevations <2 times the upper limit of normal, repeat in 2-4 wk
  - For elevations >2 times but <3 times the upper limit of normal, closely monitor, repeat in 2-4 wk, and decrease dose as needed
  - For persistent elevations in 5/9 AST levels during a 12 mo period or if there is a decline in the serum albumin below the normal range with normal nutritional status, in a patient with well-controlled disease, a liver biopsy should be performed
- Consider liver biopsy after 3.5 to 4.0 g total cumulative dose
- Consider switching to another agent or discontinuing therapy after 3.5 to 4.0 g total cumulative dose
- Consider continuing to follow up according to above guidelines without biopsy

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AST, aspartate aminotransferase; LFT, liver function test.
Apremilast

Apremilast, an oral phosphodiesterase 4 inhibitor, modulates the production of proinflammatory and anti-inflammatory mediators that play a role in the pathogenesis of psoriasis. Although its exact mechanism of action in psoriasis is unclear, it reduced the severity of moderate to severe plaque psoriasis, alleviated signs and symptoms, and improved physical function in patients with psoriatic arthritis in phase 2 and 3 clinical trials. Consequently, in September 2014, apremilast was granted approval for the treatment of psoriasis and psoriatic arthritis in the United States at a recommended dose of 30 mg twice daily (Table 3). In patients with severe renal impairment, the dose should be reduced to 30 mg once daily because of possible increased systemic exposure to apremilast. Patients and caregivers should be advised to be alert for emergence or worsening of depression and other mood changes; they should also regularly monitor body weight, as decreases of 5% to 10% have been observed in some patients treated with apremilast. Apremilast should not be used with strong cytochrome P450 enzyme inducers, because of possible loss of efficacy.

Biologic Agents

The monitoring principles are similar for tumor necrosis factor (TNF)-α inhibitors and ustekinumab, and the key aspects are summarized in Table 5. At the onset of treatment, a thorough patient history, physical examination, and medication review are critically important, as is a comprehensive baseline laboratory profile. In general, at baseline, it is recommended to check CBC and LFTs; viral hepatitis screening and tuberculosis testing for patients about to initiate biologic therapy for psoriasis are also recommended. Patients should obtain all necessary vaccinations before initiating biologic therapy. The use of live vaccines is generally avoided during biologic therapy. If a patient requires live vaccine while on therapy, the recommendation is to withhold the agent for 3 months or 5 half-lives (6 months for infliximab) and then administer the live vaccine 1 month after the agent for 3 months or 5 half-lives (6 months for infliximab) and then administer the live vaccine 1 month after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after therapy can be resumed. A study found no increased incidence of infection in patients using biologics <42 days after...
National Psoriasis Foundation Web site (https://www.psoriasis.org) is an important source of guidance for how to overcome insurance hurdles. The Web site includes a variety of resources, including sample letters for requesting information regarding how to appeal a denial, submitting an appeal for the denial of a claim, or requesting an external review by the state insurance commission (https://www.psoriasis.org/access-care/insurance-center/appeal-a-claim/sample-letters). As outlined in the sample templates, it is critical that a sufficient level of detail be provided on the patient’s history, implications in the event of suboptimal care, and the recommendations made in the most current clinical practice guidelines that are relevant to the biologic agent being requested. The National Psoriasis Foundation Web site also includes a section reviewing biologic drug manufacturer programs, which may be a source of financial support for patients who are uninsured, are unable to afford the medication despite insurance, or have Medicare or Medicaid coverage (https://www.psoriasis.org/access-care/insurance/financial-assistance/biologics). Listings of private foundations that provide financial assistance with high out-of-pocket costs, which may include copays, are also available on the Web site (https://www.psoriasis.org/access-care/insurance/financial-assistance/copay).

### General Strategies to Overcome Treatment Challenges

#### Addressing Adherence

In clinical practice, we often encounter patients with psoriasis who do not respond to standard therapy and require more advanced management strategies (Table 6). First, it is important to assess patient adherence to therapy to ensure that all medications have been taken as scheduled. If a patient is not taking the medications as directed, it is important to elicit the reasons for the nonadherence, such as forgetfulness, inability to afford the medication, life events, or changes in comorbidities or concomitant medications. If an agent is known to take at least a few weeks or even a few months to provide significant relief, the clinician should convey that expectation to the patient at the outset. Clear communication of expectations will encourage adherence. Therefore, it is important to identify reasons for nonadherence and individualize the adherence discussion on the basis of the patient’s stated challenge to achieving adherence.

#### Managing Chronic Disease Exacerbation

If consistent adherence is confirmed and the patient is still experiencing significant disease, modification of the treatment regimen may be considered to improve long-term clinical outcomes. Strategies for the management of chronic disease exacerbation in patients with moderate to severe psoriasis include intensifying or escalating the dose of the primary systemic medication, combining the primary systemic medication with another systemic or topical agent or phototherapy, or switching to another primary systemic agent with a better efficacy, safety, and tolerability profile. Although the selection of one therapy over another is a complex topic that is beyond the scope of this review, any change in therapy will signal a heightened attention to monitoring for both efficacy and side effects.

#### Managing Flares

The natural history of psoriasis is still not well understood; however, one feature of the disease involves episodic flares or exacerbations, even in patients who are well managed with a good treatment regimen. First, the clinician needs to determine if the exacerbation represents a flare (episodic and nonsustained) or a sustained chronic worsening of psoriasis. If the patient is experiencing a disease flare while receiving a biologic medication, the extent of the disease flare will guide the choice of adjunctive therapy options. For a mild disease flare, reassurance regarding the natural history of psoriasis may be sufficient in some patients. For individuals experiencing a moderate flare, the provider may consider adding a class I topical steroid, combination formulations of topical steroids and topical vitamin D analogs, or intralesional injections of corticosteroids at troublesome lesions. For patients experiencing severe flares, the provider may consider a temporary dose intensification or dose escalation of the biologic, addition of another systemic agent, such as methotrexate, or adding phototherapy (especially for pregnant patients). These adjunctive options are typically used temporarily to control the flare until the patient returns to the baseline state of disease control, at which time these adjunctive options can be tapered.

#### Special Populations

Guidelines and general strategies provide approaches for managing the majority of patients with psoriasis, yet patients with certain characteristics require additional clinical judgment in establishing a therapeutic regimen. The following

| Table 6. Strategies to Overcome Treatment Challenges. |
|------------------------------------------------------|
| Confirm patient adherence to therapy                  |
| Assess medication administration pattern of patient   |
| Examine refill history                                |
| Check for factors that may affect efficacy            |
| Use of new medication                                 |
| Development of new comorbidity                        |
| Insufficient duration of treatment                    |
| Recent significant emotional event                    |
| Modify treatment, if necessary                        |
| Dose adjustment                                       |
| Change of therapy                                     |
| Combination therapy                                   |
| Reassess for efficacy and safety                      |
| Repeat laboratory testing as necessary                |
sections provide examples of the special circumstances in the form of simulated case studies.

Pregnant Patients

L.P. is a 28-year-old woman with severe psoriasis who had been previously treated with etanercept for 3 years. She is pregnant with her first child and has an affected body surface area (BSA) of 23%.

Managing psoriasis during pregnancy can be challenging because of the unpredictable nature of the disease course, with many patients (at least 30% and possibly as high as 65%) experiencing alleviation of symptoms; however, up to 20% of patients may be negatively affected by worsening symptoms. In addition, psoriasis has been associated with an increased poor outcome composite risk in pregnancy, with higher proportions of women with psoriasis experiencing complications, including spontaneous abortion, preterm birth, and low-birthweight infants, than unaffected women. Response to treatment can likewise be unpredictable, requiring a truly individualized approach, even in the prenatal period. The 5 pregnancy categories for pharmaceutical agents are summarized in Table 7, which can be used as a general guide but is limited by its simplicity and the lack of distinction between different types and degrees of developmental toxicity. In the treatment of moderate to severe disease, narrow-band ultraviolet B (NB-UVB) therapy has been used successfully in pregnancy and should be regarded as first-line treatment when a systemic approach is necessary. No teratogenic effects have been documented for broadband ultraviolet B or NB-UVB therapy. Systemic therapy with compounds related to psoralen plus ultraviolet A (PUVA) should be approached carefully; for example, methoxsalen is in pregnancy category C. Topical application is preferred over systemic administration when PUVA must be used in pregnant patients. Cyclosporine also falls under pregnancy category C, primarily on the basis of experiences in the transplantation population; in these patients, the use of other agents confounds the determination of fetal risk. However, reported pregnancy outcomes have generally been favorable, other than an increased incidence of intrauterine growth retardation and prematurity (which may be attributable to the underlying disease or the use of corticosteroids). In contrast, both methotrexate and acitretin are in pregnancy category X, and thus their use is contraindicated during pregnancy. Risks with methotrexate include miscarriage and well-documented dose-related abnormalities of growth, craniofacies, limb development, and neurodevelopment, collectively termed the aminopterin/methotrexate syndrome. Acitretin (like all systemic retinoids) poses a risk for congenital malformation that is nearly 26 times higher than that expected in the general population and includes cardiac, thymic, and central nervous system defects.

Biologics carry a pregnancy category of B. Recommendations regarding biologics are confounded by limited data from both human and animal studies; most case reports focus on patients with rheumatologic diseases. A case study of a pregnant patient treated with etanercept described an infant with VATER (vertebral anomalies, anal atresia, tracheoesophageal fistula, esophageal atresia, renal anomalies, and radial dysplasia); however, no association between etanercept or other TNF-α antagonists and VATER was observed in a subsequent prospective cohort study. Observational data suggest that pregnancy outcomes after exposure to infliximab shortly before or during pregnancy are similar to those expected in the general population. A published animal study of ustekinumab demonstrated no effects on development of the fetus or offspring. Practitioners should have thoughtful discussions with their patients with psoriasis of childbearing age with regard to potential risks associated with psoriasis and pregnancy, as well as treatment options during pregnancy.

Children

S.B. is an 8-year-old girl with severe psoriasis. Her family history is positive for psoriasis and psoriatic arthritis, which affects her mother. She has an affected BSA of 27%. She has no joint symptoms and enjoys ballet.
Vogel et al\textsuperscript{50} found that topical agents (primarily corticosteroids) were most often used for the treatment of psoriasis in children, whereas systemic and biologic therapies were rarely used, suggesting that management of psoriasis in children may be limited by safety concerns and a lack of appropriate guidance for this population. Phototherapy can be a valuable tool for treating psoriasis in children,\textsuperscript{51} offering a safer alternative relative to biologic and other systemic therapies. NB-UVB is generally considered more efficacious than broadband ultraviolet B phototherapy, whereas broadband ultraviolet B is less irritating than NB-UVB.\textsuperscript{52} Experiences with each are limited to small case series that have collectively demonstrated efficacy and safety, although long-term effects remain unknown. PUVA is often avoided in children because psoralen poses a risk for skin cancer and a number of adverse events (including nausea, cataracts, phototoxic reactions, hepatotoxicity, and headaches), as well as practical challenges associated with the avoidance of sunlight exposure.\textsuperscript{52} The American Academy of Dermatology cautions against the use of PUVA in children because of the risk for skin cancer.\textsuperscript{10} Some clinics restrict the pediatric use of psoralen to patients who weigh >100 lb and administer it only approximately 1 to 1.5 hours before exposing the skin to ultraviolet A light.\textsuperscript{52,53} Excimer lasers can be used to treat psoriasis in children. They have the ability to target plaques while sparing surrounding skin\textsuperscript{52} and appear safe on the basis of the consensus of expert opinion.\textsuperscript{19}

To date, no biologic agent has been approved by the Food and Drug Administration for use in children with psoriasis.\textsuperscript{53} However, the use of biologic therapy may be considered in children with psoriasis refractory to conventional therapies. The best evidence available pertains to etanercept, which can be considered the preferred biologic agent at this time and for which efficacy and tolerability have been demonstrated for up to 96 weeks in children aged 4 to 17 years with moderate to severe plaque psoriasis.\textsuperscript{54}

The safety and efficacy of adalimumab have been demonstrated in pediatric patients with juvenile rheumatoid arthritis (for up to 2 years)\textsuperscript{55} and Crohn’s disease (up to 1 year),\textsuperscript{56} and it has been approved in the United States for these indications in children.\textsuperscript{57}

**Patients With Human Immunodeficiency Virus Infection or Otherwise Immunocompromised**

M.P. is a 42-year-old man with a 10-year history of human immunodeficiency virus (HIV) infection (being managed by a stable antiviral regimen) who presents with moderate plaque psoriasis. He has been undergoing phototherapy for the past 6 months, but his psoriasis has progressed despite an initial brief improvement. He has an affected BSA of 22%.

Psoriasis is not necessarily more common among patients with HIV infection, but it has a propensity to be more severe.\textsuperscript{3} Immunosuppressant agents are generally discouraged in patients with HIV infection whenever possible\textsuperscript{3,5}; thus, the use of cyclosporine, methotrexate, and TNF-\(\alpha\) inhibitors is not ideal in this patient population.\textsuperscript{3} First-line therapy is phototherapy in conjunction with antiretroviral therapy; because they lack immunosuppressive properties, oral retinoids are the systemic agents recommended as a second-line option for managing moderate to severe psoriasis in patients with HIV infection.\textsuperscript{7} Monitoring parameters for these patients include LFTs, fasting lipids, CBC, and renal function tests. In addition, HIV testing should be done for patients at risk for infection or who do not respond to conventional and biologic therapies.

**Patients With Hepatitis C Virus Infection**

T.C. is a 56-year-old man with a history of intravenous drug use and chronic hepatitis C virus (HCV) infection who presents with severe plaque psoriasis. He is unable to attend regular phototherapy sessions, and his insurance does not cover home-based phototherapy. He has an affected BSA of 32%.

Chronic HCV infection is a well-established risk factor for both cirrhosis and hepatocellular carcinoma.\textsuperscript{58} Both methotrexate and acitretin have hepatotoxic potential. Treating patients who have HCV infection and psoriasis with TNF-\(\alpha\) antagonists might provide a viable alternative. Interestingly, as noted in a systematic review by Brunasso et al,\textsuperscript{58} TNF inhibition may make peripheral T cells more reactive to antigens, such as those derived from microbes, and increase the effects of interferon-\(\alpha\) on HCV. On the basis of the same systematic review by Brunasso et al, in a population of 153 patients with HCV infection, the safety profile of anti-TNF-\(\alpha\) therapy in the 23 patients with psoriasis, psoriatic arthritis, or both appeared acceptable. Of 22 patients with available data, most had stable viral and hepatic outcomes, several had improvement in 1 or both areas, and only 1 had an increase in viral load (which was not statistically significant).\textsuperscript{58} Cyclosporine has demonstrated antiviral activity in the HCV patient population but is regarded as a third-line option after the first-line use of topical and ultraviolet-based therapies and the second-line use of TNF-\(\alpha\) inhibitors.\textsuperscript{54}

A hepatologist should be consulted before starting anti-TNF-\(\alpha\) therapy in a patient with HCV infection. In this group of patients, regular LFTs and periodic quantitative HCV ribonucleic acid testing are warranted.

**Patients With Hepatitis B Virus Infection**

A.B. is a 45-year-old woman with chronic inactive hepatitis B virus (HBV) infection, presenting with moderate to severe psoriasis. She has normal LFT results and is negative for both hepatitis B e antigen and HBV deoxyribonucleic acid but positive for hepatitis B s antigen, hepatitis B core antibody, and hepatitis B e antibody. She has an affected BSA of 23%.

Reactivation of HBV occurs when the ratio of HBV replication and immune response is altered, as occurs during the treatment of malignancies with chemotherapy and the immunosuppression of autoimmune disorders.\textsuperscript{59} Manifestations...
are variable, ranging from asymptomatic to acute hepatitis, which carries a risk for death. Before initiating therapy for psoriasis, a patient with HBV infection should be referred to a hepatologist to determine disease status and whether there is an immediate need for antiviral therapy. Methotrexate is not to be used in patients with HBV infection. All TNF-α inhibitors may cause reactivation of HBV infection because of the mechanism by which they suppress the immune response; the overall frequency of HBV reactivation with infliximab may be similar to that with chemotheraphy. In a retrospective case series focused on characterizing the safety of TNF-α inhibitors in patients with plaque psoriasis with prior HBV or chronic HCV infection, there was no evidence of viral reactivation among 11 patients with past HBV infection who were treated with etanercept or adalimumab (mean duration, 7.8 months), consistent with the findings of a prior case series in which this treatment approach was concluded to be safe. Despite the case studies supporting the safety of these agents, repeated monitoring of viral load and liver function is necessary throughout treatment.

**Patients With Internal Malignancy**

Jeff is a 67-year-old man with severe psoriasis unable to attend regular phototherapy sessions. He has a history of stage II colorectal cancer successfully treated with resection and adjuvant chemotherapy (5-fluorouracil, leucovorin, and oxaliplatin) 6 years ago, with no evidence of recurrence. He has expressed an interest in biologic therapy for his psoriasis. He has an affected BSA of 18%.

Patients with histories of cancer and comorbid psoriasis represent a complex scenario, one that many dermatology providers will face. To help guide decision making for this particular patient, consulting with his medical oncologist would be worthwhile. Immunosuppressive medications may exert effects on cancer development, meaning that patients with histories of malignancy may be at risk for recurrence when treated with immunosuppressive agents, although successful experiences have been described. Information is limited on the safety of systemic agents in patients with preexisting cancers. The German Rheumatoid Arthritis-Observation of Biologic Therapy registry examined malignancy recurrence rates in 122 patients receiving anti-TNF-α agents and anakinra who had histories of cancer, finding a nonsignificant 40% increase in recurrence rates with anti-TNF-α therapy relative to disease-modifying antirheumatic drug therapy (incidence rate ratio, 1.4; \( P = .63 \)). Another study, the British Society for Rheumatology Biologics Register, assessed the incidence of recurrence of internal malignancies among 177 patients treated with anti-TNF-α agents and 117 patients treated with disease-modifying antirheumatic drugs. After 3 years of follow-up, incident malignancy in the anti-TNF-α treatment group was 25.3 events per 1000 person-years, compared with 38.3 events per 1000 person-years in the group treated with disease-modifying antirheumatic drugs; this difference was not significant in any analyses. The limited data available on the use of biologic agents for psoriasis in patients with histories of cancer complicate the necessary assessment of the risk-to-benefit ratio for a given patient, making consultation with the patient’s medical oncologist a prudent path forward.

**Conclusions**

In the current era, most patients with psoriasis can be managed successfully by a diversity of practitioners with existing therapies, although dose escalation and combination therapy may be needed in some cases. For special populations, searches of the published literature and input from colleagues from other fields should help guide decisions. Various health care providers, not limited to dermatologists, play an important role in patient management. Referrals to dermatologists who treat psoriasis, as well as rheumatologists when necessary, are appropriate when there is any doubt surrounding the best course of action. Ongoing monitoring is important for all patients with psoriasis but especially those receiving systemic agents. Finally, although practical challenges with insurance approval exist, they can be overcome with an organized demonstration of clear clinical need (https://www.psoriasis.org/health-care-providers/working-with-health-plans).

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