

Supplement to



January 2019

The Mind-Skin Connection: Psoriasis and Psychological Comorbidities

Leon Kircik, MD

Jerry Bagel, MD

Richard G. Fried, MD, PhD

Jashin Wu, MD

A CME activity provided by Evolve Medical Education LLC.
Distributed with *Practical Dermatology*.

This continuing medical education activity is supported through
an educational grant from Ortho Dermatologics.



The Mind-Skin Connection: Psoriasis and Psychological Comorbidities

FACULTY



**LEON KIRCIK, MD,
MODERATOR**

*Clinical Associate Professor
of Dermatology, Mount Sinai
Medical Center, New York, NY*

*Clinical Associate Professor of
Dermatology*

*Indiana University School of
Medicine, Indianapolis, IN
Medical Director
Physicians Skin Care, PLLC
Louisville, KY*



JERRY BAGEL, MD

*Director, Psoriasis Treatment
Center of Central New Jersey,
Windsor Dermatology,
Windsor, NJ*

*Clinical Associate Professor
of Dermatology, Mount Sinai
Medical Center, New York, NY*



**RICHARD G. FRIED,
MD, PHD**

*Yardley Dermatology Associates,
Yardley, PA*



JASHIN WU, MD

*Director of Dermatology
Research at the Department of
Dermatology,
Kaiser Permanente Los Angeles
Medical Center,
Los Angeles, CA*

CONTENT SOURCE

This continuing medical education (CME) activity captures content from an expert clinicians roundtable discussion.

ACTIVITY DESCRIPTION

Recent research suggests that the psychological effects of psoriasis are more complex than a simple response to living with a skin disease associated with stigma. Psychiatric conditions such as depression, anxiety, and suicidal ideation are now understood as comorbidities of psoriasis.

This roundtable discussion brings together expert clinicians to discuss the psychological comorbidities of psoriasis. They also discuss how clinicians treating patients with psoriasis can screen for these comorbidities. The goal is to provide the best possible outcome for the whole patient.

TARGET AUDIENCE

This certified CME activity is designed for dermatologists, physician assistants, and nurse practitioners that treat patients with psoriasis.

LEARNING OBJECTIVES

Upon completion of this activity, the participant should be able to:

- **Describe** the psychological comorbidities associated with psoriasis.
- **Review** the proposed role of systemic inflammation in the pathophysiology of the psychological comorbidities associated with psoriasis, and the implications these findings have for the treatment of psoriasis.
- **Review** and **identify** strategies to assess patients with psoriasis for psychological comorbidities.

GRANTOR STATEMENT

Supported through an educational grant from Ortho Dermatologics.

ACCREDITATION STATEMENT

Evolve Medical Education LLC (Evolve) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Evolve designates this enduring material for a maximum of 1 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

TO OBTAIN AMA PRA CATEGORY 1 CREDIT™

To obtain *AMA PRA Category 1 Credit™* for this activity, you must complete the pretest, read the activity in its entirety and complete the posttest/Activity Evaluation Form, which consists of a series of multiple-choice questions. To answer these questions online and receive real-time results, as well as print out your CME certificate awarding 1 *AMA PRA Category 1 Credit™*, please visit <http://evolvemed.com/online-courses/1821-suppl/>. Alternatively, please complete the Pretest/Posttest/Activity Evaluation and mail or fax to Evolve Medical Education LLC, 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950.

DISCLOSURE POLICY

It is the policy of Evolve that faculty and other individuals who are in the position to control the content of this activity disclose any real or apparent conflict of interests relating to the topics of this educational activity. Evolve has full policies in place that will identify and resolve all conflicts of interest prior to this educational activity.

The following faculty/staff members have the following financial relationships with commercial interests:

Jerry Bagel, MD, has had a financial agreement or affiliation during the past year with the following commercial interests in the form of *Grant/Research Support*: AbbVie; Boehringer-Ingelheim, Celgene, Eli-Lilly, Janssen, and Novartis. *Speaker's Bureau*: AbbVie; Celgene, Eli-Lilly, Janssen, and Novartis.

Richard G. Fried, MD, PhD, has no financial relationships with commercial interests.

Leon Kircik, MD, has had a financial agreement or affiliation during the past year with the following commercial interests in the form of *Advisory Board*: Aclaris, Allergan, Inc., Almirall, Anacor Pharmaceuticals, Biogen-Idec, Colbar, Celgene, Cipher, Connetics Corporation, EOS, Exeltis, Ferndale Laboratories, Inc., Galderma Laboratories, LP, Genentech, Inc., Intendis, Innocutis, ISDIN, Johnson & Johnson, Nano Bio, OrthoNeutrogena, Promius, Quinova, SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Valeant Pharmaceuticals Intl./Ortho Dermatologics, and Warner-Chilcott. *Consultant*: Allergan, Inc., Almirall, Amgen, Inc., Anacor Pharmaceuticals, Colbar, Cipher, CollaGenex, Connetics Corporation, Exeltis, Galderma Laboratories, LP, Genentech, Inc., Intendis, Isdin, Johnson & Johnson, Laboratory Skin Care Inc., Leo, Medical International Technologies, Merck, Merz, Novartis AG, OrthoNeutrogena, Promius, PuraCap, SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Taro, UCB, Valeant Pharmaceuticals Intl./Ortho Dermatologics, and ZAGE. *Grant/Research Support*: Acambis, Allergan, Inc., Amgen, Inc., Anacor Pharmaceuticals, Astellas Pharma US, Inc., Asubio, Berlex Laboratories, Biolife, Biopelle, Boehringer-Ingelheim, Breckinridge Pharma, Celgene, Centocor, Inc., Cellceutix, Coherus, CollaGenex, Combinatrix, Connetics Corporation, Coria, Dermavant, Dermira, Dow Pharmaceutical Sciences, Inc., Dusa, Eli Lilly, Exeltis, Ferndale Laboratories, Inc., Galderma Laboratories, LP, Genentech, Inc., GlaxoSmithKline, PLC, Health Point, LTD, Idera, Intendis, Johnson & Johnson, Leo, L'Oréal, 3M, Maruho, Merck, Medicis Pharmaceutical Corp., Nano Bio, Novartis AG, Noven Pharmaceuticals, Nucrust Pharmaceuticals Corp, Obagi, Onset, OrthoNeutrogena, Promius, QLT, Inc., PharmaDerm, Pfizer, Quinova, Quatrix, SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, TolerRx, UCB, Valeant Pharmaceuticals Intl./Ortho Dermatologics, Warner-Chilcott, and XenoPort. *Speaker's Bureau*: Abbott Laboratories, Allergan, Inc., Amgen, Inc., Assos Pharma, Astellas Pharma US, Inc., Cipher, CollaGenex, Connetics Corporation, Dermik Laboratories, Embil Pharmaceuticals, Exeltis, Galderma Laboratories, LP, Genentech, Inc., Innocutis, Innovail, Johnson & Johnson, Leo, L'Oréal, 3M, Onset, OrthoNeutrogena, PediaPharma, PharmaDerm, Sero, SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Taro, Triax, UCB, Valeant Pharmaceuticals Intl./Ortho Dermatologics, and Warner-Chilcott. *Stock/Shareholder*: Johnson & Johnson.

Jashin Wu, MD, has had a financial agreement or affiliation during the past year with the following commercial interests in the form of *Consultant*: AbbVie, Almirall, Amgen, Bristol-Myers Squibb, Celgene, Dermira, Dr. Reddy's Laboratories, Eli Lilly, Janssen, LEO Pharma,

Novartis, Ortho Dermatologics, Promius Pharma, Regeneron, Sun Pharmaceutical, and UCB. *Grant/Research Support*: AbbVie, Amgen, Eli Lilly, Janssen, and Novartis. *Speaker's Bureau*: Celgene, Novartis, Sun Pharmaceutical, UCB, and Valeant Pharmaceuticals North America LLC/Ortho Dermatologics.

EDITORIAL SUPPORT DISCLOSURES

Erin K. Fletcher, MIT, director of compliance and education, Evolve; Susan Gallagher-Pecha, director of client services and project management, Evolve; and Kristen Richardson, writer, have no financial relationships with commercial interests.

Neil Shah, MD, peer reviewer, has no financial relationships with commercial interests.

OFF-LABEL STATEMENT

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The opinions expressed in the

educational activity are those of the faculty. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

DISCLAIMER

The views and opinions expressed in this educational activity are those of the faculty and do not necessarily represent the views of Evolve, *Practical Dermatology*®, or Ortho Dermatologics.

DIGITAL EDITION

To view the online version of the material, please visit <http://evolvemeded.com/online-courses/1821-suppl/>.



PRETEST QUESTIONS

Please complete prior to accessing the material and submit with Posttest/Activity Evaluation

INSTRUCTIONS FOR CME CREDIT

To receive *AMA PRA Category 1 Credit™*, you must complete the attached pretest/posttest/Activity Evaluation Form and mail or fax to Evolve Medical Education LLC; 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. To answer these questions online and receive real-time results, please visit <http://evolvemeded.com/online-courses/1821-suppl/>. If you are experiencing problems with the online test, please email us at info@evolvemeded.com. Certificates are issued electronically, please be certain to provide your email address below.

Please type or print clearly, or we will be unable to issue your certificate.

Name _____

☐ MD/DO participant ☐ non-MD participant

Phone (required) _____

Email (required) _____

Address _____

City _____

State _____

Zip _____

License Number _____

1. Rate your level of confidence in your ability to discuss psychological comorbidities with your psoriasis patients.

- A. Not at all confident
- B. Not very confident
- C. Neutral
- D. Confident
- E. Very confident

2. How often do you discuss psychological comorbidities with psoriasis patients (based on a scale of 1 to 5, with 1 = "Never" and 5 = "Always")?

- A. 1
- B. 2
- C. 3
- D. 4
- E. 5

3. Which of the following is the most common psychological comorbidity associated with psoriasis?

- A. Depression
- B. Sexual dysfunction
- C. Sleep disorders
- D. Suicidality

4. Which one of the following proinflammatory cytokines has not been definitively shown to be elevated in both psoriasis and depression?

- A. IL-1
- B. IL-17
- C. TNF- α
- D. IL-6

5. You are treating a 52-year-old man who was diagnosed with psoriasis at age 30. He recently moved to the area and this is his first visit to your office. You want a baseline evaluation of depression. What would be the most useful, user-friendly instrument to use?

- A. HADS
- B. PHQ-9
- C. C-SSRS
- D. DLQI

The Mind-Skin Connection: Psoriasis and Psychological Comorbidities

Those of us who treat patients with psoriasis have long recognized the profound quality of life effects of this chronic disease. But recent research suggests that the psychological effects of psoriasis are more complex than a simple response to living with a skin disease associated with stigma. Psychiatric conditions such as depression, anxiety, and suicidal ideation are now understood as comorbidities of psoriasis. The following roundtable brings together expert clinicians to discuss the psychological comorbidities of psoriasis. We will also discuss how clinicians treating patients with psoriasis can screen for these comorbidities. The goal, as always, is to provide the best possible outcome for the whole patient.

— Leon Kircik, MD

PSYCHOLOGICAL COMORBIDITIES OF PSORIASIS

Leon Kircik, MD: Our first task is to review the psychological comorbidities associated with psoriasis. Patients with psoriasis bear a greater burden of mental health comorbidities compared with the general population as well as people with other cutaneous conditions.¹ In a systematic review of the literature, the estimated prevalence of psychological conditions in people with psoriasis ranged from 24% to 90%.²

Depression is one of the most recognized psychological comorbidities, and patients with psoriasis face an increased risk of depression even after controlling for other comorbidities.^{3,4} A meta-analysis showed that people with psoriasis were at least 1.5 times more likely to have depression than people without the disease.⁵ If patients with psoriasis experience stigmatization, have severe pruritus, or have been diagnosed with psoriatic arthritis, they are more likely to have depression.⁶

There is also a high prevalence of anxiety among adult patients with psoriasis, compared to those without the disease.⁷ Data show that anxiety is slightly elevated in patients with psoriasis compared to people with other dermatologic diseases.¹

Jerry Bagel, MD: We need to do a better job recognizing depression in our patients with psoriasis. There's an article that looked at the concordance between clinical assessments of depression and anxiety by dermatologists and assessments made using the Hospital Anxiety and Depression Scale (HADS).⁸ [HADS is a 14-item patient-administered questionnaire that measures anxiety and depression.⁹] Only 44% of dermatologists recognized depression in patients who had depression as determined by the

*"A study has estimated the prevalence of alexithymia in patients with psoriasis at 25%.
I see it a lot in my patients with psoriasis.
They're stoic; they're like granite."*

—Jerry Bagel, MD

HADS.⁸ So we're not understanding what our patients are going through.

Richard Fried, MD, PhD: As a psychologist and a dermatologist, I think the concept of subclinical depression is underrecognized in the literature. Every measure we have of depression is based on the classic signs described in the Diagnostic and Statistical Manual of Mental Disorders (DSM). But I think we have more subclinical depression among psoriasis patients. Subclinical depression is basically an overall feeling of "blah." Food doesn't taste as good, flowers don't smell as sweet, sex—if there is any—doesn't feel as good. The depression often manifests as a general withdrawal from family and friends. Patients' interests fade away: They stop coaching the kids, they aren't interested in going to the movies, they stop playing sports.

The insidious nature of how chronic skin disease robs people not only of their happiness but also of their inter-

actions with people, places, things, and work is underrecognized by standard measures. In addition, patients don't identify these feelings as depression.

I cannot tell you how many times I've had the experience of putting a patient with psoriasis on sertraline or duloxetine along with their biologic, and having their partner come in later and say, "I don't know what's in this bottle, what's in this syringe, but I feel like I've gotten my spouse back."

Jashin Wu, MD: Patients with psoriasis also are at high risk for sleep disorders and sexual dysfunction. Actually, a recent review of the literature cites sleep disorders and sexual dysfunction as the most frequent psychological comorbidities associated with psoriasis (Table 1). So even though we talk about depression and anxiety all the time, the prevalence of sleep disorders and sexual dysfunction, which we probably have not talked about enough in the literature, is even higher.

TABLE 1. COMMON PSYCHOLOGICAL COMORBIDITIES ASSOCIATED WITH PSORIASIS²

Sleep disorders	62%
Sexual dysfunction	46%
Anxiety	30%
Depression	28%

Dr. Bagel: Does the high prevalence of obesity among patients with psoriasis play a role in sleep disorders?

Dr. Wu: It's probably all related. Perhaps patients have sleep apnea because they have obesity. Perhaps they can't sleep because they are scratching all night. I'm sure it's all related.

Dr. Fried: As are the dysesthesias. It is perhaps underestimated how much psoriatic skin itches, tingles, burns, crawls, or just has diffuse hypersensitivity. Everyone thinks about itch with psoriasis, and if it's impetiginized or if there are fissures, we think about pain.

I think psoriatic skin often just feels crappy. It wakes people up at night. It makes them feel uncomfortable. It makes them incredibly reticent about any kind of touch, whether it's a blanket or clothing or someone touching their skin. I think that sleep interlaced with dysesthesia, depression, and alcohol abuse probably interacts and then spirals.

Dr. Bagel: Jennifer Cather, MD, has done interesting work on the sexual component of psoriasis. In a qualita-

tive study of 20 patients with moderate to severe genital psoriasis, 90% reported at least one negative effect on sexual activity, including reduced frequency of sex, avoidance of sexual relationships, and reduced sexual desire.¹⁰ In another study, treatment of moderate to severe psoriasis with ustekinumab produced significant improvements in sexual problems.¹¹

Dr. Fried: The Cather study is interesting because it focuses on the subjective experiences of people with psoriasis. Some studies of sexuality and psoriasis focus on the frequency of intercourse and erectile difficulties, and I'm not sure that really taps into the lived experience of patients. Patients ask themselves, "Can I cuddle with my partner? Do I feel comfortable enough to take my shirt off in front of my partner?" I think we're looking at the tip of the iceberg when we think about sexual dysfunction and psoriasis.

Dr. Bagel: I'd like to ask the group about alexithymia—the difficulty identifying or expressing emotions. A study has estimated the prevalence of alexithymia in patients with psoriasis at 25%.¹² I see it a lot in my patients with psoriasis. They're stoic; they're like granite. They don't talk until you ask specific questions like, "When was the last time you went to the beach? When was the last time you got into a hot tub?" Some patients with psoriasis are very emotional, but some just can't express how they feel. Do other people have thoughts about the concept of alexithymia?

Dr. Fried: Let's put alexithymia in a few buckets. Bucket number one is patients who don't know or understand that they have depression. Bucket number two is patients who are terrified to express their emotions. Bucket number three is people who are tuned into their emotions but have no idea how to sort through them or express them. I'm guessing that all of us have had the experience of asking a patient who has had psoriasis for 25 years, "How are you doing, Joe?" And he replies, "Ah, same ol' same ol'." Then you look him in the eye and hold eye contact for a few seconds and ask, "Honestly, how difficult is it?" And you watch his eyes start to fill up with tears.

I think those feelings are under the surface for so many people with psoriasis. We don't always appropriately evaluate these feelings of depression and anxiety because patients aren't always able to be honest, they aren't always aware of their feelings, and they may not understand what is going on other than that their lives feel like a total mess. I think sharing with these patients that it's exceedingly difficult to live with psoriasis while reassuring them that we now have many more effective treatments than we did in the past is so important.

"In a recent systematic review and meta-analysis of 18 studies, patients with psoriasis were twice as likely to consider suicide as people without psoriasis. Patients with psoriasis had a 32% higher likelihood of attempting suicide than people without psoriasis and a 20% higher likelihood of completing suicide than people without psoriasis."

—Leon Kircik, MD

Dr. Kircik: Effective treatment is key. A recently published observational study showed that phototherapy or systemic therapy significantly decreased alexithymia in patients with moderate to severe psoriasis.¹³ Alexithymia reversed in more than half of patients after one year of treatment. It's also interesting that excessive use of alcohol was reduced by almost 3-fold.¹³

Dr. Bagel: Based on the data I've read, psoriasis has a greater impact on suicidality than other dermatologic disorders.¹⁴ Why?

Dr. Fried: Other than eczema, and some of the more common diffuse skin diseases, there's not another skin disease that is so capricious in where, when, and with what intensity it shows itself. So what part of your body do you dare expose next Friday night if you're anticipating an intimate interaction? It's just so overwhelming and overwhelmingly unpredictable. And then, because of the exuberant presentation of psoriasis, patients have experienced psychosocial rejection and perhaps even bullying in the past. Patients anticipate what the next person is going to say, how the next person is going to react. It leaves patients thinking that they just want to escape. That escape might be in alcohol, it might be in drugs, or it might be in suicide.

Dr. Kircik: Let's review some of the data on psoriasis and suicide. People with psoriasis are at increased risk for suicidality, which includes suicidal ideation, suicide attempts, and completed suicide. In a recent systematic review and

Apremilast and Depression

Apremilast is an oral selective phosphodiesterase 4 (PDE4) inhibitor approved for the treatment of moderate to severe psoriasis and psoriatic arthritis. Apremilast labeling carries a warning, although not a boxed warning, for depression. During the controlled clinical trials conducted for the drug's approval in psoriasis, 1.3% of patients treated with apremilast reported depression compared with 0.4% of patients treated with placebo. This rate of depression as an adverse event with apremilast is lower than the background rate of people with psoriasis. One patient receiving placebo committed suicide, and 1 patient receiving apremilast attempted suicide. No patients receiving apremilast completed suicide. A comprehensive analysis of apremilast clinical trials found no evidence of an increased risk of psychiatric events with apremilast treatment. However, patients and caregivers should be counseled to be alert for new or worsening depression, suicidal thoughts, or any other mood changes, and to let the treating clinician know if these changes occur.

Gooderham M, Papp K. Selective phosphodiesterase inhibitors for psoriasis: Focus on apremilast. BioDrugs. 2015; 29:327-339.

meta-analysis of 18 studies, patients with psoriasis were twice as likely to consider suicide as people without psoriasis.¹⁵ Patients with psoriasis had a 32% higher likelihood of attempting suicide than people without psoriasis and a 20% higher likelihood of completing suicide than people without psoriasis.¹⁵ Younger patients and patients with more severe disease are at particular risk.¹⁵

Dr. Wu: When thinking about psychological comorbidities, we should also mention alcohol consumption and smoking. In my clinical practice, patients with psoriasis tend to struggle more with alcohol and smoking compared with patients with other cutaneous diseases. The data show that as many as one-third of people with moderate to severe psoriasis consume alcohol excessively, and excessive drinking is associated with increased body surface area involvement.¹⁶ People with psoriasis also have a significantly greater risk of dying from alcohol-related causes than people without the disease.¹⁶ Smoking is an independent risk factor for psoriasis, and people with psoriasis smoke more than people without psoriasis.¹⁷

PATHOPHYSIOLOGY OF PSYCHOLOGICAL COMORBIDITIES

Dr. Kircik: Let's move on to a discussion of the pathophysiology of psychological comorbidities. Are people with psoriasis depressed because of psychosocial stressors? Are people with psoriasis depressed because of an innate

pathologic mechanism that we don't yet fully understand? Do psoriasis and the psychological comorbidities of psoriasis have an overlapping pathophysiology?

Dr. Wu: It may be a chicken and egg situation, but levels of some proinflammatory cytokines are elevated in both psoriasis and depression.¹⁸ Interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-α are all elevated.¹⁸ So it may be the chicken and the egg, but I think it also could be the cytokines themselves.

Dr. Fried: It is now being suggested that inflammatory cytokines cross the blood-brain barrier and increase reuptake of neurotransmitters at the level of the synapse.¹⁹ So the question becomes, as the panel suggested, is psoriasis depressing because of living with the psychosocial stigma or does the increased reuptake of serotonin, norepinephrine, and dopamine at the synapse give us a clear biological explanation for why patients are depressed and anxious centrally?

Dr. Bagel: Another interesting line of research is that proinflammatory cytokines stimulate indoleamine activity, which catalyzes the conversion of tryptophan to kynurenine.^{18,19} Kynurenine metabolism dysfunction may contribute to neuropsychiatric conditions.¹⁹

Dr. Fried: I think it's probably all of the above. But I think newer data on depression as an inflammatory disorder and inflammatory skin disorders depleting neurotransmitters centrally, is important and should be recognized.

Dr. Wu: There is a related point that I would like to bring up. As you're all aware, brodalumab carries a boxed warning for suicidal ideation and behavior and can be prescribed only through a Risk Evaluation and Mitigation Strategy program.²⁰ The drug, which is indicated for the treatment of adult patients with moderate to severe plaque psoriasis, selectively binds to the IL-17 receptor A. Does anyone have any thoughts?

Dr. Bagel: The mechanism of action of brodalumab is different in that it inhibits the IL-17 receptor, compared with the 2 other currently FDA-approved IL-17 inhibitors, secukinumab and ixekizumab, which inhibit the IL-17A molecule itself.²¹

Dr. Kircik: The role of IL-17 in psychological conditions is not clear currently. One study found that IL-17 was elevated in patients with rheumatoid arthritis, especially those who also had anxiety.²² But another small study

found that IL-17 levels were not significantly higher in patients with major depressive disorder compared with controls.²³

During the clinical development of brodalumab for psoriasis, there were 4 completed suicides and 10 attempted suicides in brodalumab-treated subjects.²⁴ The majority of these events were during the long-term, open-label phase of the studies. There were no completed suicides during the 12-week placebo-controlled part of the trials. It's important to note that the brodalumab clinical study program did not exclude subjects with a history of psychiatric events or previous suicide attempts, unlike clinical trials for other recently approved biologics.²⁴

Dr. Wu: We should also note that brodalumab has been shown to improve depression and anxiety. One of the Phase 3 trials of brodalumab, AMAGINE-1, included the outcome of changes in the HADS score.^{25,26} The HADS questionnaire was given at baseline and at week 12. A greater proportion of brodalumab-treated patients had improvements in anxiety and depression after 12 weeks of treatment compared with patients who received placebo.²⁶

I was a coauthor of a paper by Mark Lebwohl, MD, that evaluated data from clinical trials of brodalumab: a placebo-controlled Phase 2 clinical trial, the open-label, long-term extension of that trial, and the three Phase 3 pivotal trials and their open-label, long term-extensions.²⁷ No causal relationship was found between suicidality and treatment with brodalumab.²⁷

Dr. Bagel: When apremilast, which has a warning for depression, came out, I started asking patients about depression. (See box, previous page.) But remember, we asked patients about depression when considering acitretin. Once the IL-17s came out, I started asking about personal or family history of inflammatory pathology because of the increased expression of IL-17 in inflammatory bowel disease.

So now, as part of my review of systems, I talk about history of depression and suicidal ideation. But what is the best strategy for a dermatologist to determine the likelihood that a patient has severe depression or might be at risk for suicide?

Dr. Fried: When considering prescribing isotretinoin or when considering prescribing biologics for psoriasis, I ask 3 questions.

Number 1: "When it's been one of those weeks, or months, or years and everybody and everything is closing in, has hurting yourself or somebody else ever been an option?"

Number 2 (If the answer to question 1 is "yes"): "What would stop you from doing it?"

TABLE 2. PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)²⁸

Over the past 2 weeks, how often have you been bothered by any of the following problems? (Use “y” to indicate your answer.)	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling asleep, staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3
Scoring 0-4: No depression • 5-9: Minimal symptoms • 10-14: Mild symptoms • 15-19: Moderate symptoms • 20 or more: Severe symptoms				

Number 3: “Where are you now?”

If a patient is at high risk, I want them to see a psychiatric professional before I prescribe anything.

SCREENING FOR PSYCHOLOGICAL COMORBIDITIES

Dr. Kircik: This brings us to another topic I want to cover, which is screening for the psychological comorbidities of psoriasis. As Dr. Bagel mentioned earlier, studies have shown that dermatologists don’t do a great job recognizing psychological comorbidities such as anxiety and depression.

Several validated instruments are available to assess psychological comorbidities in people with psoriasis. The Columbia Suicide Severity Rating Scale (C-SSRS) is recommended by the FDA to assess suicidality in clinical trials.¹⁸ The HADS is frequently used in clinical trials of psoriasis medications, although it can also be used in clinical practice.⁹

There are more user-friendly options. I use the Patient Health Questionnaire-9, or PHQ-9, on every single psoriasis patient as a baseline (See Table 2). The PHQ-9 asks 9 questions based on DSM criteria to assess depression.²⁸ A small study of patients with mild to moderate psoriasis showed that the PHQ-9, which takes only 1 to 3 minutes to complete, is a useful screening tool.²⁹ I think that sometimes people feel more comfortable filling out a questionnaire rather than having a conversation with their physician. Of course, some patients may be more comfortable talking with a physician.

There is also the PHQ-2, which uses the first 2 questions of the PHQ-9. It isn’t intended to establish a diagnosis of depression but it is a first-step screen.³⁰ Adding the question

“Have you had thoughts or plans to hurt yourself or hurt others?” can help detect suicidal ideation.³¹

Do any of you use validated screening tools?

Dr. Wu: I think it’s a great idea, but I haven’t used any of these validated surveys in my patients in clinic. If I have any sense that they have depression, anxiety, or suicidal ideation, I generally send them straight to the psychiatry department. But in my own clinic, I don’t use screening tools.

Dr. Fried: With the rampant occurrence of depression among adolescents now, anything we can use for the benefit of patients as well as medicolegal considerations is a great idea.

Dr. Kircik: I find the PHQ-9 easy and fast. I think some sort of screening instrument makes sense, both medically and legally, as well as for the good of patients. There aren’t any recognized guidelines for psychological comorbidity screening, but a European expert panel consensus document recommends that patients with psoriasis be assessed regularly for anxiety, depression, and addictive behaviors and referred to a psychiatrist if psychological comorbidities affect psoriasis management or if the dermatologist suspects depression.³² If I see a trend toward depression or suicidality, I suggest that the patient see a psychiatrist.

Dr. Bagel: I think the crucial question is how can we help ourselves—dermatologists—become comfortable evaluating suicidal ideation and depression? And where’s the gray area? What methods can we use? Is it the HADS? I don’t

have a good system other than my own questions and intuition.

Dr. Kircik: We have to recognize that dermatologists are pressed for time. It's similar to screening for psoriatic arthritis: time-consuming but necessary.

Dr. Bagel: Dermatologists had to get used to asking questions about inflammatory bowel disease in patients with psoriasis. Perhaps that's more straightforward than screening for psychological comorbidities, but the key is for physicians to get comfortable.

Dr. Fried: We have a euphemism in our center: skin emotion specialist. The skin emotion specialists are psychiatrists and psychologists in the community. If we think a patient is at risk for psychiatric comorbidities we'll say, "We have skin emotion specialists who have extensive experience with psoriasis. I'd love for you to see one of them, because psoriasis in its purest sense is your skin behaving in a neurotic fashion. You're not neurotic, but your skin is. We'd like you to see a skin emotion specialist once, just to see if there is anything else we can safely add to make your skin feel better. And, given how difficult it is to live with psoriasis, you'll feel better too."

Dr Wu: We already mentioned that brodalumab treatment decreased depression and anxiety in the AMAGINE-1 study. I'd also like to note that in the pivotal clinical trials for adalimumab, etanercept, ustekinumab, and infliximab, depressive symptoms decreased with treatment.³³ In a study that analyzed patients in the Psoriasis Longitudinal Assessment and Registry (PSOLAR), treatment with biologics appeared to be associated with a lower incidence of depressive symptoms than treatment with traditional systemics and phototherapy in patients with psoriasis.³³ In my clinical experience, I can attest that successful treatment of psychological comorbidities has a real effect that greatly improves the lives of people with psoriasis.

Dr. Fried: The unknown entity in any given person is how much clinical improvement is enough to minimize short- and long-term comorbidities. We can measure glycated hemoglobin, we can measure blood pressure, we can even perform cardiac scans for calcification, but we have no scan to determine how people are affected psychologically. We have an obligation to make people with psoriasis as physiologically and psychologically free of burden as we can.

Dr. Bagel: I've been around a little longer than some of you: 33 years in private practice. The one thing I learned

"In my clinical experience, I can attest that successful treatment of psychological comorbidities has a real effect that greatly improves the lives of people with psoriasis."

—Jashin Wu, MD

early on is: how do you make people happier? You make them clear.

Dr. Kircik: And now we have the National Psoriasis Foundation treatment targets for plaque psoriasis.³⁴ The target response 3 months after the initiation of treatment is a body surface area (BSA) of 1% or less. A response of 3% BSA at 3 months is considered acceptable. Evaluation every 6 months during the maintenance period is recommended, and the target response at maintenance evaluations is a BSA of 1% or less.

CONCLUSIONS

Dr. Kircik: I'd like to close this discussion by asking each of you for your final thoughts on our topic of the psychological comorbidities of psoriasis.

Dr. Wu: Psoriasis is a terrible disease, so it's not surprising that many people with psoriasis have concomitant mental health issues. Dermatologists should be aware of these comorbidities and be willing to address them or send patients to a specialist who can.

Dr. Bagel: For 6 months of my dermatology residency at Columbia Presbyterian Medical Center, I worked on the inpatient service, where there were always 30 patients with severe psoriasis who were hospitalized for 1 month. I initiated weekly group therapy sessions in collaboration with a psychiatrist. What soon became apparent is that in addition to being frustrated and angry about their disease, many patients were depressed and experienced suicidal ideation.

Thirty-five years later, we have much better therapies for psoriasis. But until patients receive the appropriate treatment, patients are depressed and many experience suicidal ideation.

Dr. Fried: Clinicians should be aware that each patient with psoriasis has his or her own comorbidity threshold that once crossed results in irreparable damage to the body and psyche. Our obligation is to be sensitive to and vigilant for these comorbidities and to guide our patients toward effective therapies that may avert the many negative sequelae of psoriasis. ■

1. Wu JJ, Feldman SR, Koo J, Marangell LB. Epidemiology of mental health comorbidity in psoriasis. *J Dermatol Treat*. 2018; 29: 487–495.
2. Ferreira BR, Pio-Abreu JL, Reis JP, Figueiredo A. Analysis of the prevalence of mental disorders in psoriasis: The relevance of psychiatric assessment in dermatology. *Psychiatr Danub*. 2017; 29: 401–406.
3. Cohen BE, Martires KJ, Ho RS. Psoriasis and the risk of depression in the US population: National Health and Nutrition Examination Survey 2009–2012. *JAMA Dermatol*. 2016; 152: 73–79.
4. Wu JJ, Penfold RB, Primates P, et al. The risk of depression, suicidal ideation and suicide attempt in patients with psoriasis, psoriatic arthritis or ankylosing spondylitis. *J Eur Acad Dermatol Venereol*. 2017; 31: 1168–1175.
5. Dowlatshahi EA, Wakke M, Arends LR, Nijsten T. The prevalence and odds of depressive symptoms and clinical depression in psoriasis patients: a systematic review and meta-analysis. *J Invest Dermatol*. 2014; 134: 1542–1551.
6. Korman AM, Hill D, Alikhan A, Feldman SR. Impact and management of depression in psoriasis patients. *Expert Opin Pharmacother*. 2016; 17: 147–152.
7. Fleming P, Bai JW, Pratt M, et al. The prevalence of anxiety in patients with psoriasis: a systematic review of observational studies and clinical trials. *J Eur Acad Dermatol Venereol*. 2017; 31: 798–807.
8. Dalgard FJ, Svensson Å, Gielor U, et al. Dermatologists across Europe underestimate depression and anxiety: results from 3635 dermatological consultations. *Br J Dermatol*. 2018; 179: 464–470.
9. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res*. 2002; 52: 69–77.
10. Cather JC, Ryan C, Meeuwis K, et al. Patients' perspectives on the impact of genital psoriasis: a qualitative study. *Dermatol Ther (Heidelb)*. 2017; 7: 447–461.
11. Guenther L, Han C, Szapary P, et al. Impact of ustekinumab on health-related quality of life and sexual difficulties associated with psoriasis: results from two phase III clinical trials. *J Eur Acad Dermatol Venereol*. 2011; 25: 851–857.
12. Sampogna F, Puig L, Spuls P, et al. Prevalence of alexithymia in patients with psoriasis and its association with disease burden: a multicentre observational study. *Br J Dermatol*. 2017; 176: 1195–1203.
13. Sampogna F, Puig L, Spuls P, et al. Reversibility of alexithymia with effective treatment of moderate to severe psoriasis: longitudinal data from EPIDEPSO. *Br J Dermatol*. 2018; Sep 30. doi: 10.1111/bjd.17259. [Epub ahead of print]
14. Pompili M, Innamorati M, Trovarelli S, et al. Suicide risk and psychiatric comorbidity in patients with psoriasis. *J Int Med Res*. 2016; 44 (1 suppl): 61–66.
15. Singh S, Taylor C, Kormmehl H, Armstrong AW. Psoriasis and suicidality: A systematic review and meta-analysis. *J Am Acad Dermatol*. 2017; 77: 425–440.
16. Parisi R, Webb RT, Carr MJ, et al. Alcohol-related mortality in patients with psoriasis: a population-based cohort study. *JAMA Dermatol*. 2017; 153: 1256–1262.
17. Armstrong AW, Harskamp CT, Dhillon JS, Armstrong EJ. Psoriasis and smoking: a systematic review and meta-analysis. *Br J Dermatol*. 2014; 170: 304–314.
18. Koo J, Marangell LB, Nakamura M, et al. Depression and suicidality in psoriasis: review of the literature including the cytokine theory of depression. *J Eur Acad Dermatol Venereol*. 2017; 31: 1999–2009.
19. Farzanfar D, Dowlati Y, French LE, Lowes MA, Alavi A. Inflammation: a contributor to depressive comorbidity in inflammatory skin disease. *Skin Pharmacol Physiol*. 2018; 31: 246–251.
20. Siliq [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC.
21. Roman M, Chiu MW. Spotlight on brodalumab in the treatment of moderate-to-severe plaque psoriasis: design, development, and potential place in therapy. *Drug Des Devel Ther*. 2017; 11: 2065–2075.
22. Liu Y, Ho RC, Mak A. The role of interleukin (IL)-17 in anxiety and depression of patients with rheumatoid arthritis. *Int J Rheum Dis*. 2012; 15: 183–187.
23. Kim JW, Kim YK, Hwang JA, et al. Plasma levels of IL-23 and IL-17 before and after antidepressant treatment in patients with major depressive disorder. *Psychiatry Investig*. 2013; 10: 294–299.
24. Hashim PW, Chen T, Lebwohl MG, Marangell LB, Kircik LH. What lies beneath the face value of a box warning: A deeper look at brodalumab. *J Drugs Dermatol*. 2018; 17: s29–s34.
25. Papp KA, Reich K, Paul C, et al. A prospective phase III, randomized, double-blind, placebo-controlled study of brodalumab in patients with moderate-to-severe plaque psoriasis. *Br J Dermatol*. 2016; 175: 273–286.
26. Papp K, Reich K, Paul C, et al. Improvements in depression and anxiety with brodalumab therapy in AMAGINE-1, a phase 3 study for moderate to severe plaque psoriasis. *J Am Acad Dermatol*. 2016; 74 (suppl 1): AB254.
27. Lebwohl MG, Papp KA, Marangell LB, et al. Psychiatric adverse events during treatment with brodalumab: Analysis of psoriasis clinical trials. *J Am Acad Dermatol*. 2018; 78: 81–89.
28. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001; 16: 606–613.
29. Singh SM, Narang T, Dogra S, et al. Screening for depressive disorders in outpatients with mild to moderate psoriasis: a study from North India. *Indian J Dermatol Venereol Leprol*. 2015; 81: 148–150.
30. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care*. 2003; 41: 1284–1292.
31. Bujara S. Mental health screening in dermatology: Uncovering comorbid psychopathology. *Dermatology Advisor*. November 2, 2017. Available at: <https://www.dermatologyadvisor.com/general-dermatology/psychiatric-comorbidities-dermatology-patients/article/704709/>
32. Strohal R, Kirby B, Puig L. Psoriasis beyond the skin: an expert group consensus on the management of psoriatic arthritis and common comorbidities in patients with moderate-to-severe psoriasis. *J Eur Acad Derm Venereol*. 2014; 28: 1661–1669.
33. Strober B, Gooderham M, Elke MGJ, et al. Depressive symptoms, depression, and the effect of biologic therapy among patients in Psoriasis Longitudinal Assessment and Registry (PSOLAR). *J Am Acad Dermatol*. 2018; 78:70–80.
34. Armstrong AW, Siegel MP, Bagel J, et al. From the medical board of the National Psoriasis Foundation: treatment targets for plaque psoriasis. *J Am Acad Dermatol*. 2017; 76: 290–298.

INSTRUCTIONS FOR CME CREDIT

To receive *AMA PRA Category 1 Credit™*, you must take the pretest, read the activity in its entirety and complete the post-test/Activity Evaluation Form, which consists of a series of multiple-choice questions. To answer these questions online and receive real-time results, as well as print out your CME certificate awarding 1 *AMA PRA Category 1 Credit™*, please visit <http://evolvedmeded.com/online-courses/1821-suppl/>. Alternatively, please complete the Pretest/Posttest/Activity Evaluation and mail or fax to Evolve Medical Education LLC, 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. Please type or print clearly, or we will be unable to issue your certificate.

Name _____

☐ MD/DO participant ☐ non-MD participant

Phone (required) _____ ☐ Email (required) _____

Address _____

City _____ State _____ Zip _____

License Number _____

DEMOGRAPHIC INFORMATION

Profession	Years in Practice	Patients Seen Per Week	Region	Setting	Models of Care
<input type="checkbox"/> MD/DO	<input type="checkbox"/> > 20	(with the disease targeted in this activity)	<input type="checkbox"/> Northeast	<input type="checkbox"/> Solo Practice	<input type="checkbox"/> Fee for Service
<input type="checkbox"/> NP	<input type="checkbox"/> 11-20		<input type="checkbox"/> Northwest	<input type="checkbox"/> Community Hospital	<input type="checkbox"/> ACO
<input type="checkbox"/> Nurse/APN	<input type="checkbox"/> 6-10	<input type="checkbox"/> 0	<input type="checkbox"/> Midwest	<input type="checkbox"/> Government or VA	<input type="checkbox"/> Patient-Centered
<input type="checkbox"/> PA	<input type="checkbox"/> 1-5	<input type="checkbox"/> 1-5	<input type="checkbox"/> Southeast	<input type="checkbox"/> Group Practice	<input type="checkbox"/> Medical Home
<input type="checkbox"/> Other	<input type="checkbox"/> < 1	<input type="checkbox"/> 6-10	<input type="checkbox"/> Southwest	<input type="checkbox"/> Other	<input type="checkbox"/> Capitation
		<input type="checkbox"/> 11-15		<input type="checkbox"/> I do not actively practice	<input type="checkbox"/> Bundled Payments
		<input type="checkbox"/> 15-20			<input type="checkbox"/> Other
		<input type="checkbox"/> 20+			

LEARNING OBJECTIVES

Did the program meet the following educational objectives?	Agree	Neutral	Disagree
Describe psychological comorbidities associated with psoriasis	_____	_____	_____
Review the proposed role of systemic inflammation in the pathophysiology of and the implications these findings have for the treatment of psoriasis	_____	_____	_____
Review and identify strategies to assess patients with psoriasis for psychological comorbidities	_____	_____	_____

POST TEST QUESTIONS

1. Rate your level of confidence in your ability to discuss psychological comorbidities with your psoriasis patients.

- A. Not at all confident
- B. Not very confident
- C. Neutral
- D. Confident
- E. Very confident

2. How often do you discuss psychological comorbidities with psoriasis patients (based on a scale of 1 to 5, with 1= "Never" and 5= "Always")?

- A. 1
- B. 2
- C. 3
- D. 4
- E. 5

3. Which of the following is the most common psychological comorbidity associated with psoriasis?

- A. Depression
- B. Sexual dysfunction
- C. Sleep disorders
- D. Suicidality

4. Which one of the following proinflammatory cytokines has not been definitively shown to be elevated in both psoriasis and depression?

- A. IL-1
- B. IL-17
- C. TNF-α
- D. IL-6

5. You are treating a 52-year-old man who was diagnosed with psoriasis at age 30. He recently moved to the area and this is his first visit to your office. You want a baseline evaluation of depression. What would be the most useful, user-friendly instrument to use?

- A. HADS
- B. PHQ-9
- C. C-SSRS
- D. DLQI

ACTIVITY EVALUATION/SATISFACTION MEASURES

Your responses to the questions below will help us evaluate this continuing medical education (CME) activity. They will provide us with evidence that improvements were made in patient care as a result of this activity as required by the Accreditation Council for Continuing Medical Education (ACCME).

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low _____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low _____

This activity improved my competence in managing patients with this disease/condition/symptom. ____ Yes ____ No

I plan to make changes to my practice based on this activity. ____ Yes ____ No

Please identify any barriers to change (check all that apply):

- | | |
|--|---|
| <input type="checkbox"/> Cost | <input type="checkbox"/> Lack of consensus or professional guidelines |
| <input type="checkbox"/> Lack of administrative support | <input type="checkbox"/> Lack of experience |
| <input type="checkbox"/> Lack of time to assess/counsel patients | <input type="checkbox"/> Lack of opportunity (patients) |
| <input type="checkbox"/> Reimbursement/insurance issues | <input type="checkbox"/> Lack of resources (equipment) |
| <input type="checkbox"/> Patient compliance issues | <input type="checkbox"/> No barriers |
| <input type="checkbox"/> Other. Please specify: _____ | |

The design of the program was effective for the content conveyed.

____ Yes ____ No

The content supported the identified learning objectives.

____ Yes ____ No

The content was free of commercial bias.

____ Yes ____ No

The content was relative to your practice.

____ Yes ____ No

The faculty was effective.

____ Yes ____ No

You were satisfied overall with the activity.

____ Yes ____ No

Would you recommend this program to your colleagues?

____ Yes ____ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

- | | |
|--|---|
| <input type="checkbox"/> Patient Care | <input type="checkbox"/> Medical Knowledge |
| <input type="checkbox"/> Practice-Based Learning and Improvement | <input type="checkbox"/> Interpersonal and Communication Skills |
| <input type="checkbox"/> Professionalism | <input type="checkbox"/> System-Based Practice |

Additional comments:

____ I certify that I have participated in this entire activity.

This information will help evaluate this CME activity. May we contact you by email in 3 months to see if you have made this change?

practical
 dermatology™


evolve
medical education