Psoriasis care is ever changing. As researchers analyze new modes of therapy and look for new ways to harness existing therapies for various forms of psoriatic disease, clinicians encounter patients on a daily basis that are affected by psoriasis in different ways. Thus, it is important that physicians keep informed regarding the latest advances in therapy as well as the latest data on comorbidities and the psychosocial impact of psoriatic disease.

The National Psoriasis Foundation Medical Advisory Board recently published new consensus guidelines for the treatment of moderate to severe psoriasis in the January issue of the Archives of Dermatology. The guidelines address a range of issues, from severity to treatment regimens. Ahead, I will summarize the central points and provide commentary on implications for care.

**CONSENSUS GUIDELINES**

Among the tasks of the guidelines was to provide an update on each of the treatment modes available. Here is a brief recap of the guidelines for psoriasis therapy:

**Oral Therapies.** Acitretin holds a place as a first-line oral treatment for palmoplantar or pustular psoriasis but should not be used in women of child bearing potential. As a monotherapy for plaque psoriasis, its use is limited due to a slow onset of action and its known difficulty to achieve complete clearing of plaques.

The guidelines indicate that cyclosporine, although approved by the US Food and Drug Administration for up to one year of use, be limited to 12-week treatment to control a flare. After this, therapy should be transitioned to another long-term agent, which does not have nephrotoxicity.

The final oral agent used in psoriasis, methotrexate, seems to have less efficacy than cyclosporine but can be used more long-term. However patients with risk of fatty liver—i.e., diabetics, obese patients—will require liver biopsies whenever a cumulative dose of 1.5g is taken.

**Biologic Agents.** Despite the newfound prominence of the new consensus guidelines provide a blueprint for the evolving standard of psoriasis care. In addition to these, developments in research, development, and clinical practice are likely to continue changing how clinicians understand and treat psoriasis, as well as care for patients with psoriatic disease. It is important to recognize that certain regions of psoriasis—i.e. scalp, palmar-plantar, groin involvement—may have less than 10 percent BSA but are severe in nature and may not be responsive to topical therapies. As new data and improved therapeutic delivery continue to usher developments that are changing the face of psoriasis care, ultimately the most important element of successful treatment is your relationship with the patient.
of IL-12/23 inhibitors, anti-tumor necrosis factor (TNF) agents are still considered a mainstay therapy for moderate to severe psoriasis. While efficacy data on the TNF inhibitors are fairly clear, safety has long been an area of debate. The guidelines clarify the current safety concerns with TNF inhibitors. Risks associated with adalimumab (Humira, Abbott), etanercept (Enbrel, Amgen), and infliximab (Remicade, Janssen) include sepsis, tuberculosis, infections, exacerbation of congestive heart failure, lymphoma, and demyelination. These must be taken into account when evaluating, monitoring, and discussing these treatments with patients. While data on the IL-12/23 agents is less robust, ustekinunumb (Stelara, Janssen) is also considered well tolerated and effective as a first-line treatment.

**Phototherapy.** Although psoralen + UVA (PUVA) is slightly more effective than Narrowband UVB (NB-UVB), it leads to more skin aging and freckling, while also increasing the risk of squamous cell and basal cell carcinoma. If opting for NB-UVB, the guidelines suggest that it should be administered three times per week, whereas PUVA can be effective at two times per week. Moreover, the addition of acitretin to NB-UVB or PUVA enhances efficacy.

**CIRCUMSTANTIAL TREATMENT**

The guidelines also update the treatment of psoriasis in specific situations:

**Pregnancy.** For patients who are pregnant with severe disease, NB-UVB is an option. The guidelines also indicate that cyclosporine, PUVA, and biologics may be offered when the benefits outweigh the risks.

**Hepatitis B.** Methotrexate should not be prescribed for patients with hepatitis B. In addition, isolated hepatitis B virus (HBV) reactivation has been observed with TNF antagonists. TNF pre-treatment evaluations should include HBV screening and if seropositive for r-HBV surface antigen, a course of antiviral therapy is recommended starting two to four weeks before TNF treatment.

**Hepatitis C.** Small studies have shown that TNF inhibitors do not increase viral load or elevate liver enzymes in patients with hepatitis C virus (HCV). Monitoring viral load and liver enzymes is recommended. The guidelines also highlight a case report of using cyclosporine successfully without HCV exacerbation.

**TNF Treatment and Elective Surgery.** The conservative choice of suspending anti-TNF treatment in psoriatic patients undergoing elective surgery is supported. Consider discontinuing for four half lives prior to surgery. Half lives for etanercept, adalimumab, and infliximab are four, 12, and 29 days, respectively, and 15 to 46 days for ustekinunumb.

**COMORBIDITIES**

Importantly, research continues to reveal new findings about psoriasis comorbidities. This represents a most challenging area of psoriasis therapy, as so much of the data is built on correlation and association. Nevertheless, the mounting data paint a broader picture of psoriasis that warrants serious consideration in how we conceptualize and treat psoriatic disease.

Apart from the psychological toll psoriasis takes on patients, the disease is associated with various other conditions that are worth noting. Currently, the data indicate that 25 percent of psoriasis patients get psoriatic arthritis. Psoriasis patients also show a three-fold increase in diabetes, hyperlipidemia, and hypertension over non-psoriasis patients. In addition, by the age of 30, psoriasis patients are at five-fold increased risk of heart attacks and strokes; more specifically, that’s one extra stroke per 530 people and one extra heart attack per 500 people. Psoriasis patients also exhibit an increased frequency of lymphoma and leukemia. In addition, pregnant woman with severe psoriasis have a three- to four-fold increased frequency of spontaneous abortion, preterm birth, severe pre-eclampsia and eclampsia, ectopic pregnancy, and placenta previa.

**Vaccination.** Administering an inactivated or subunit-based vaccine is generally safe with methotrexate, cyclosporine, or biologic agents. However, it is not recommended to administer a live vaccine to someone on the above-listed agents. A few examples of live-attenuated vaccines include measles, mumps, rubella, varicella, yellow fever, nasal-spray flu, rabies, BCG, and typhoid.

**THERAPEUTIC UPDATE**

The new consensus guidelines provide a blueprint for the evolving standard of psoriasis care. In addition to these, developments in research, development, and clinical practice are likely to continue changing how clinicians understand and treat psoriasis, as well as care for patients with psoriatic disease.

**Topical and Combination Therapy.** Topical therapy has seen key advances in recent years, particularly given the emergence of combination therapy as a highly efficacious approach to psoriasis. For example, calcipotriene 0.005% + betamethasone dipropionate 0.064% (Taclonex, LEO Pharma) ointment and topical suspension (Taclonex Scalp) combine the potency of a class II topical steroid with a vitamin D derivative that provides over a 70 per-
cent improvement in psoriasis within four weeks. Using a class II steroid minimizes the risk of class I adverse events such as atrophy, striae, and telangiectasias, and takes advantage of the vitamin D-induced normalization of keratinization. Additionally, compliance tends to be enhanced because calcipotriene plus betamethasone dipropionate is only used once daily. Safety studies with thousands of patients for up to a year show a very reassuring safety profile.3

As psoriasis is a multifactorial disease, with hyperproliferation of the epidermis as well as an upregulated dermal immune process, it is not surprising that monotherapy is not as efficacious as combination therapy. The COBRA study revealed that by adding clobetasol propionate 0.05% (Clobex, Galderma) spray to moderate to severe psoriatic patients receiving either methotrexate, phototherapy, or biologic therapy would increase efficacy to the extent that 20 percent more patients obtained a clear or almost clear status, as compared to when they were only receiving monotherapy.4

Other studies have found great benefit in combination approaches, as well. The Pristine study showed that 90 percent of patients and their physicians were happy with their response when they added topical steroids to etanercept.5

Phototherapy can also be a strong adjunctive therapy to biologic treatment. For instance, one study showed that the addition of NB-UVB for 12 weeks to either etanercept or adalimumab increased the Psoriasis Area and Severity Index 75 to 71 percent and 90 percent, respectively.6 Also, the addition of methotrexate has been shown to elevate the efficacy of etanercept therapy in the treatment of moderate to severe psoriasis.7

For patients with intense flaring, cyclosporine 5mg/kg is often required to control the flare. Once improved (usually within six weeks), the addition of a biologic agent with tapering of cyclosporine over six weeks will minimize nephrotoxicity associated with cyclosporine.

IL Inhibitors Update. As biologic therapies continue to exhibit strong efficacy and are more integrated into psoriasis therapy, questions abound regarding the long-term safety of TNF inhibitors and the new frontier of interleukin inhibitors. In January 2011, Abbott withdrew its new drug application for briakinumab (Abbott) due to findings related to major adverse cardiovascular events (MACE). While the future of briakinumab remains uncertain, the data for the anti-IL-12/23 agent ustekinumab continue to show its relative safety.

Four-year data was presented at the recent American Academy of Dermatology Meeting in San Diego, showing that rates of MACE remained low and stable without an observed dose response with up to four years of follow-up.8 In addition, overall major infection and stroke rates with up to four years of follow-up were consistent with or lower than expected in the general US population. Another poster study found that non-melanoma skin cancer rates and other malignancies have remained stable compared with earlier analyses and show no apparent dose effect through up to four years of follow-up.9 Additionally, malignancy with up to four years of follow-up was consistent with the expected rate of US population, while overall infections remained stable.10 No new patterns were observed with increased exposure, and

BUILD A TRUSTING RELATIONSHIP WITH THE PATIENT

Here is a step-by-step walkthrough for facilitating healthy interaction and a relationship of trust:

When introducing yourself, shake the patient’s hand and maintain consistent eye contact, as this helps put the patient at ease and establishes a safe, open environment to disclose her or his feelings. Then ask the patient, “How can I help you?” This question conveys not just your willingness to treat the patient’s disease, but also your desire to help the patient by whatever means necessary. In response, the patient usually shares her or his experience with psoriasis to varying degrees. Some patients are direct in their wish for successful treatment, while others come across as more affected by the psychosocial effects of the disease. How each patient responds should help you to understand how that patient is affected by her or his experience with the disease and can help you to decide on the degree to which you treat the patient. During this conversation, I also ask patients if they wear long sleeves in the summer to hide their psoriasis. This re-enforces that as their physician, I understand the extent to which their psoriasis impacts their life.

Once you are ready to examine the patient’s skin, I recommend placing your hand on their psoriasis, as this reminds the patient that the disease is not contagious. In addition, most patients are accustomed to people not wanting to look at or touch their psoriasis, so a “hands-on” approach communicates a level of trust that patients often welcome. This lets patients know that you will take their problems seriously while ensuring an objective evaluation of their psoriasis.

These simple steps may increase patients’ compliance and willingness to try different therapies and help build the long-term relationships necessary for effective psoriasis management.
serious infection rates were comparable to psoriatic patient population with no systemic or biologic treatment.

Forthcoming data in coming months and years will continue to elucidate the safety profiles of biologic therapies and provide a clearer outlook on risk/benefit profiles in specific circumstances. Nevertheless, as another poster study articulates, clinicians should recognize that the long-term safety of biologics remains unclear. Moreover, when prescribing biologic agents, keep in mind that patient perceptions matter and that a frank discussion about adverse events is critical.

UNDERSTANDING THE BURDEN OF DISEASE
One of the most important aspects of the recent consensus guidelines is the emphasis on variability of the impact of psoriatic disease. Although Body Surface Area (BSA) has been used in the past, it is important to recognize that certain regions of psoriasis—i.e., scalp, palmar-plantar, groin involvement—may have less than 10 percent BSA but are severe in nature and may not be responsive to topical therapies. This point underlines the reality that psoriasis impacts individuals suffering from it in various capacities.

Studies have shown that patients with psoriatic disease are roughly 50 percent more likely to be depressed. They have a 78 percent increased use in selective serotonin reuptake inhibitors, a two-fold increased risk of obesity, and a three-fold increase in smoking. In addition, they have an increased frequency of anxiety, especially in women and even in those who have been treated effectively and worry that psoriasis will reoccur. Psoriatic patients also sleep on average about 20 minutes less a night than those without psoriasis.13 And in the pediatric population, psoriatic patients are at an increased risk of psychiatric disorders, including depression and anxiety.14 These data—particularly when coupled with the recent findings on comorbidities (see sidebar on previous page)—highlight the importance of maintaining an aggressive but also cautious approach to treatment. Achieving this balance is difficult and will likely vary depending on the individual patient. But it starts with a strong, trusting relationship with the patient, which is truly the foundation of successful psoriasis care. As new data and improved therapeutic delivery continue to usher developments that are changing the face of psoriasis care, ultimately the most important element of successful treatment is your relationship with the patient. Conveying your total attention and listening to your patient’s concerns and frustration establishes you as someone the patient can trust, increases your ability to treat the disease effectively, and enables the patient to better cope with this chronic condition.

Dr. Bagel has served as consultant, researcher, or speaker for Amgen, LEO, Abbott, Janssen, Caldera, and GlaxoSmithKline.

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Weigh in on this topic now!

To take this survey online, using your smartphone, photograph the QR code. If you do not have a QR reader on your phone, you can download one at www.getscanlife.com. Alternatively, to take the survey you can visit research.net/s/PDerm6.

1. Do you currently use biologic therapies for psoriasis in your practice?
  - Yes
  - No

2. If you do not, which of the following have influenced your prescribing? (Choose all that apply)
  - Not appropriate for my patient base
  - Not comfortable/familiar with the agents
  - Not prepared for complex management
  - Don’t want to deal with insurance issues
  - Concerned about long-term safety
  - Patients prefer other therapies