Psoriasis

Topicals:

- Corticosteroids
- Dovonex (vitamin D)
- Taclonex
- Retinoids (Tazorac)
- Tacrolimus/Pimecrolimus (Protopic/Elidel)

Systemic Agents:

- UVL
  - NB-UVB
  - PUVA (Psoralen + UVA)
    - -nausea
    - -sun sensitivity esp. eyes
    - -increased risks for skin cancer/melanoma
  - UVL – wand
    - -for localized disease

- Acitretin/Soriatane (Vit A derivative)
  - -Taken by mouth; 10-25 mg/day
  - -SE: sticky skin, hair loss, photosensitivity
  - -Lab abnormalities: elevated lipids +/- LFTs
  - -*Contraindicated* in childbearing

- Methotrexate (chemo agent)
  - -Long track record of safety, even in children
  - -Inexpensive
  - -PASI 75 = 26%
  - -Taken by mouth; 7.5 – 25 mg/week
  - -SE: liver damage, bone marrow, lungs
  - -Caution in diabetics, drinkers, Bactrim

- Cyclosporin (anti-rejection agent)
  - -Oral agent
  - -Relatively inexpensive
  - -SE: Nephro (kidney) toxicity, high blood pressure, gingival hyperplasia

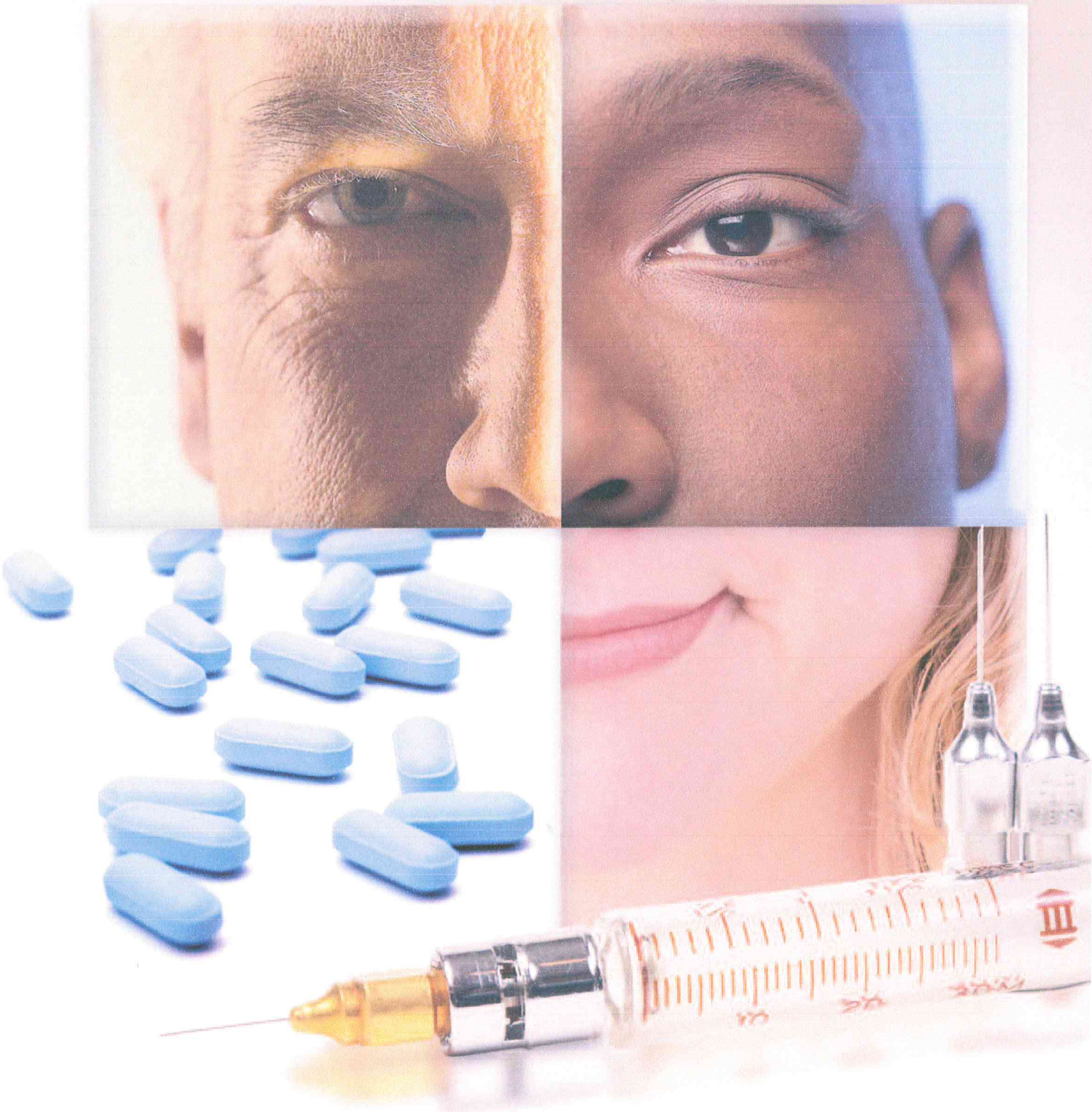
- Biological Agents
  - -T-Cell Inhibitors: Amevive (Alefacept)
    Raptiva (Efalizumab
  - -TNF Inhibitors: Enbrel (Etanercept)
    Remicaide (Infliximab)
    Humira (Adalimumab)
  - -Fusion Protein Inhibitors: Enbrel(Entanercept)
  - -IL-12 & IL-23 Inhibitors: Stelara (Ustekinumab)

TNF INHIBITORS	T CELL INHIBITORS
-Watch CHF, MS, TB/Infections w/Remicaide & Humira; Malignancy -↑ efficacy -↓ adverse reactions	-Watch for infection, malignancy/solid tumors (lymphoma & aplastic anemia) -↓ efficacy; doesn't work in pso arthritis -↓ adverse reactions

MONOCLONAL ANTIBODIES	
REMICAIDE (Infliximab) Monoclonal chimeric antibody IV 5 mg/kg x 50 weeks Weeks 9, 2, 6, 14 then q 8 weeks PASI 75 = 60% Sustained response, but dose creep Better in 2 weeks SE: infusion site rxn, flu-like (16%),↑LFT	**AMEVIVE** (Alefacept) Blocks CD-2 on T cells; deletes memory cells IM; 12 weeks on, 12 weeks off 5 treatment courses; PASI 30%, 40%....55% SE: hepatic injury (20%), H/A, itch, infection Labs: CD-4; hold if less than 250 (4%) Sustained response
HUMIRA (Adalimumab) Human antibody Subcutaneous 80 mg then 40 mg q week Utilized for 60 weeks PASI 75 – 67% (75% if weekly) Sustained response Improvement in 2 weeks	**RAPTIVA** (Efalizumab) Humanized monoclonal ab to CD11a of LFA-1 Works on Tcell activat'n trafficking,cytokine rel 0.7 mg/kg conditioning dose then 1 mg/kg utilized for 3 years w/PASI 75 = 40-50% SE: flu-like during initiation; expect ↑wbc (2xly) H/A, infection, hemolytic anemia,↓plts (.3%) Labs: check plt q mo x 3 then q 3 mo Okay to use w/UVB Works fast, *but* REBOUND on discontinuation
FUSION PROTEIN INHIBITORS	**IL-12 AND IL-23 INHIBITORS**
ENBREL (Entanercept) Fusion protein, binds TNFα 50 mg twice/wk x 3 mo, then 25 mg twice/wk PASI 75 = 47% Slower onset ~ 6 weeks	**STELARA** (Ustekinumab) Blocks IL-12 & IL-23, 2 proteins in immune system Every 12 weeks after 2 starting doses wks 0&4 PASI 75 = 80% at 12 weeks 5 year data available

***ANY MEDICATION THAT SUPPPRESSES YOUR IMMUNE SYSTEM RUNS THE RISK OF INFECTION, ALLERGIC RXN, MALIGNANCY & RPLS (A REVERSIBLE NEURO DISORDER)

Patient-Centered Approaches to



Moderate-to-Severe Psoriasis

An expanding treatment arsenal means dermatologists can better manage patients based on each individual's unique needs.

By Abby S. Van Voorhees, MD

Any dermatologist knows that therapeutic response in moderate to severe plaque psoriasis varies from patient to patient and may even change for an individual over time. To some extent, the emergence of multiple systemic agents to treat moderate to severe psoriasis reflects this variability of the disease. The expansion of the treatment arsenal means that clinicians must consistently re-evaluate their approach to management so that they are able to choose a treatment that is most likely to meet each patient's specific needs with the fewest risks and side-effects.

With the still relatively recent advent of biologic therapies for psoriatic disease, clinicians wonder where and how these agents fit into treatment of moderate to severe disease. Reviewing the therapeutic approach to a few different patient populations helps identify when and how clinicians may consider use of the various treatment options.

Need for Effective Interventions

The importance of implementing effective therapies for psoriasis is increasingly clear as dermatologists learn more about the impact of the disease on patients. The National Psoriasis Foundation conducted a survey in 1998 that provided valuable insight into the effect of psoriasis on patients.[1] A remarkable 43 percent of the foundation's membership (n=17,488) completed the four-page questionnaire, which was focused on capturing patient experience rather than quantifying quality of life. The survey was not powered for statistical analysis.

Of note, more than three-quarters (78 percent) of patients with severe psoriasis reported frustration with treatment, while about half (49 percent) of patients with severe psoriasis reported they were "only somewhat" or "not at all" satisfied with treatment. Thirty-two percent of patients reported treatment was not aggressive enough.

Psoriasis clearly impacts patients' functioning. Roughly 20 percent of patients in any age group reported that psoriasis negatively impacted sleep. More than one quarter of patients younger than age 54 reported a negative impact on sexual activities. Many patients also face limitations walking and washing their hands, and these limitations appear to increase with age.

About one in six patients 18 to 34 years old reported psoriasis-related problems interacting in the workplace, interacting with family and/or spouse, and making and/or keeping friends. This rate was only slightly lower for those 35 to 54 years of age.

Many patients also said they experienced exclusion from a public facility or trouble obtaining jobs. As many as 10 percent of the youngest responders said they even considered suicide due to their disease.

Greater sensitivity to the treatment needs of patients coupled with the emergence of new therapies has changed our approach to management of moderate to severe psoriasis. Psoriasis is more prevalent than previously thought. Dermatologists must understand the disease process and keep abreast of emerging treatments, such as biologics, that may inhibit disease progression and improve long-term patient outcomes and quality of life. The appropriate use of emerging therapies will help address these significant health concerns.

Starting Point

To begin, it's important to identify what constitutes moderate to severe psoriasis. Though several indices are available to measure the severity or impact of psoriasis, for the sake of discussion, a moderate to severe presentation will involve 10 percent or more body surface area or will include involvement of a more limited area that is associated with morbidity, such as plantar involvement.

For many cases of moderate to severe psoriasis, UVB phototherapy (preferably narrow-band, NBUVB) warrants consideration as an initial treatment. Though there are inherent risks associat-

TABLE 1

	Advantages	Disadvantages
PUVA	• Useful in the following settings: Moderate to severe disease or specific sites resulting in disability; Thin to thick plaques; Minimal to moderate severe erythema; All skin types ; Elderly • Need for maintenance therapy • Need for ltd. tx over time (<250 treatments)	• Hassles/difficulties associated with access • Risk of phototoxicity and photosensitivity • Risks of potential skin cancer • Tolerabilty of Oxsoralen Ultra • Cost of Oxsoralen + co-pays
ReUVB & RePUVA**	• Greater efficacy • More rapid clearing w/fewer number of UVB or PUVA treatments • Lower cumulative doses NB-UVB or PUVA • Fewer side effects from systemic retinoids secondary to low-dose therapy • Option for maintenance with either agent	• Potential side effects associated with retinoid: Lipid and hepatic monitoring; Special concerns in women of child-bearing potential • Enhanced risk of phototoxicity • Hassle/lack of access of phototherapy • Cost of acitretin + copays
Methotrexate & Cyclosporine	• Efficacy • Convenience • Oral formulation • Potential risks/side effects well established • Relatively inexpensive	• Risk of potential toxicities: MTX: hepatic, bone marrow, pulmonary, Liver bx indicated every 1.5 gm; CsA: nephrogenic, hypertension, gingival hyperplasia • Risk of potential side effects: MTX: nausea, fatigue; CsA: HA, muscle aches • Risk of potential drug interactions: MTX: ie Bactrim; CsA: ie Coumadin
Alefacept (Amevive)	• Intermittent therapy/remittive: Appealing to travelers, college students, elderly • Administered by office staff: Useful when patients do not want to self-inject • Useful w/concerns of non-compliance/lack of responsibility • Medicare coverage • Possible Role in PsA	• Patients requiring rapid response of psoriasis • Lower response rate after 1 course • Cost
Efalizumab (Raptiva)	• Long-term, control of psoriasis • Efficacy and convenience • Usefulness with comorbidities such as CHF	• Concerns in non-compliant patients/need for selection of responsible patients • Risk of rebound/inflammatory flare • Lack of benefit in PsA - ? New onset • Risk of thrombocytopenia • Risk of anemia • Cost
Etanercept (Enbrel)	• Long term control of psoriasis • Efficacy and convenience • Concurrent treatment of PsA • Prior use in children 4+ for other indications	• Need for avoidance with comorbidities such as: CHF; Prior malignancies; Lupus erythematosis; Personal/family Hx of MS, other neurological syndromes • Infections • Cost
Infliximab (Remicade)	• Long term control of psoriasis • Rapid response • Highly efficacious • Intermittent tx (infusions Q4-8wks)/remittive • Avoidance of self-injections • Medicare coverage • Concurrent treatment of psoriatic arthritis	• Hospital/office-based administration • Avoid with Hx of sensitivity to murine products • Need for avoidance with comorbidities such as: CHF; Prior malignancies; Hepatic abnormalities; Lupus erythematosis; Personal/family Hx of MS, other neurological syndromes • Infections / TB; Blood dyscrasias • ? Escalating dose • Cost
Adalimumab (Humira)	• Long-term control of psoriasis • Efficacy and convenience • Concurrent treatment of PsA	• Need to avoid with comorbidities such as:CHF; Prior malignancies; Lupus erythematosis; Personal/family Hx of MS, other neurological syndromes • Infections / TB; Blood dyscrasias • Cost

ed with ultraviolet irradiation of the skin, UVB phototherapy can quickly and effectively yield control of psoriasis without the use of significant doses, allowing dermatologists to minimize long-term risks.

NB-UVB is useful across a range of presentations, including moderate to severe disease, in plaques of thin to moderate thickness, in patients with minimal to moderate erythema, and in patients with lighter skin types. Among its benefits, UVB phototherapy avoids use of systemic agents. NB-UVB is a potentially safe and effective option for all ages, from children to the elderly. The emergence of effective at-home units is another benefit.

However, there are contraindications and practical considerations that limit the usefulness of UVB phototherapy in certain cases. Disadvantages associated with NB-UVB phototherapy include difficulties associated with access. These include lack of access within the dermatologist's office or a nearby practice, as well as patient convenience issues, such as work/personal schedule conflicts, lack of transportation, etc. Additionally, NB-UVB phototherapy can be expensive, even for patients with otherwise good insurance coverage. Several co-pays each week quickly add up. There are risks of phototoxicity and potential skin cancer, which clinicians can work to minimize. Finally, though UVB phototherapy can quickly yield clearance, patients can require regular

***Note:* ReUVB phototherapy**
RePUVA photochemotherapy

Systemic retinoid
- Acitretin, Dosage: 10-25mg PO daily
- Isotretinoin, Dosage: 0.5mg/kg PO daily

PLUS: UVB or PUVA 2-3 times each week

maintenance treatments. This too, can be inconvenient, especially over the long-term.

Table 1 offers a review of the advantages and disadvantages of several other interventions to be discussed in this article, including PUVA.

Moderate to Severe Psoriasis in the Healthy Adult

Generally speaking, a healthy adult with moderate to severe psoriasis may be a prime candidate for UVB (narrow-band or broad-band) phototherapy.[2] (Table 2) To augment or extend the efficacy of UVB phototherapy, consider add-on therapies, such as UVB plus systemic retinoids, UVB plus adjuvant topical therapies, or even Goeckerman therapy, which though effective remains frequently overlooked. While combined use of drugs with UVB exposes patients to the risks and possible adverse effects of both agents, the combination approach can maximize the efficacy of each intervention, thereby limiting the duration of exposure to and cumulative dose of either treatment.

In the event that UVB phototherapy is unavailable, contraindicated, ineffective, or simply impractical (due to any number of factors including patient noncompliance), other treatment options include: Systemic retinoids, alefacept (Amevive, Biogen), cyclosporine, etanercept (Enbrel, Amgen-Wyeth), adalimumab (Humira, Abbott), methotrexate, PUVA, efalizumab (Raptiva, Genentech), or infliximab (Remicade, Centocor). Choice of an agent for any individual patient will depend on various factors including previous treatment history, unique patient characteristics, patient comorbidities, compliance, insurance coverage, and in the case of biologics patient preference (self-injection, etc.). I do not recommend acitretin for any female patient of childbearing potential.

Should these options alone prove ineffective, consider a combination approach. Effective appropriate combinations include cyclosporine plus methotrexate, methotrexate plus a biologic, a retinoid plus a biologic, or a biologic in combination with UVB phototherapy. Note that while several of these combinations have been used safely and effectively in the clinic, extensive data may not be available for all approaches.

Moderate to Severe Psoriasis in Childhood

The approach to the healthy adult provides a basic framework for psoriasis therapy, though the approach will change to meet the specific needs of patients in special populations, such as children. Patients under age 18 account for about 0.3 percent of all cases of psoriasis, with 10 percent of all psoriasis patients diagnosed by age 10, and 30 percent diagnosed by age 15.

> UVB photochemotherapy remains the cornerstone of treatment of moderate to severe psoriasis in the healthy patient under 18.

Family history is variable with about 15 percent of pediatric patients having one parent with psoriasis but 75 percent having a history of psoriasis in both parents. The male/female ratio is variable.

UVB photochemotherapy remains the cornerstone of treatment of moderate to severe psoriasis in the healthy patient under 18. However, there are child-related challenges associated with UVB phototherapy. Specifically, compliance can be challenging because patients are obviously dependent on an adult for transportation and will have school and activities that limit access to treatment. Having a young child sit still in the light box can be a challenge; patient boredom can compound the challenge. Younger children especially may be tempted to remove goggles or shielding, which is obviously problematic.

Having a parent in the lightbox to hold the young child may be an option. We have found that providing headsets is a good way to distract patients, minimize boredom, and improve the phototherapy experience, especially among pediatric patients. Similar challenges exist when administering UVA, which is a second-line option for some healthy children. NB or BB-UVB can be combined with adjuvant topical agents or in special cases with systemic retinoids. Goeckerman is also an option.

If UVB in unavailable, contraindicated, ineffective, or not practical, systemic options include cyclosporine, Enbrel, methotrexate, and for dark-skinned patients PUVA.

Liver toxicity is the most common adverse event associated with methotrexate in this population. Pediatric patients receiving methotrexate must avoid live vaccines. Clinicians must recognize and alert parents/patients to risks associated with certain concurrent medications, i.e. tetracyclines. Additionally, inform patients/parents that concurrent milk intake can decrease bioavailability. Guidelines for use of methotrexate in pediatric rheumatology patients do not require liver biopsy.

The recommended pediatric dose of acitretin is 0.25-0.6mg/kg/day. Use of this agent has been linked to a risk of premature epiphyseal closure and spinal hyperostosis, prompting some specialists to encourage bone scans every 12 to 18 months for pediatric patients on chronic

TABLE 2. Management of Moderate to Severe Psoriasis in a Healthy Adult (without PsA)[2]

If UVB available, feasible, practical, and suitable	If UVB unavailable, contraindicated, ineffective, or patient unable to comply
NB or BB UVB Photochemotherapy • UVB Photochemotherapy alone • UVB plus systemic retinoids • UVB plus adjuvant topical therapies • Goeckerman therapy	• Systemic retinoids • Alefacept • Cyclosporine • Etanercept • Adalimumab • Methotrexate • PUVA • Efalizumab • Infliximab
	• Cyclosporine plus methotrexate • Methotrexate plus a biologic • Retinoid plus biologic • Biologic plus UVB phototherapy

therapy. It is important to consider the risk of conversion to etretinate with alcohol consumption, especially when treating teen patients.

The dose for cyclosporine in pediatric patients is 3.0-3.5mg/kg/day.[3] There are risks associated with concurrent medication use, particularly Trimethoprim-sulfamethoxazole. Patients must avoid live vaccines. Treatment is linked to an increased risk of lymphoma. The most common side-effect associated with treatment is headache.

Enbrel is the biologic of first-choice in pediatric patients because it is approved for and has a history of use in juvenile rheumatoid arthritis (JRA). Data from the JRA trials show an increased risk of infections, such as upper respiratory infections and sinusitis. Patients must avoid live vaccines. Recommended dosage is 0.4mg/kg twice weekly.

Moderate to Severe Psoriasis in Patients of Color

While the frequency of psoriasis is lower among African-Americans than in the overall US population (1.3 percent African-Americans versus 2.5 percent Caucasians), there is no difference in severity between the two groups.[4]

During the initial evaluation of a patient of color, screen for possible hypertension or diabetes mellitus, which tend to be more prominent in African-American patients. Patients with hypertension treated with systemic retinoids, regardless of ethnicity, require ongoing lipid monitoring if concurrent hyperlipidemia is present.

UVA may be considered earlier for patients of color due to the decreased risk of skin cancers. If phototherapy is feasible, suitable, and practical, first-line treatment options include NB or BB-UVB phototherapy alone, UVB plus systemic retinoids, UVB plus adjuvant topical agents, Goeckerman, PUVA, or PUVA plus adjunctive retinoids.

With the exception of PUVA moving up in the algorithm, the approach is otherwise the same as for the healthy adult patient.

Moderate to Severe Psoriasis in Patients who Abuse Alcohol

The incidence of alcohol abuse is increased in psoriasis patients, perhaps due to the emotional burden of the disease (though this is speculative). Beyond the obvious concerns associated with enhanced drug toxicity of the liver, alcohol abuse presents a challenge to compliance, with a possible lack of consistency in medication administration. This is true not only for systemic medications but for phototherapy as well; patients may not present for treatment or not comply with instructions during UV administration.

Aside from recognizing the risk of poor compliance, dermatologists may approach the patient who abuses alcohol much as they would the healthy adult patient—with some caveats. Limit use of cyclosporine to the short-term and monitor patients on all therapies for signs of developing hepatoxicity. Generally, acitretin use is not encouraged for any patient who abuses alcohol.

Psoriasis: Disease Facts[6,7]

- Psoriasis affects 4.5 million to 7 million people in the US
- 150,000 to 260,000 new cases reported per year
- Mean age of onset: 28 years
- Peak onset in late teens /early twenties
- Second peak of onset: 50-60 years
- 1.7 million people with psoriasis are being treated
- 600,000 patients with moderate to severe disease
- Incidence of psoriatic arthritis between 5-30%

Psoriasis in Patients with Hepatitis C

The incidence of Hepatitis C in psoriasis patients is about 10 percent and is slightly higher (12 percent) in patients with psoriatic arthritis. Findings that skin lesions can be positive for hepatitis virus particles have led some to speculate that the virus could actually be a trigger for psoriasis. Additionally, interferon therapy often exacerbates psoriasis.[5]

In light of potential liver toxicity as well as issues related to immunosuppression, the approach to management is cautious. As in the healthy adult patient, UVB phototherapy is first line. If unavailable, ineffective, or impractical, systemic options include retinoids, Enbrel, or PUVA. Should these fail to yield control, consider other biologic agents or systemic treatments: Humira, Amevive, azathioprine, short-term cyclosporine, Raptiva, Remicade, or myophenomofetil.

Erythrodermic Psoriasis

Affecting just 0.8 to 4.1 percent of the population, erythrodermic psoriasis can be a diagnostic and therapeutic challenge. The condition, with a mean age of onset of 50 years, affects twice as many men as women. It may be acute or chronic in nature.

It is important to distinguish between etiologies, including drugs, PRP, and other systemic diseases. Appropriate patient evaluation is critical. Question patients regarding a history of congestive heart failure or other heart disease. On the physical exam, check vital signs and be vigilant for lower leg edema. Laboratory evaluation should include CBC, hepatic profile, chemistry profile, skin biopsy, and sepsis evaluation.

Due to the need for immediate institution of therapy and desire for rapid control, first line treatment options are systemic retinoids, Remicade, methotrexate, Enbrel (50mg twice per week), cyclosporine, or Humira. Any of these should be used in conjunction with adjunctive topical measures, including wet compresses, cool baths, and/or mid-potency steroid ointments. Consider hospitalization if indicated; rule out sepsis.

Once erythrodermic psoriasis is stable, maintain clearance based on the standard algorithm for a healthy adult.

Psoriatic Arthritis plus Psoriasis

Estimates suggest that 10 to 30 percent of psoriasis patients will develop psoriatic arthritis (PsA). Onset of PsA tends to be in the fourth to sixth decade, and the disease is often preceded by plaque psoriasis. PsA affects about one percent of the population in the US, affecting men and women equally.

The appropriate approach to treatment considers the needs of both diseases and in many cases, given that PsA may develop in a patient already being treated for psoriasis, involves an "additive" approach. For limited joint stiffness or minimal disability, non-steroidal anti-inflammatory agents (NSAIDS) may be added to the current psoriasis therapy. Alternatively, first-line treatment options for patients with psoriasis and PsA include Enbrel, Humira, Remicade, or methotrexate. Any of the preceding biologics may be used in conjunction with methotrexate, which is particularly beneficial if the patient is transitioning from methotrexate.

A dermatologist may consider referral to a rheumatologist for complete evaluation and possible early detection of progressive, deforming arthritis.

Importance of Individualizing Treatment

The biologic agents are a welcome addition to the therapeutic array that enhance our ability to treat psoriasis across a range of patient populations. Nonetheless, there is no one treatment that is right for every patient or every type of disease. In order to make the best treatment decisions, dermatologists in the clinic must consider all relevant information about a patient and their comorbidities, avoid possible drug interactions, allow for enhanced patient satisfaction, and attempt to maximize compliance. These considerations will guide selection of the best intervention for a given patient.

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