Psoriasis and comorbid diseases

Implications for management

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See related articles on pages 377 and 531

Learning objectives

After completing this learning activity, participants should be able to determine psoriasis treatment options for patients who also have significant cardiovascular risk factors, such as obesity and/or diabetes; provide appropriate screening for psoriasis patients according to recommended guidelines; and identify optimal treatment regimens for patients with moderate to severe psoriasis and associated cardiovascular, infectious, or rheumatologic comorbidities.

Disclosures

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As summarized in the first article in this continuing medical education series, the currently available epidemiologic data suggest that psoriasis may be a risk factor for cardiometabolic disease. Emerging data also suggest associations between psoriasis and other comorbidities beyond psoriatic arthritis, including chronic kidney disease, inflammatory bowel disease, hepatic disease, certain malignancies, infections, and mood disorders. Recognizing the comorbid disease burden of psoriasis is essential for ensuring comprehensive care of patients with psoriasis. The clinical implications of the comorbid diseases that are associated with psoriasis and recommendations for clinical management are reviewed in this article. (J Am Acad Dermatol 2017;76:393-403.)

Key words: cardiovascular disease; chronic kidney disease; comorbidities; Crohn's disease; depression; infection; lymphoma; metabolic syndrome; nonalcoholic fatty liver disease; psoriasis; psoriatic arthritis; screening; vaccination.

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Abbreviations used:

BMI:	body mass index
BSA:	body surface area
CD:	Crohn's disease
CDC:	Centers for Disease Control and Prevention
CIRT:	Cardiovascular Inflammation Reduction Trial
CTCL:	cutaneous T-cell lymphoma
CV:	cardiovascular
CVD:	cardiovascular disease
FDA:	US Food and Drug Administration
IBD:	inflammatory bowel disease
IL:	interleukin
MACE:	major adverse cardiovascular events
NAFLD:	nonalcoholic fatty liver disease
NMSC:	nonmelanoma skin cancer
PASI:	Psoriasis Area and Severity Index
PUVA:	psoralen plus ultraviolet A light phototherapy
RA:	rheumatoid arthritis
RCT:	randomized controlled trial
TB:	tuberculosis
TNF:	tumor necrosis factor
UC:	ulcerative colitis

CARDIOMETABOLIC DISEASE

Key points

- **Patients with psoriasis are underscreened and undertreated for cardiovascular risk factors**
- **At a minimum, patients with psoriasis should be screened for cardiovascular risk factors according to recommendations for the general adult population**
- **Observational data suggest that treatment with methotrexate or tumor necrosis factor inhibitors is associated with a decrease in cardiovascular events; however, data from randomized controlled trials are not yet available, and data for other psoriasis therapies are lacking**

In spite of the evidence supporting an increased prevalence of cardiovascular (CV) risk factors and increased risks of CV disease (CVD) and mortality among patients with psoriasis, data suggest that patients are inadequately screened and undertreated for CV risk factors.[1-5] For example, in a cross-sectional study of National Ambulatory Medical Care Survey data from 2005 to 2009, only 41% of patients with psoriasis versus 66% of those without psoriasis were screened for ≥1 CV risk factor (ie, blood pressure, glucose, cholesterol, or body mass index [BMI]).[4] Specifically among dermatologists, screening for CV risk factors was infrequent (blood pressure, 2.6%; glucose, 1.2%; cholesterol, 4.3%; and BMI, 9.7%). Similarly, a 2015 survey of 127 US dermatologists revealed that <50% screened for hypertension, dyslipidemia, or diabetes in patients with psoriasis.[5] In addition, in a cross-sectional study of patients with hypertension in the United Kingdom, patients with psoriasis were more likely to have uncontrolled hypertension compared with patients without psoriasis.[3] Together, these data highlight an important health care systems gap in screening for and treating CV risk factors among patients with psoriasis. Therefore, as recommended by clinical practice guidelines,[6,7] dermatologists should, at a minimum, advise patients with moderate to severe psoriasis of their possible increased risk of CVD and recommend that they see their primary care physician for appropriate medical screenings and assessment.

Major adverse cardiovascular events

Screening for CV risk factors among patients with psoriasis, particularly those with more severe disease, is essential to minimizing risk of major adverse cardiovascular events (MACE). Screening and management of CV risk factors in patients with psoriasis should, at a minimum, follow recommendations for the general adult population (level of evidence, IB).[6-8] In addition, lifestyle interventions, such as weight loss and smoking cessation, should be encouraged among psoriasis patients who are obese and who are current smokers, respectively (level of evidence, IB). According to the American College of Cardiology and American Heart Association guidelines, CV risk assessment should include evaluation of traditional risk factors every 4 to 6 years among persons 20 to 79 years of age and estimation of 10-year CVD risk among those 40 to 79 years of age (Table I).[9]

Important questions that remain unanswered include what the particular CV risk factor treatment goals should be for psoriasis patients and whether the presence of psoriasis alone warrants different or more aggressive screening and management strategies for CV risk factors compared with the general population. Mehta et al's study[10] of the impact of psoriasis on the Framingham Risk Score found that the addition of psoriasis warranted a change in CV risk factor treatment plans and goals for >60% of patients.[10] Therefore, psoriasis itself—especially severe disease—may indeed necessitate clinically significant changes in prevention and treatment goals for CV risk factors in a similar manner to what has been recommended by the European League Against Rheumatism for patients with rheumatoid arthritis (RA).[11]

Critically, it remains unknown if successful treatment of psoriasis will lower the risk of future CV events. The treatment of psoriasis is currently

Table I. American College of Cardiology/American Heart Association guidelines for assessing cardiovascular disease risk factors*

Age, y	Recommendation	Frequency	Level of evidence
20-79	Check traditional risk factors†	Every 4-6 y	IB
40-79	Estimate 10-year risk for Atherosclerotic Cardiovascular Disease‡ using Pooled Cohort Equations§	Every 4-6 y	IB

Level of evidence definitions: IA, evidence from metaanalysis of randomized controlled trials; IB, evidence from ≥1 randomized controlled trial; IIA, evidence from ≥1 controlled study without randomization; IIB, evidence from ≥1 other type of experimental study; III, evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies; IV, evidence from expert committee reports or opinions or clinical experience of respected authorities, or both.
*Data from Goff et al.[9]
†Age, sex, total and high-density lipoprotein cholesterol, systolic blood pressure, use of antihypertensive therapy, diabetes, and current smoking.
‡Defined as nonfatal myocardial infarction, coronary heart disease death, and nonfatal and fatal stroke.
§Pooled cohort equation for estimating risk takes the following variables into account: sex, race, age, treated or untreated systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, current smoking status, and history of diabetes.

considered to be elective, and systemic treatments are reserved for patients with severe disease that is physically or psychologically disabling to the patient. As a result, the overwhelming majority of patients, even with objectively severe psoriasis, do not receive adequate treatment to control their skin disease.[12-14] This view of psoriasis may be similar to that of hypertension in the 1960s when treatment was considered elective and potentially harmful in the elderly until randomized controlled trials (RCTs) showed improved CV outcomes and decreased mortality among those receiving antihypertensive therapy.[15,16] Unlike hypertension, there are currently no RCTs to prove that psoriasis therapies lower the risk of CVD. Meta-analyses of observational studies suggest that methotrexate and tumor necrosis factor (TNF) inhibitors may lower the risk of CV events in patients with RA.[17-19] Similarly, emerging data from observational studies of psoriasis suggest that methotrexate and TNF inhibitors may lower the risk of CV events in patients with psoriasis[20-22]; however not all studies have observed a protective effect,[23,24] and the observational nature of the studies limits the conclusions that can be drawn. Mixed results from studies of psoriasis therapy effects on the risk of CV events, which have also been observed in the RA population, may be related to differences in study design, uses of different comparator groups, and misclassification of treatment status, and they highlight the need for RCTs to better address this question.[25] Therefore, RCTs evaluating the effects of psoriasis therapy on CVD using rigorous surrogate markers, such as vascular inflammation[26,27] and, ultimately, on CV events are essential. Initial studies in RA[28] and psoriasis[29] suggest that TNF inhibitors may reduce vascular inflammation as measured by 18-fluorodeoxyglucose positron emission tomography-computed tomography. Multiple studies are ongoing to evaluate the effects of ultraviolet B phototherapy (ClinicalTrials.gov identifier NCT01553058), TNF inhibition (NCT01553058, 01866592), interleukin (IL) 12/23 inhibition (NCT02187172), and IL-17 inhibition (NCT02690701) on vascular inflammation. Finally, underscoring the importance of testing the inflammatory hypothesis in CVD, the Cardiovascular Inflammation Reduction Trial (CIRT; NCT01594333) is an ongoing RCT studying the effect of methotrexate on the incidence of MACE in patients with type 2 diabetes or metabolic syndrome who have had a previous MI.[30] The CIRT trial is not a study of patients with psoriasis, but it will be important in establishing whether methotrexate treatment of inflammation reduces the residual risk of CVD. If these or other future RCTs reveal a protective effect of psoriasis treatments on CVD, a paradigm shift in the current view of psoriasis therapy will be needed, and support for a causal relationship between psoriasis and CVD would be strengthened.

Obesity

Obesity may have important effects on psoriasis severity and response to therapies. The impact of weight loss interventions (either diet modification or exercise) on psoriasis severity was assessed in a systematic review and meta-analysis of 7 RCTs of 878 participants.[31] The meta-analysis of 3 RCTs found a significantly greater reduction in the Psoriasis Area and Severity Index (PASI) score among patients receiving the weight loss intervention than those who did not receive the intervention (pooled mean PASI difference, −2.49 [95% confidence interval {CI}, −3.90 to −1.08). Similarly, among 4 studies that assessed 75% reduction in the PASI score (PASI-75) as an outcome, more participants in the intervention versus the control group achieved PASI-75 (pooled

odds ratio [OR], 2.92 [95% CI, 1.39-6.13]). Therefore, the current data suggest that weight loss improves psoriasis, but the clinical significance is modest. There was at least substantial heterogeneity among the studies included in the meta-analyses; thus, additional studies are needed to better understand the effects of specific weight loss interventions on psoriasis.

Increased weight and BMI may also negatively impact response to systemic treatments, including biologic therapies and cyclosporine. Subanalyses of data from RCTs have found that higher weight or BMI is associated with poorer response to fixed-dose biologic therapies (ie, adalimumab, etanercept, and ustekinumab 45 mg), whereas the response to infliximab, whose dose is weight-based, does not vary with BMI.[32,33] A US cross-sectional study of patients with psoriasis who were seen in the routine clinical setting supports the RCT findings.[34] The likelihood of having clear or almost clear skin as defined by a 6-point physician global assessment was found to decrease with increasing BMI among psoriasis patients who were receiving adalimumab or etanercept but not among those taking methotrexate. Together, these data suggest that obese psoriasis patients may be underdosed with fixed-dose biologics. Importantly, weight loss may improve response to biologic therapy as suggested by a single RCT evaluating the effect of weight reduction by diet modification on treatment efficacy among obese psoriasis patients who were receiving adalimumab, etanercept, infliximab, or ustekinumab.[35] Another similarly designed RCT also found an improved response to treatment with low-dose cyclosporine among obese patients with psoriasis randomized to a low-calorie versus normal diet.[36] While weight has not been found to have an effect on initial response to treatment with methotrexate, a single-center study suggests that obese psoriasis patients are more likely to experience loss of response to methotrexate than nonobese patients.[37]

Lastly, obese patients with psoriasis may be at increased risk of medication side effects from methotrexate. Nonalcoholic fatty liver disease (NAFLD) is a relative contraindication to methotrexate and is more common among obese patients.[38,39] Being overweight may also be a risk factor for severe hepatic fibrosis among patients with psoriasis who are taking methotrexate.[40] Therefore, it has been recommended that obese patients with psoriasis who are taking methotrexate undergo more aggressive monitoring, including obtaining liver biopsies both at baseline (ie, within 2-6 months of starting therapy) and at a cumulative dose of 1.0 to 1.5 g of methotrexate.[38]

Collectively, these data highlight the importance of providing counseling to overweight and obese patients with psoriasis about weight loss and the impact of their weight on both psoriasis severity and treatment response (level of evidence, IB). In addition, dermatologists should be cautious of methotrexate use in obese patients with psoriasis.

Hypertension

Given the association between psoriasis and hypertension, patients with psoriasis should undergo at least standard blood pressure screening that is recommended for the general population (Table II).[41] Data suggest that psoriasis patients with hypertension may have more severe hypertension[42] and may be more likely to have poorly controlled blood pressure than hypertensive patients without psoriasis[3]; therefore, appropriate management and monitoring of blood pressure is important to emphasize. Lastly, as hypertension is a well-known potential adverse effect of cyclosporine, dermatologists should use cyclosporine cautiously in patients with psoriasis who have pre-existing hypertension.[43]

Diabetes

As psoriasis is associated with an increased risk of diabetes, patients with psoriasis should be screened for diabetes at least according to the standard recommendations for the general population (Table III).[44-47] Based on observational data that suggest more aggressive diabetes[48] and greater prevalence and risk of micro- and macrovascular complications[49,50] among patients with than without psoriasis, it may be reasonable to consider more frequent monitoring of diabetes and screening for diabetic complications among psoriasis patients. However, additional studies are needed to support these initial findings and before such recommendations are implemented widely.

Dyslipidemia

More prevalent dyslipidemia among patients with psoriasis supports lipid screening at least per standard recommendations for the general population (Table I). Hyperlipidemia is a potential adverse effect of treatment with acitretin[51] and cyclosporine[43]; therefore these medications should be used with caution in patients with psoriasis who also have dyslipidemia, and close lipid monitoring is necessary.

In summary, it is essential for both clinicians and patients to understand the possibly heightened risk of CVD in patients with psoriasis, which may increase with greater disease severity and longer duration. At a minimum, screening for and management of CV risk factors in patients with psoriasis

Table II. Guidelines for hypertension screening*

Target population	Screening recommendation	Level of evidence
18-39 years old and blood pressure <130/85 mm Hg without any risk factors†	Screen every 3-5 y	IB
Yes to any of the following:	Screen annually	IB
>40 years old		
At increased risk for hypertension†		

Level of evidence definitions: IA, evidence from metaanalysis of randomized controlled trials; IB, evidence from ≥1 randomized controlled trial; IIA, evidence from ≥1 controlled study without randomization; IIB, evidence from ≥1 other type of experimental study; III, evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies; IV, evidence from expert committee reports or opinions or clinical experience of respected authorities, or both.
*Data from the US Preventative Services Task Force.[97]
†Risk factors: systolic blood pressure >130-139 mm Hg, diastolic blood pressure >85-89 mm Hg, overweight or obese, and African American.

Table III. Guidelines for diabetes screening in asymptomatic patients*

Target population	Screening recommendation†	Level of evidence
Yes to both of the following‡:	Screen every 3 y‖	II-IV
40-70 years of age§		
Overweight or obese (ie, body mass index ≥25 kg/m^2)		

Level of evidence definitions: IA, evidence from metaanalysis of randomized controlled trials; IB, evidence from ≥1 randomized controlled trial; IIA, evidence from ≥1 controlled study without randomization; IIB, evidence from ≥1 other type of experimental study; III, evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies; IV, evidence from expert committee reports or opinions or clinical experience of respected authorities, or both.
*Data from the US Preventative Services Task Force.[44]
†Screen with any one of the following: hemoglobin A1c, fasting plasma glucose, or oral glucose tolerance test.
‡Persons who have a family history of diabetes, history of gestational diabetes or polycystic ovarian syndrome, or are members of certain racial/ethnic groups (ie, African Americans, American Indians or Alaskan Natives, Asian Americans, Hispanics or Latinos, or Native Hawaiians or Pacific Islanders) may be at increased risk of diabetes at a younger age or at a lower body mass index and should be considered for earlier screening.
§The American Diabetes Association recommends screening for diabetes in adults ≥45 years of age and screening in persons with multiple risk factors regardless of age.[46,98]
‖More frequent testing may be considered for those with abnormal tests results or those at higher risk.

should be according to the recommendations for the general adult population (Tables I-III).[6,7] Continued basic, translational, and epidemiologic research will be essential to support the development of evidence-based psoriasis-specific recommendations for comorbid disease screening and management. In addition, ongoing and future well-conducted RCTs will be necessary to answer the critical question of whether or not treatment of psoriasis itself has an effect on CV disease, events, morbidity, and mortality.

GASTROINTESTINAL DISEASE

Key points

- **Adalimumab and infliximab are approved by the US Food and Drug Administration for the treatment of both psoriasis and inflammatory bowel disease (Crohn's disease and ulcerative colitis); ustekinumab is approved for the treatment of both psoriasis and CD**
- **Secukinumab and ixekizumab should be used with caution in patients with both psoriasis and Crohn's disease**
- **Methotrexate and acitretin should be used cautiously in patients with psoriasis and liver disease**
- **Tumor necrosis factor inhibitors should be avoided in patients with psoriasis and moderate to severe alcoholic hepatitis**

Inflammatory bowel disease

It is important to understand the therapeutic implications of comorbid inflammatory bowel disease (IBD), which is more prevalent among patients with than without psoriasis. Adalimumab and infliximab are approved by the US Food and Drug Administration (FDA) for the treatment of both psoriasis and IBD (ie, Crohn's disease [CD] and ulcerative colitis [UC]), and ustekinumab was also recently approved for the treatment of Crohn's disease. Therefore, these biologics are the treatments of choice in patients with both psoriasis and UC or CD.

Notably, dosing of systemic medications for treatment of CD and UC is often higher than that for psoriasis. Unexpectedly, secukinumab, an IL-17A inhibitor and biologic that was recently approved by the FDA for the treatment of moderate to severe psoriasis, was not only found to be ineffective for treatment of CD but was also suggested to be associated with higher adverse event rates than placebo in a single clinical trial.[52] Exacerbations of CD were observed in clinical trials of secukinumab[53] and ixekizumab[54] for the treatment of psoriasis, and should therefore be used with caution in patients with both psoriasis and CD.

Hepatic disease

The greater prevalence of NAFLD among patients with psoriasis suggests cautious use of potentially hepatotoxic medications, such as methotrexate and acitretin, in patients with both diseases. As discussed previously, NAFLD is a relative contraindication to treatment with methotrexate, and more aggressive monitoring with liver biopsies obtained at baseline and at a cumulative dose of 1.0 to 1.5 g of methotrexate may be considered (level of evidence, IV).[38] Noninvasive tests to detect hepatic fibrosis, such as various serologic tests and radiologic imaging, such as ultrasound-based elastography, magnetic resonance elastography, acoustic radiation force impulse imaging, and cross-sectional imaging, have also been suggested as promising tools but have yet to be established in the setting of long-term methotrexate use among patients with psoriasis.[55]

Moderate to severe alcoholic hepatitis is a relative contraindication to treatment with TNF inhibitors, specifically etanercept. In a single RCT of etanercept in the treatment of moderate to severe alcoholic hepatitis, higher mortality and serious infection rates at 6 months were detected in the etanercept versus placebo group.[56] Therefore, etanercept and other TNF inhibitors should be avoided in psoriasis patients with moderate to severe alcoholic hepatitis (level of evidence, IB). Importantly, patients with psoriasis, especially those being considered for systemic treatment with potentially hepatotoxic medications, should be screened for alcohol use and counseled appropriately.

CHRONIC KIDNEY DISEASE

Key point

- **Patients with more severe psoriasis may warrant closer monitoring for kidney disease, and potentially nephrotoxic medications, such as cyclosporine, should be used with caution**

With data suggesting increased risks of chronic kidney disease and end-stage renal disease among patients with psoriasis,[57,58] the risks versus benefits of treating patients with moderate to severe psoriasis with potentially nephrotoxic medications, such as cyclosporine, should be carefully considered. Closer monitoring for renal insufficiency with serum creatinine, blood urea nitrogen, and urinalysis to screen for microalbuminuria may also be considered for patients with psoriasis affecting ≥3% of their body surface area (BSA; level of evidence, III).

MALIGNANCY

Key points

- **Tumor necrosis factor inhibitors may be associated with increased risks of nonmelanoma skin cancer and melanoma**
- **Chronic oral psoralen plus ultraviolet A phototherapy is associated with an increased risk of nonmelanoma skin cancer, particularly squamous cell carcinoma**
- **Patients with psoriasis on immunosuppressive therapy should adhere to guidelines for age-appropriate cancer screening**
- **Annual skin cancer screening may be considered in patients with psoriasis who are receiving immunosuppressive medications or phototherapy**

The risk of malignancy among patients with psoriasis is most convincing for lymphoma, particularly cutaneous T-cell lymphoma (CTCL),[59-61] although misdiagnosis of CTCL as psoriasis may at least partially explain this association. Increased risks of other cancers have also been suggested.[62] Malignancy risk is of special concern among patients treated with immunosuppressive systemic therapies or phototherapy. Most studies to date have assessed malignancy risk related to TNF inhibitors received by patients with RA or a combination of immune-mediated diseases (ie, RA, IBD, psoriatic diseases, or ankylosing spondylitis) for which TNF inhibitors are indicated. A meta-analysis of RCTs[63] and observational studies[64] of patients taking TNF inhibitors found no increased risk of internal malignancy, but suggested that risks of nonmelanoma skin cancer (NMSC)[63,64] and melanoma[64,65] may be increased. Skin cancer is also of particular concern among patients who have received phototherapy. The evidence is strongest for an increased risk of NMSC, particularly squamous cell carcinoma, among patients treated with psoralen plus ultraviolet A (PUVA) phototherapy whereby treatment with >200 sessions of PUVA is associated with a 14-fold increased risk of squamous cell carcinoma.[66] The

Table IV. Guidelines for age-appropriate cancer screening*

Malignancy	Age, y	Screen	Frequency	Level of evidence
Breast cancer[99]	50-74	Mammogram	Every 2 y	IA
Cervical cancer[100]	21-65	Papanicolaou smear	Every 3 y	IB
Colon cancer[101]	50-75	FOBT	Yearly	IB
		Flexible sigmoidoscopy + FOBT	Every 5 y (flexible sigmoidoscopy); every 3 y (FOBT)	
		Colonoscopy	Every 10 y	
Lung cancer[102]	55-80 with ≥30 pack-year history and current smoker or quit within 15 y	Low-dose computed tomography scan of the chest	Yearly	IA

Level of evidence definitions: IA, evidence from metaanalysis of randomized controlled trials; IB, evidence from ≥1 randomized controlled trial; IIA, evidence from ≥1 controlled study without randomization; IIB, evidence from ≥1 other type of experimental study; III, evidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case-control studies; IV, evidence from expert committee reports or opinions or clinical experience of respected authorities, or both.
FOBT, Fecal occult blood test.
*Refer to guideline reference documents for full screening recommendations.

risk of melanoma with oral PUVA remains controversial, and increased risk of skin cancer with topical PUVA or narrowband ultraviolet B phototherapy remains unproven.[67]

Especially considering the potential cancer risks and malignancy warnings that accompany adalimumab, etanercept, infliximab, and ustekinumab, it is important that clinicians recommend and patients adhere to age-appropriate cancer screening guidelines (Table IV). Screening and appropriate counseling for important behavioral risk factors for cancer (eg, smoking) is also suggested, and at least yearly skin cancer surveillance may be considered (level of evidence, III-IV). Importantly, malignancy, other than NMSC, is at least a relative contraindication for treatment with immunosuppressive therapies for psoriasis. Guidelines for treatment of RA indicate that treatment with biologics may be cautiously considered in patients with history of malignancy if they have been cancer-free for ≥5 years (level of evidence, III-IV).[68,69] Among psoriasis patients with multiple NMSCs, acitretin may be considered for both psoriasis treatment and its potential chemopreventive effects.[70,71] Lastly, obtaining a skin biopsy should be considered in patients with psoriasis who have atypical lesions or disease that fails to appropriately respond to treatment in order to rule out CTCL.

INFECTION

Key points

- **Screening for hepatitis B and C and HIV should be considered before starting immunosuppressive therapy in patients with psoriasis**
- **Screening for tuberculosis before and annually during immunosuppressive therapy in patients with psoriasis is recommended**
- **Patients with psoriasis are recommended to keep up to date with vaccinations, ideally before receiving immunosuppressive therapies**

Infection risk attributable to psoriasis itself and immunosuppressive therapies used to treat moderate to severe disease remains a matter of debate. Observational studies suggest increased risks of serious infections,[72,73] including pneumonia,[74,75] among patients with psoriasis. Both a meta-analysis of RCTs[76] and an observational study[77] have not found higher risks of serious infection caused by TNF inhibitors compared with other systemic therapies; the effects of specific psoriasis treatments on serious infection risk remain unclear. An observational study of psoriasis patients suggests that the risk of herpes zoster may be increased among patients receiving combination biologic and methotrexate therapy.[78] Considering the serious infection warnings that accompany methotrexate, cyclosporine, adalimumab, etanercept, infliximab, ustekinumab, secukinumab, and ixekizumab, it is recommended that patients with psoriasis, particularly those requiring immunosuppressive systemic therapy, remain up to date with their vaccinations according to the Advisory Committee for Immunization Practices (level of evidence, IV).[79-81] As respiratory infections were found to be the most common serious infections in patients with psoriasis,[72,73] influenza and pneumonia vaccinations may be particularly important. Live vaccines should be avoided in patients who are currently taking and are within at least 1 month of starting immunosuppressive therapy.[79]

Infections of special concern, especially in the setting of treatment with immunosuppressive systemic medications, include viral hepatitis B and C, HIV, and tuberculosis (TB). The Centers for Disease Control and Prevention (CDC) and the Medical Board of the National Psoriasis Foundation recommend screening all patients for hepatitis B infection before initiating immunosuppressive therapy with triple serology and baseline liver function tests.[82,83] Screening for hepatitis C is more controversial, but several guidelines recommend screening at least high-risk populations before initiating immunosuppressive, particularly biologic, therapy.[84-86] The CDC also recommends ≥1 HIV screening test in every person between the ages of 13 and 64.[87] Finally, considering the potential for TB reactivation, particularly with TNF inhibition, whereby the greatest risk may be associated with adalimumab and infliximab,[88,89] TB screening before starting and annually while on biologic therapy has been recommended (level of evidence, IV).[90]

MOOD DISORDERS

Key point

- **Screening for mood disorders should be considered in patients with psoriasis, particularly those with more severe disease**

Reports of increased risks of depression, anxiety, and suicidality among patients with psoriasis[91,92] suggest that clinicians should consider screening psoriasis patients for depression and suicidality, especially if they have more severe disease. Because both acitretin and apremilast have been labeled with warnings for mood changes and depression, respectively, patients who are taking these medications should be monitored for depression or other mood instability (level of evidence, III).

PSORIATIC ARTHRITIS

Key points

- **All patients with psoriasis should be screened for psoriatic arthritis**
- **The presence of psoriatic arthritis is an indication for systemic therapy**

Psoriatic arthritis is associated with decreased functional ability and quality of life and may result in permanent joint damage. A diagnosis of psoriatic arthritis is an indication for treatment with systemic therapy. Early detection and treatment is essential to prevent progression of this potentially debilitating joint disease.[93] All patients with psoriasis should be asked if they have joint symptoms, including joint swelling, tenderness, and morning stiffness that lasts for ≥30 minutes and improves with activity (level of evidence, III-IV). Diagnostic tests and treatment recommendations are reviewed in more detail elsewhere.[94-96]

In conclusion, clinicians and patients must understand the wide range of medical comorbidities associated with psoriasis in order to ensure respective provision and receipt of appropriate screening and treatment in an attempt to reduce morbidity and mortality. Importantly, ongoing and future well-conducted RCTs are necessary to determine the effect of psoriasis treatment on the associated risks of cardiometabolic, renal, malignant, infectious, psychiatric, and other emerging comorbid diseases.

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Answers to CME examination

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