EXCALIBUR
MEDICAL EDUCATION

HANDLING THE HARD QUESTIONS:

WHAT OUR PATIENTS ARE ASKING US ABOUT PSORIATIC ARTHRITIS

THE PURPOSE OF THIS DOCUMENT

Patients with newly diagnosed psoriatic arthritis (PsA) often ask many questions about their disease and how it can best be managed. It is important for rheumatologists and other providers involved in the management of PsA to be able to properly and effectively communicate appropriate responses to these questions. This pocket guide includes a brief summary of evidence surrounding some of the most common—and challenging—questions rheumatologists and other providers are likely to face from their patients with PsA. We hope you find this guide useful for your professional development.

CONTENTS

WHY DID I GET PSORIATIC ARTHRITIS?

We don't know for certain how or why you developed PsA. There are a variety of potential contributing issues, including genetic, environmental, and immunologic factors.[1,2]

While PsA is clearly an immune-mediated disease, there is still some debate over whether it is a classic autoimmune disease wherein rogue immune cells that have lost the ability to recognize the body as "self" attack healthy tissue, or if the disease results from inflammation caused by trauma or physical stress in the joints. In either case, persistent inflammation in patients with PsA causes joint damage and bone deterioration.[2–4]

PsA most commonly occurs in patients who already have a diagnosis of psoriasis—an autoimmune skin disease—and particularly in patients with plaque psoriasis. In rare cases, however, PsA can occur outside of these pre-existing diagnoses, especially in patients with a family history of psoriasis or PsA.[5-7]

Skin symptoms of psoriasis precede the musculoskeletal symptoms of PsA by an average of 10 years. Patients with psoriasis that affects the scalp, nails, and intergluteal/perianal regions have a greater risk of developing PsA than those with psoriasis in other areas.[5,8]

Genetic factors play an important role in the development of both psoriasis and PsA. In particular, genetic abnormalities in the human leukocyte antigen (HLA; also called the major histocompatibility complex [MHC]) genes show an association with both psoriasis and PsA, although they are more strongly associated with PsA than psoriasis. Environmental factors such as stress, physical trauma, infection, obesity, smoking, and changes to the microbiota

WHY DID I GET PSORIATIC ARTHRITIS?

have also all been implicated as potential triggers of PsA.[6,9,10]

Internationally agreed-upon criteria for classification of PsA have been developed that can assist us in a diagnosis of PsA. To classify a patient as having PsA, we would look to confirm that you have inflammatory articular disease plus a combination of the following features:[11]

1. Current psoriasis
2. A history of previous psoriasis
3. A family history of psoriasis
4. Dactylitis
5. Nail lesions
6. Juxta-articular bone formation on radiographs
7. Negative rheumatoid factor

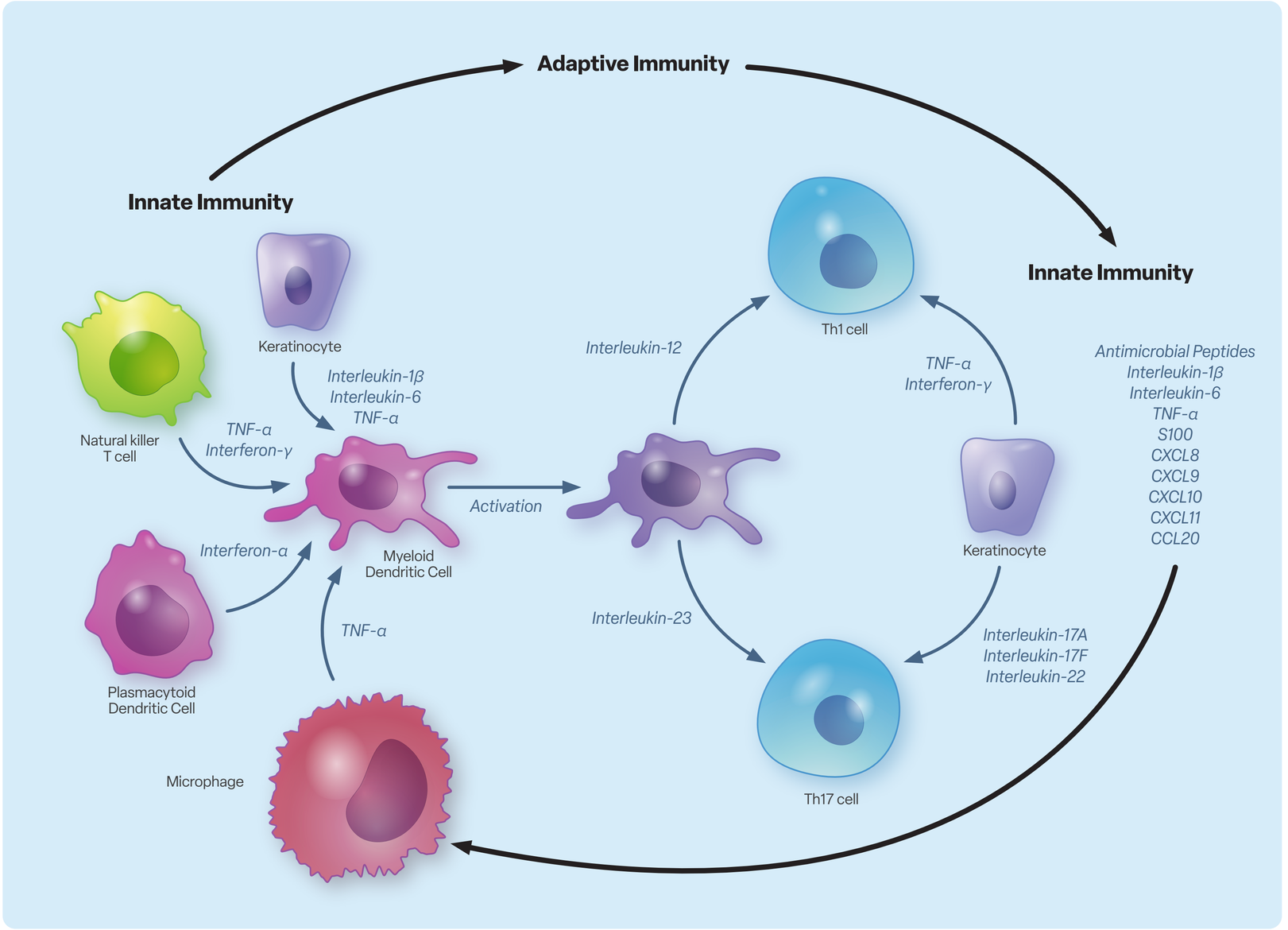
REFERENCES

1. Ocampo D V, Gladman D. Psoriatic arthritis. *F1000Res*. 2019;8:F1000 Faculty Rev-1665.
2. Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. *Lancet*. 2018;391(10136):2273-2284.
3. Kerschbaumer A, Fenzl KH, Erlacher L, Aletaha D. An overview of psoriatic arthritis – epidemiology, clinical features, pathophysiology and novel treatment targets. *Wien Klin Wochenschr.* 2016;128(21):791-795.
4. Emmungil H, Ilgen U, Direskeneli RH. Autoimmunity in psoriatic arthritis: pathophysiological and clinical aspects. *Turk J Med Sci.* 2021;51(4):1601-1614.
5. Kishimoto M, Deshpande GA, Fukuoka K, et al. Clinical features of psoriatic arthritis. *Best Pract Res Clin Rheumatol.* 2021;35(2):101670.
6. American College of Rheumatology. Diseases and conditions: Psoriatic arthritis. Available at www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Psoriatic-Arthritis. Accessed May 18, 2022.
7. Ritchlin CT, Colbert RA, Gladman DD. Psoriatic arthritis. *N Engl J Med*. 2017;376(10):957-970.
8. Winchester R, FitzGerald O. The many faces of psoriatic arthritis: their genetic determinism. *Rheumatology.* 2020;59(Supplement_1):i4-i9.
9. Yan D, Gudjonsson JE, Le S, et al. New frontiers in psoriatic disease research, part I: Genetics, environmental triggers, immunology, pathophysiology, and precision medicine. *J Invest Dermatol*. 2021;141(9):2112-2122.e3.
10. Carvalho AL, Hedrich CM. The molecular pathophysiology of psoriatic arthritis—The complex interplay between genetic predisposition, epigenetics factors, and the microbiome. *Front Mol Biosci*. 2021;8.
11. Mease PJ, Armstrong AW. Managing patients with psoriatic disease: the diagnosis and pharmacologic treatment of psoriatic arthritis in patients with psoriasis. *Drugs*. 2014;74(4):423-441.

WHY DID I GET PSORIATIC ARTHRITIS?

FIGURE 1

Mechanisms of Inflammation in Psoriasis and PsA[11]



WHAT OUR PATIENTS ARE ASKING US ABOUT PSORIATIC ARTHRITIS

WHAT OUR PATIENTS ARE ASKING US ABOUT PSORIATIC ARTHRITIS

HOW DO YOU KNOW I HAVE PSORIATIC ARTHRITIS?

Since there is no single definitive test that will tell us that you have PsA, we base our diagnosis on a number of different factors that help us to rule out other conditions—mostly other forms of arthritis—with a similar clinical presentation.

A physical exam is used to help us determine how many of your joints are impacted and any other physical symptoms you have that are indicative of PsA. While PsA can affect any joint, it most commonly affects the peripheral joints such as the elbows, knees, feet, and hands. PsA can also sometimes affect the axial joints within the spine and sacroiliac joints that link your pelvis and lower spine. One particularly distinctive feature of PsA is that inflammation often occurs within the entheses, the connective tissue that attaches the tendons and ligaments to the bone, facilitating the movement of the skeleton.[1,2] The most common sites of enthesitis include the plantar fascia and Achilles tendon.[3]

Another distinguishing characteristic of PsA is that swelling often involves the whole digit instead of just around the joint. This is known as dactylitis (or sausage digit) and can occur in up to half of all patients diagnosed with PsA. In most patients with PsA, the joints affected are asymmetrical.[3] Outside of the joints, the finger and toenails, eyes (uveitis), and gastrointestinal system can also be affected by PsA. Patients with PsA have an increased risk of cardiovascular disease and other comorbidities, including obesity, diabetes, anxiety and depression, which we will be mindful of during your management.[1,2,4]

HOW DO YOU KNOW I HAVE PSORIATIC ARTHRITIS?

In addition to results from a physical exam, blood tests may be ordered to aid in our diagnosis. For example, we can test for the presence of specific biomarkers known as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP). The presence of these autoantibodies tends to be associated with a diagnosis of rheumatoid arthritis (RA) since 70-80% of patients with RA are "seropositive." The majority of patients with PsA, on the other hand, are seronegative for RF and anti-CCP antibodies.[5,6]

Other blood tests that can help in a potential diagnosis of PsA include a complete blood count, erythrocyte sedimentation rate (ESR), and C-reactive protein. Finally, radiography, ultrasound, and magnetic resonance imaging can help us visualize the characteristic joint erosions that are indicative of a diagnosis of PsA.[5]

REFERENCES

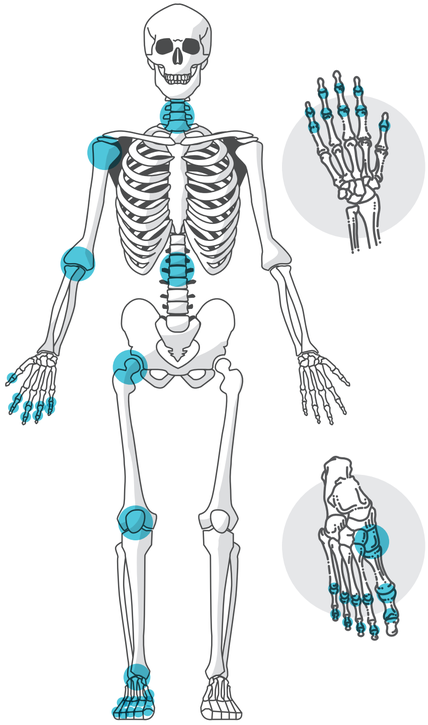
1. Kishimoto M, Deshpande GA, Fukuoka K, et al. Clinical features of psoriatic arthritis. *Best Pract Res Clin Rheumatol*. 2021;35(2):101670.
2. Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. *Lancet*. 2018;391(10136):2273-2284.
3. Saalfeld W, Mixon AM, Zelie J, Lydon EJ. Differentiating psoriatic arthritis from osteoarthritis and rheumatoid arthritis: A narrative review and guide for advanced practice providers. *Rheumatol Ther*. 2021;8(4):1493-1517.
4. Stober C. Pathogenesis of psoriatic arthritis. *Best Pract Res Clin Rheumatol*. 2021;35(2):101694.
5. Merola JF, Espinoza LR, Fleischmann R. Distinguishing rheumatoid arthritis from psoriatic arthritis. *RMD Open*. 2018;4(2):e000656.
6. Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis: A review. *JAMA*. 2018;320(13):1360-1372.

HOW DO YOU KNOW I HAVE PSORIATIC ARTHRITIS?

WHAT OUR PATIENTS ARE ASKING US ABOUT PSORIATIC ARTHRITIS

Differential Diagnosis of PsA[3]

OSTEOARTHRITIS



Asymmetric peripheral disease

Distal and proximal involvement

DIP joints

Synovitis

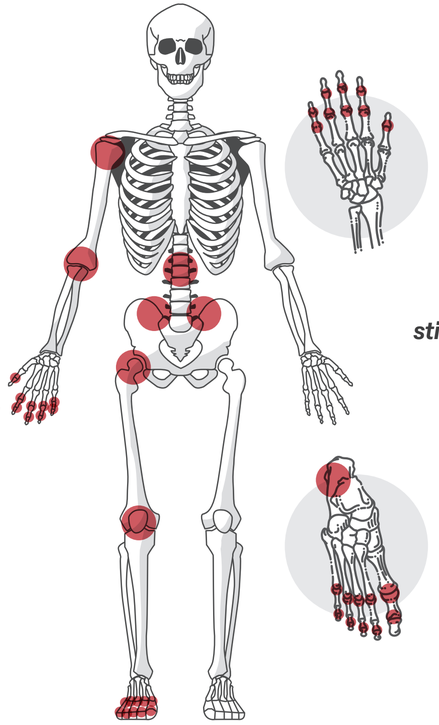
Stiffness with activity

Sclerosis

Bone spurs

Joint space narrowing

PSORIATIC ARTHRITIS



Psoriasis

Nail dystrophy

Ankylosis

Dactylitis

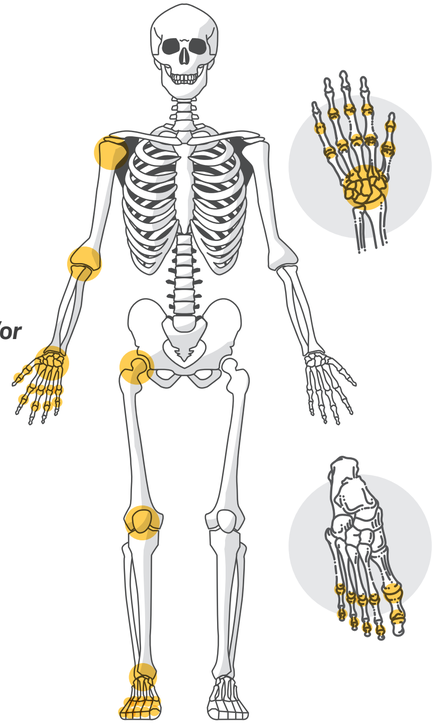
Enthesitis

RHEUMATOID ARTHRITIS

Synovitis

Morning stiffness and/or immobility

PIP joints



Systemetric peripheral disease

Bone erosion

Proximal involvement

Destructive bone lesions

ARE MY CHILDREN GOING TO GET PSORIATIC ARTHRITIS?

Many patients worry about the possibility of their children inheriting PsA, and genetic factors do contribute to the risk of developing both psoriasis and PsA.[1,2] Unfortunately, we are in the early stages of understanding the genetic basis of these complex diseases, so it's impossible to predict with any certainty whether your children are likely to inherit the condition.

To unravel the genetic riddle in PsA, researchers gather evidence from several different types of studies. Epidemiological studies, for example, look at the distribution of a particular disease across a population over time and tell us about the risk of relatives of people with specific diseases inheriting that disease over their lifetime. These kinds of studies have been performed in patients with PsA and show that first-degree relatives of patients with PsA have a 30- to 55-fold higher risk of acquiring PsA compared to the general population. Approximately 8% of individuals currently diagnosed with PsA have an affected first-degree relative.[3] Data like this supports a strong genetic component to PsA. In fact, there appears to be a stronger genetic association in PsA than psoriasis, in which the inherited risk is only 8- to 10-fold higher for first-degree relatives of affected individuals compared to the general population.[3,4]

Researchers have identified some of the genes that contribute to susceptibility to psoriasis and PsA. Variants in the HLA genes play a central role in the development of both conditions, although the specific HLA genes involved are thought to vary. PsA, for example, has a stronger association

ARE MY CHILDREN GOING TO GET PSORIATIC ARTHRITIS?

with HLA-B genes, while psoriasis is more closely associated with HLA-C genes.[5]

As they grow older, children of individuals with PsA should be made aware of their potential risk for inheriting this disease as well as the primary signs and symptoms of psoriasis and PsA so that they can seek prompt evaluation and treatment should these appear.

REFERENCES

1. Ocampo D V, Gladman D. Psoriatic arthritis. *F1000Res*. 2019;8:F1000 Faculty Rev-1665.
2. Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. *Lancet*. 2018;391(10136):2273-2284.
3. Chandran V, Schentag CT, Brockbank JE, et al. Familial aggregation of psoriatic arthritis. *Ann Rheum Dis*. 2009;68(5):664-667.
4. Rahmati S, Tsoi L, O'Rielly D, et al. Complexities in genetics of psoriatic arthritis. *Curr Rheumatol Rep*. 2020;22(4):10.
5. Winchester R, Minevich G, Steshenko V, et al. HLA associations reveal genetic heterogeneity in psoriatic arthritis and in the psoriasis phenotype. *Arthritis Rheum*. 2012;64(4):1134-1144.

SHOULD I STILL SEE MY DERMATOLOGIST NOW THAT I'VE BEEN DIAGNOSED WITH PSORIATIC ARTHRITIS?

Ideally, your dermatologist should continue to be an integral part of your treatment team. In many instances, we will collaborate with them in the management of your disease. There is evidence, in fact, that close collaboration between dermatologists and rheumatologists is a key factor in improving outcomes for patients with PsA.[1]

Since the majority of patients with PsA have had psoriasis for many years prior to their diagnosis of PsA, it is likely that you have already developed a relationship with a dermatologist. Psoriasis affects more than 7 million adults in the United States and is among the most common diseases that dermatologists treat.[2] It is possible that it was your dermatologist who initially suggested a referral to rheumatology since they are ideally positioned to screen patients for PsA.[3,4]

Our rheumatology team has expertise in managing conditions that cause joint pain and swelling while dermatologists are experts in the management of skin conditions. Because PsA impacts both of these areas, it is often important for each specialty to collaborate on your care. The management of PsA should be highly individualized and tailored to the main symptoms you are experiencing, and rheumatologists, dermatologists, and other members of your healthcare team will work together to select the best treatment course for you.[5,6]

Treatment options that are available for patients with psoriasis and PsA have exploded over the past decade. Treatment of both diseases centers on the use of disease-modifying anti-rheumatic drugs (DMARDs), including synthetic DMARDs (small molecule drugs that are administered orally) and

SHOULD I STILL SEE MY DERMATOLOGIST NOW THAT I'VE BEEN DIAGNOSED WITH PSORIATIC ARTHRITIS?

biologic DMARDs (made from proteins and other substances found in nature and administered through an infusion or injection). Synthetic DMARDs can be further subdivided into conventional synthetics (e.g., methotrexate, sulfasalazine, leflunomide) and targeted synthetics (e.g., Janus kinase inhibitors, a newer drug class). Two classes of biologic DMARDs are currently approved by the U.S. Food and Drug Administration for the treatment of PsA: tumor necrosis factor-alpha (TNF) inhibitors and interleukin (IL) inhibitors.[7]

Broadly speaking, many of the same DMARDs are used in the treatment of both psoriasis and PsA, so most dermatologists and rheumatologists have clinical experience using these drugs. Exceptions include golimumab, a TNF inhibitor, and abatacept, a small molecule drug. These are both approved for the treatment of PsA but not psoriasis. In addition, while there are no JAK inhibitors approved for the treatment of psoriasis, tofacitinib and baricitinib are both approved for the treatment of PsA. There are also some instances where particular drugs show greater efficacy in the treatment of joint symptoms compared to skin symptoms and vice versa; for example, leflunomide has been shown to have limited efficacy in the treatment of skin symptoms but can be very effective in some patients with PsA to help manage their pain.[8]

To help us make the right treatment decisions, a number of organizations, including the American College of Rheumatology, the American Academy of Dermatology, and the National Psoriasis Foundation, have published PsA treatment guidelines.[9,10] In patients with PsA, these guidelines suggest use of a biologic DMARD as the recommended first option. Skin symptoms of PsA can also be managed with a variety of topical agents and other therapies, such as ultraviolet (UV) light therapy. A dermatologist can help to integrate these into your treatment plan as warranted.[5,6]

SHOULD I STILL SEE MY DERMATOLOGIST NOW THAT I'VE BEEN DIAGNOSED WITH PSORIATIC ARTHRITIS?

WHAT OUR PATIENTS ARE ASKING US ABOUT PSORIATIC ARTHRITIS

Drug Class	FDA Approved for Psoriasis	FDA Approved for PsA
Conventional DMARDs		
Methotrexate	✓	✓
Cyclosporine	✓	
Leflunomide	✓	✓
TNF Inhibitors		
Etanercept	✓	✓
Infliximab	✓	✓
Adalimumab	✓	✓
Certolizumab pegol	✓	✓
Golimumab		✓
Interleukin Inhibitors		
Ustekinumab	✓	✓
Secukinumab	✓	✓
Ixekizumab	✓	✓
Brodalumab	✓	
Tildrakinzumab-asmn	✓	
Risankizumab-rzaa	✓	✓
Guselkumab	✓	✓
JAK Inhibitors		
Tofacitinib		✓
Upadacitinib		✓
CTLA4 Inhibitor		
Abatacept		✓
PDE4 Inhibitor		
Apremilast	✓	✓

DMARDs Approved by the FDA for the Management of Psoriasis and/or Psoriatic Arthritis[6]

SHOULD I STILL SEE MY DERMATOLOGIST NOW THAT I'VE BEEN DIAGNOSED WITH PSORIATIC ARTHRITIS?

REFERENCES

1. Ziob J, Behning C, Brossart P, Bieber T, Wilsmann-Theis D, Schäfer VS. Specialized dermatological-rheumatological patient management improves diagnostic outcome and patient journey in psoriasis and psoriatic arthritis: a four-year analysis. *BMC Rheumatol*. 2021;5:45.
2. Armstrong AW, Mehta MD, Schupp CW, Gondo GC, Bell SJ, Griffiths CEM. Psoriasis prevalence in adults in the United States. *JAMA Dermatol*. 2021;157(8):940-946.
3. Zhang A, Kurtzman DJB, Perez-Chada LM, Merola JF. Psoriatic arthritis and the dermatologist: An approach to screening and clinical evaluation. *Clin Dermatol*. 2018;36(4):551-560.
4. Belinchón I, Salgado-Boquete L, López-Ferrer A, et al. Dermatologists' role in the early diagnosis of psoriatic arthritis: Expert recommendations. *Actas Dermosifiliogr*. 2020;111(10):835-846.
5. Boehncke WH, Anliker MD, Conrad C, et al. The dermatologists' role in managing psoriatic arthritis: Results of a Swiss Delphi exercise intended to improve collaboration with rheumatologists. *DRM*. 2015;230(1):75-81.
6. Shapiro S. A dermatologist's perspective on choosing an anti-psoriatic drug. Available at www.the-rheumatologist.org/article/a-dematologists-perspective-on-choosing-an-anti-psoriatic-drug/. Accessed May 19, 2022.
7. Bellinato F, Gisondi P, Girolomoni G. A dermatologist perspective in the pharmacological treatment of patients with psoriasis and psoriatic arthritis. *Expert Rev Clin Pharmacol*. 2020;13(5):481-491.
8. Kaltwasser JP, Nash P, Gladman D, et al. Efficacy and safety of leflunomide in the treatment of psoriatic arthritis and psoriasis: a multinational, double-blind, randomized, placebo-controlled clinical trial. *Arthritis Rheum*. 2004;50(6):1939-1950.
9. American Academy of Dermatology Association. Psoriasis clinical guideline. Available at www.aad.org/member/clinical-quality/guidelines/psoriasis. Accessed May 19, 2022.
10. Singh JA, Guyatt G, Ogdie A, et al. Special article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Rheumatol*. 2019;71(1):5-32.

WILL I NEED TO TAKE THIS MEDICATION FOR THE REST OF MY LIFE?

Unfortunately, because there is no cure for PsA, it requires lifelong management to prevent irreversible joint damage. Without treatment, 40-70% of patients with PsA will experience destructive joint damage, making it vital to diagnose PsA early and initiate treatment promptly.[1,2]

Even with treatment, however, you will likely experience a waxing and waning of your disease over time, with a series of remissions and flares.[2] It's also unlikely that you'll receive the same drug regimen for the rest of your life. Fewer than 20% of patients with PsA experience sustained remission with one treatment regimen. As the effectiveness of your medication predictably wanes, we'll discuss different therapeutic strategies; there are fortunately lots of current options. For this reason, it's very important that you come in for regular follow-up appointments so we can assess your level of disease activity.[3]

Many providers suggest following a treat-to-target (T2T) approach to therapy, in which a specific goal (usually remission or minimal disease activity) is pursued, and treatment is adjusted as needed to maintain the therapeutic target. Multiple studies have shown that a T2T approach can be effective for patients with RA, and although it is less well documented in patients with PsA, it is thought to be a viable option in this disease state as well. In fact, current PsA treatment guidelines already support the use of a T2T strategy, although it is not yet considered standard of care in PsA.[4–6]

With expanding treatment options and more targeted strategies, disease remission is becoming an increasingly achievable goal for

WILL I NEED TO TAKE THIS MEDICATION FOR THE REST OF MY LIFE?

patients with PsA. There is some preliminary research exploring the possibility of tapering the dose or even discontinuing one or more medications in patients who achieve sustained disease remission. While limited, the available evidence suggests that tapering the dose of TNF inhibitors and even discontinuing treatment is feasible in some patients with PsA but carries a risk of loss of disease control and relapse, with the highest risk of relapse following treatment discontinuation.[7,8]

REFERENCES

1. Ziob J, Behning C, Brossart P, Bieber T, Wilsmann-Galante CM. Supporting young adults with psoriatic arthritis. *Nursing*. 2020;50(11):24-31.
2. Menter A. Psoriasis and psoriatic arthritis overview. Am *J Manag Care*. 2016;22(8 Suppl):s216-224.
3. Lubrano E, Perrotta FM, Scriffignano S, et al. Sustained very low disease activity and remission in psoriatic arthritis patients. *Rheumatol Ther*. 2019;6(4):521-528.
4. Arthritis Foundation. Using Treat-to-Target for PsA. Available at www.arthritis.org/diseases/more-about/using-treat-to-target-for-psa. Accessed May 20, 2022.
5. Zhang AD, Kavanaugh A. Treat to target in psoriatic arthritis. *Rheum Dis Clin North Am*. 2019;45(4):505-517.
6. Rombach I, Tillett W, Jadon D, et al. Treating to target in psoriatic arthritis: assessing real-world outcomes and optimising therapeutic strategy for adults with psoriatic arthritis—study protocol for the MONITOR-PsA study, a trials within cohorts study design. *Trials*. 2021;22(1):185.
7. Ye W, Tucker LJ, Coates LC. Tapering and discontinuation of biologics in patients with psoriatic arthritis with low disease activity. *Drugs*. 2018;78(16):1705-1715
8. Coates LC, Moverley AR, McParland L, et al. Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a UK multicentre, open-label, randomised controlled trial. *Lancet*. 2015;386(10012):2489-2498.

ARE THERE ANY SPECIFIC SAFETY RISKS OF BIOLOGIC MEDICATIONS THAT I NEED TO WORRY ABOUT?

In order to be approved by the FDA, all medications have to undergo extensive clinical testing, and current biologic therapies are no exception. In clinical and post-marketing surveillance trials, all currently approved biologics were found to have a tolerable safety profile.[1,2] That said, there are some class- and drug-specific side effects that impact a small percentage of patients with PsA that we will closely monitor over the coming months.

Biologic agents work by blocking components of your immune system that have been implicated in driving the inflammation that we see in patients with PsA. What that means is, while these medications can help to alleviate the symptoms of your PsA and prevent disease progression, they also suppress your immune system, which can have unintended consequences.

Because of the immunosuppressive mechanism of action of biologic agents, the most common safety concern is an increased risk of serious infections. Serious infections are those that require intravenous antibiotics or hospitalization. If improperly managed, these can even be fatal, although that is an extremely rare occurrence.

Studies show that, among approved TNF inhibitors, the highest risk of infection is associated with infliximab.[3–5] To date, few studies have been carried out to examine the risk of infection associated with different interleukin inhibitors. Notably, there is also a potential risk of tuberculosis acquisition or reactivation in patients treated with TNF inhibitors; consequently, consensus guidelines recommend all patients starting on a TNF inhibitor, as well as other biologics, be screened for tuberculosis.[4]

ARE THERE ANY SPECIFIC SAFETY RISKS OF BIOLOGIC MEDICATIONS THAT I NEED TO WORRY ABOUT?

In addition to bacterial infections, biologics also carry a risk of fungal infections, in particular candidiasis (more commonly called a yeast infection). Candidiasis is specifically associated with the use of IL-17 inhibitors. It should be noted, however, that these fungal infections are largely mild to moderate in severity.

With regard to viral infections, studies have shown that there is a potential risk of hepatitis B virus reactivation in patients treated with biologic therapy that requires regular monitoring. Although studies are limited so far, there is no evidence to suggest that biologic therapies used to treat PsA increase the risk of severe acute respiratory coronavirus-2 (SARS-CoV-2) infection.[4,5]

Infusible biologics such an infliximab can cause infusion-related reactions characterized by fever, itchy skin (pruritus), flushing, shortness of breath (dyspnea), and headache. Although rare, life-threatening infusion reactions can occur. However, your healthcare team is well-practiced in administering drugs intravenously, and we have numerous protocols in place to minimize the risk of severe infusion reactions.[4,5]

Most biologics are not administered as infusions but rather as subcutaneous injections. Injection-site reactions, which are characterized by redness of the skin, swelling, itching, and pain at the site of the injection, are common but typically mild.[6]

Finally, many patients are concerned about the potential risk of cancer with biologic therapies. While these medications do suppress the immune response, the current evidence suggests that, although there is an increased risk of cancer in patients with PsA and psoriasis in general, biologic therapies do not seem to further increase that risk. The caveat is that many of today's biologics are very new, and long-term studies have

ARE THERE ANY SPECIFIC SAFETY RISKS OF BIOLOGIC MEDICATIONS THAT I NEED TO WORRY ABOUT?

not been performed, so you should follow recommendations with respect to cancer screening programs.[4,5]

It's undoubtedly a lot to think about, but rheumatologists are experienced helping patients avoid and potentially overcome the most common of these side effects. You will need to use your judgment to weigh the potential benefits vs. risks of biologic therapy, but you can hopefully take comfort in the experience of millions of patients with PsA and other rheumatic diseases who have successfully transitioned to the use of biologic therapy to help manage their disease.

REFERENCES

1. Ruyssen-Witrand A, Perry R, Watkins C, et al. Efficacy and safety of biologics in psoriatic arthritis: a systematic literature review and network meta-analysis. *RMD Open*. 2020;6(1):e001117.
2. Migliore A, Gigliucci G, Birra D, et al. Biologics for psoriatic arthritis: network meta-analysis in review. *Eur Rev Med Pharmacol Sci*. 2021;25(18):5755-5765.
3. Jin Y, Lee H, Lee MP, et al. Risk of hospitalized serious infection after initiating ustekinumab or other biologics for psoriasis or psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2021;May 10;[Epub ahead of print]
4. Al-Janabi A, Yiu ZZN. Biologics in psoriasis: Updated perspectives on long-term safety and risk management. *Psoriasis Targets Ther*. 2022;12:1-14.
5. Kamata M, Tada Y. Safety of biologics in psoriasis. *J Dermatol*. 2018;45(3):279-286.
6. Grace E, Goldblum O, Renda L, et al. Injection site reactions in the Federal Adverse Event Reporting System (FAERS) post-marketing database vary among biologics approved to treat moderate-to-severe psoriasis. *Dermatol Ther*. 2020;10:99-106.
7. Ozen G, Pedro S, Schumacher R, et al. Safety of abatacept compared with other biologic and conventional synthetic disease-modifying antirheumatic drugs in patients with rheumatoid arthritis: data from an observational study. *Arthr Res Ther*. 2019;21(141).
8. Kelsey A, Chirch LM, Payette MJ. Tuberculosis and interleukin blocking monoclonal antibodies: Is there risk? *Dermatol Online J*. 2018.
9. Arnold J, Winthrop K, Emery P. COVID-19 vaccination and antirheumatic therapy. *Rheumatol*. 2021;60(8):3496-3502.
10. Zeng H, Wang S, Chen L, Shen Z. Biologics for psoriasis during the COVID-19 Pandemic. *Front Med*. 2021; 8:759568.
11. American College of Rheumatology. COVID-19 clinical guidance for adult patients with rheumatic diseases. Available at www.rheumatology.org/Portals/0/Files/ACR-COVID-19-Clinical-Guidance-Summary-Patients-with-Rheumatic-Diseases.pdf. Accessed June 7, 2022.

Key Safety Concerns Related to Biologic Therapy Used in the Management of Rheumatic Diseases[4,7-11]

Adverse Event Type	Summary	Risk Management Strategies
INFECTIONS		
Serious infections	Increased risk with infliximab and lower risk with ustekinumab in observational studies. Lower risk of infection with abatacept compared to other biologic DMARDs and conventional synthetic DMARDs in patients with RA.	Consider avoiding infliximab in patients at high risk of infection
Tuberculosis (TB)	Increased odds of developing TB on TNF inhibitors in meta- analysis of RA trials. Available studies do not suggest an increased risk of TB reactivation or new active infection in patients taking interleukin inhibitors, but clinical trials are ongoing.	Screen for TB with interferon gamma release assay prior to initiation of biologic therapy. Treat latent TB prior to biologic initiation.
COVID-19 infection	TNF inhibitors may be associated with better prognosis in event of COVID-19 infection compared with conventional systemic agents. Data is lacking for other biologic classes. There is limited data regarding the impact of biologic agents on COVID-19 vaccine response or SARS-CoV-2 infection outcomes.	Insufficient data to definitively inform risk management. Clinicians may consider temporarily discontinuing biologic therapy during the time immediately following vaccination and/or while patients are actively infected with SARS-CoV-2 based on an individual risk-benefit analysis.
CARDIOVASCULAR		
Heart failure	Anti-TNFs may increase the risk of heart failure, though data is inconclusive	Anti-TNF agents are relatively contraindicated in heart failure; other classes should be considered in this context
Major cardiovascular events (MACE)	Little data supporting biologics contributing to MACE	No evidence to influence biologic-selection in those at high risk of MACE
OTHER		
Mental health	Biologic initiation associated with an improvement in psychiatric symptoms	Psychiatric comorbidity should not influence choice of biologic
IBD exacerbations	Anti-IL-17s associated with new onset or exacerbation of existing IBD	Avoid anti-IL17s in patients with comorbid IBD
Interstitial lung disease	Limited reports of interstitial lung disease secondary to TNF inhibitors, ustekinumab, ixekizumab and secukinumab	Insufficient data to inform risk management
Cancer	Observational studies do not demonstrate an increased cancer risk with biologic therapies. Longer term studies required to account for potential latency between drug exposure and cancer development.	Encourage patients to participate in national cancer screening programs. Consider risks and benefits of treatment discontinuation on case-by-case basis with multidisciplinary team input.
Pregnancy	Certolizumab pegol does not cross the placenta. Limited data on TNF inhibitors, ustekinumab, and secukinumab suggests no increases in prematurity, fetal death, or teratogenicity, but studies have limitations.	Certolizumab pegol could be considered a first-line option in women planning conception. Neonates born to mothers taking biologics beyond 16 weeks' gestation should avoid live vaccines in the first 6 months.
Breastfeeding	Biologics are protein molecules and unlikely to be absorbed systemically from breastmilk, though there is no confirmatory data	Inform women that breastfeeding should be safe theoretically, but there is no evidence to confirm this

HOW SOON SHOULD I START FEELING BETTER AFTER I BEGIN TAKING THIS MEDICATION?

There are a number of factors that can affect how quickly you'll respond to a particular medication. In clinical studies, many of the drugs used to treat PsA elicited a response within 2-3 weeks. Regardless of the medication you are prescribed, you should see some improvement within a 12-week period.[1–5]

PsA is a complex disease with no one-size-fits-all therapeutic regimen. Some patients do not respond to a particular treatment or combination of treatments, while others will achieve disease remission with their first treatment. That's why it's important that you adhere to a regular schedule of checkups at our practice, typically every 3-4 months, so that we can assess your symptoms and try to determine if your current medication regimen is working.

It is also important for both of us to remember that you know your disease best. It's therefore essential that you speak up if you feel a treatment isn't working for you or if there is an issue we should know about. Even if it's after only 6-8 weeks, let us know if your symptoms don't improve or if they are getting worse—if you experience a disease flare, that is a clear sign that we need to change your treatment.[6,7]

It is typically recommended that we wait at least 3 months after initiating a treatment before switching therapy in order to be certain of whether the treatment regimen is working or not. If you're getting some benefit after 3 months, we'll likely continue with that treatment to see if things continue to improve as long as there are no significant side effects. We also have the option with some drugs to increase the dosage to see if that helps. If you haven't experienced any relief from your symptoms by 3 months, or if the drug appeared to be working at first but now has stopped impacting your

HOW SOON SHOULD I START FEELING BETTER AFTER I BEGIN TAKING THIS MEDICATION?

symptoms, we can begin to examine options for changing therapy.[6,7]

Adherence to therapy is essential to optimizing outcomes in PsA, so it's important that you maintain the suggested dose regimen for those first few months, even if the medication doesn't appear to be working. That's the only way we'll be able to conclusively tell if we should maintain you on your current regimen or switch to something different.

REFERENCES

1. Psoriatic Arthritis Dosing. COSENTYX® (secukinumab). Available at www.cosentyx.com/psoriatic-arthritis/treatment-dosing. Accessed May 21, 2022.
2. After Starting Treatment. HUMIRA® (adalimumab). Available at www.humira.com/psoriatic-arthritis/after-starting-treatment. Accessed May 21, 2022.
3. XELJANZ® (tofacitinib) For UC | Safety Info. Available at www.xeljanz.com/uc/clinical-trial-results. Accessed May 21, 2022.
4. REMICADE® (infliximab). Available at www.remicade.com/psoriatic-arthritis/learn-about-remicade.html. Accessed May 21, 2022.
5. Menter A. Psoriasis and psoriatic arthritis overview. *Am J Manag Care*. 2016;22(8 Suppl):s216-224.
6. Smolen JS, Aletaha D, Barton A, et al. Rheumatoid arthritis. *Nat Rev Dis Primers*. 2018;4(1):1-23.
7. WebMD. Is your psoriatic arthritis treatment working? Available at www.webmd.com/arthritis/psoriatic-arthritis/treatments. Accessed May 21, 2022.

WHAT SHOULD I DO ABOUT VACCINES?

Patients with PsA are at greater risk of contracting infectious diseases than the general population and of significant morbidity and higher mortality rates when they do contract such conditions. Therefore, it's critical that you remain up to date with recommended vaccines. However, there are some important considerations to be mindful of based on the type of vaccine and the timing of vaccination.[1–3]

The most important vaccines for patients with PsA are the influenza, pneumococcal, and herpes zoster (commonly known as shingles) vaccines.[2]

All patients with PsA should receive an annual influenza vaccine, with patients older than 65 years of age receiving a high-dose formulation.

There are two types of pneumococcal vaccines approved by the FDA; pneumococcal conjugate vaccines (PCV) and pneumococcal polysaccharide vaccines (PPSV). Vaccination against pneumococcal disease is recommended for all patients with PsA. In patients who have not previously received a pneumococcal vaccine, it is recommended that they receive one dose of PCV15 or PCV20. If PCV20 is administered, no further vaccination is needed. If PCV15 is administered, a PPSV23 dose should be given at least 1 year later. There is additional, recently updated guidance available on the U.S. Centers for Disease Control and Prevention website.[3]

Shingles is an illness that results from the reactivation of the chickenpox virus in the body. Patients with rheumatic diseases are at greater risk of acquiring shingles, particularly those being treated with a JAK inhibitor. The shingles vaccine should be administered to all patients ages 18 and older who are increased risk for shingles due to immunodeficiency or immunosuppression caused by known disease or therapy.

Other vaccines that should be considered in patients with PsA include those that protect against the hepatitis A and B viruses, meningococcal disease, and

WHAT SHOULD I DO ABOUT VACCINES?

tetanus, diphtheria, and pertussis. Vaccination against SARS-CoV-2, the virus that causes COVID-19 disease, is also recommended in all patients; recommendations regarding booster shots are changing too quickly to be covered in this publication.[1,2,4]

There is some evidence that some of the medications used to treat PsA, because of their immunosuppressive nature, can reduce the effectiveness of vaccines. For instance, methotrexate, which is often used as an adjunct to biologic therapies in the management of PsA, has also been shown to impact the efficacy of the influenza vaccine. To date, there is no evidence that TNF or interleukin inhibitors affect vaccine efficacy.

Three Key Vaccines for Patients with PsA[1]

Influenza	• Recommended for all patients • Patients aged ≥65 years should receive a high-dose formulation • Non-live vaccine should be preferentially used in patients being treated with immunosuppressive therapy
Pneumococcal	• Recommended for all patients with PsA who never received a pneumococcal vaccine or are uncertain of their vaccination history • Patients should receive 1 dose of PCV15 or PCV20 – If PCV20 is used, pneumococcal vaccination is complete – If PCV15 is used, it should be followed with 1 dose of PPSV23 at least 1 year later • For patients who previously received PPSV23 but not a pneumococcal conjugate vaccine, 1 dose of PCV15 or PCV20 may be administered at least 1 year after they received PPSV23
Herpes Zoster ('Shingles')	• All patients aged ≥50 years (or 18+ and on or initiating immunosuppressive medications)

Ideally, all vaccines should be administered at least 2 weeks prior to initiating treatment for PsA (4 weeks if the treatment includes rituximab) to avoid any potential impact on vaccine efficacy. For patients who have already begun receiving treatment for their PsA, there are risks and benefits of temporarily stopping treatment to receive vaccines that should be discussed. Studies have shown that withholding methotrexate

WHAT SHOULD I DO ABOUT VACCINES?

for 2 doses after administration of the influenza vaccine improves the response to vaccination and does not appear to significantly affect PsA disease activity.[5] Live vaccines—such as the measles and yellow fever vaccines—should be administered at least 4 weeks prior to starting treatment for PsA. Live vaccines are not recommended for patients with PsA once treatment has begun, unless they can't be avoided—if one was required for work or travel, for example. In those instances, it is recommended that therapy be held for at least 1 month before and after vaccination. It is also recommended that patients with PsA keep their distance as much as possible from friends or family members who have received a live vaccine to avoid the risk of infection.[1,2,4]

REFERENCES

1. Kotton KN, Winthrop K. Immunizations in autoimmune inflammatory rheumatic disease in adults. Available at www.uptodate.com/contents/immunizations-in-autoimmune-inflammatory-rheumatic-disease-in-adults. Accessed May 23, 2022.
2. Calabrese C. Vaccinations in patients with rheumatic disease: Consider disease and therapy. *Med Clin North Am*. 2021;105(2):213-225.
3. U.S. Centers for Disease Control and Prevention. Pneumococcal vaccination: Summary of who and when to vaccinate. Available at www.cdc.gov/vaccines/vpd/pneumo/hcp/who-when-to-vaccinate.html. Accessed June 6, 2022.
4. Wong PKK, Hanrahan P. Management of vaccination in rheumatic disease. *Best Pract Res Clin Rheumatol*. 2018;32(6):720-734.
5. Park JK, Lee YJ, Shin K, et al. Impact of temporary methotrexate discontinuation for 2 weeks on immunogenicity of seasonal influenza vaccination in patients with rheumatoid arthritis: a randomised clinical trial. *Ann Rheum Dis*. 2018;77(6):898-904.

Supported by an educational grant from
Pfizer *and* ***Novartis***

EXCALIBUR
MEDICAL EDUCATION

www.excaliburmeded.com