RHEUMATOLOGY NURSE
PRACTICE
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TREATMENT PATHWAYS IN ANKYLOSING SPONDYLITIS

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VOLUME **6** / ISSUE **3**

- *What do expert consensus guidelines say about the optimal treatment of patients with ankylosing spondylitis (AS)?*
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ACTIVITY DESCRIPTION

In this issue of *Rheumatology Nurse Practice*, we will review evidence-based treatment pathways aimed at improving patients' AS symptoms that may allow them to better function and enjoy their lives. We will focus on the latest clinical guidelines both for patients newly diagnosed with AS as well as those who have not responded to prior therapies. In addition, we will discuss how to manage some of the more common extra-articular manifestations and comorbidities of AS, including uveitis, inflammatory bowel disease (IBD), psoriasis, and cardiac disease.

LEARNING OBJECTIVES

After participating in the activity, learners should be better able to:

- Discuss the importance of prompt diagnosis and treatment of patients with ankylosing spondylitis (AS)
- Identify key concepts included within consensus guidelines for the diagnosis and treatment of AS
- Assess the general efficacy and safety of biologic therapies approved for the treatment of AS based on published clinical trial results
- Develop strategies to help overcome common patient adherence hurdles to AS treatment regimens

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TREATMENT PATHWAYS IN ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS), the main form of chronic inflammatory arthritis that affects the head and trunk, is present in approximately 0.1–0.5% of the U.S. population, making it one of the most common rheumatic diseases.[1,2] The back pain, stiffness, and limited flexibility that accompany AS can dramatically compromise quality of life for some patients and interfere with their ability to carry out everyday activities.[1,3] For example, the inability to bend at the waist that many patients with AS experience can make daily tasks such as getting dressed or maintaining personal hygiene difficult. With respect to reduced health-related quality of life, employment limitations, and economic costs, the burden of AS is estimated to be comparable to that of rheumatoid arthritis (RA).[4]

The symptoms of AS often emerge in a patient's teenage years or early adulthood; this means that many patients live with the condition for decades.[4,5] As a result, early, effective treatment can have a long-lasting positive impact on a patient's ability to live a full life, allowing them to fully engage in family, social, work, and leisure activities that are important to them.[4] Conversely, ineffective treatment, or the lack of treatment entirely, can lead to irreversible damage that limits a patient's ability to function in the world.

In recent years, a number of new AS treatment options have emerged, including the interleukin-17a (IL-17A) inhibitors secukinumab and ixekizumab and tumor necrosis factor (TNF) inhibitor biosimilars.[1] In addition, the JAK inhibitor tofacitinib was recently approved for the treatment of AS. In short, clinicians have more treatment choices than ever before for effectively managing AS (see Table 1). At the same time, these novel therapeutic options add complexity to the decision-making process when crafting treatment plans.

Importance of Early, Effective AS Treatment

Ultimately, the goals of treatment for patients with AS are to reduce pain, stiffness, and fatigue; maintain spinal flexibility and normal posture; reduce functional limitations; maximize work productivity; and minimize the impact of extra-articular manifestations and comorbidities.[6] Research shows that most impairment in physical function occurs within the first 10 years of AS symptom onset, underscoring the importance of promptly starting patients on effective treatment.[4] In addition, some evidence shows that the shorter a patient's disease duration, the greater the likelihood that they will respond to common AS therapies such as non-steroidal anti-inflammatory drugs (NSAIDs) and TNF inhibitors.[7]

Currently, AS often remains undiagnosed until years after symptoms emerge; in fact, delays stretching up to 14 years are routine.[8] These delays compromise the ability of clinicians to link patients to effective treatment in time to prevent unnecessary disease progression. However, these diagnostic delays are unsurprising given the difficulty that many healthcare providers have in distinguishing between the symptoms of AS and those of non-inflammatory back pain. National surveys show that approximately 25% of U.S. adults report experiencing back pain, and AS is estimated to be responsible for that pain in only 5% of these individuals.[4] Asking a series of five simple questions can help clinicians determine whether a patient's back pain is likely to be due to AS (see Table 2),[4] ensuring that diagnosis occurs promptly so that effective treatment can be initiated.

Table 1 *Approved and Emerging Therapies for the Treatment of AS*[1,22]

Class	Agent	Recommended Role in Treatment
NSAIDs	--	First-line treatment
TNF inhibitors	Adalimumab	Second-line treatment
	Certolizumab pegol	
	Etanercept	
	Golimumab	
	Infliximab	
IL-17A inhibitors	Ixekizumab	Third-line treatment
	Secukinumab	
Conventional synthetic DMARDs	Sulfasalazine	If peripheral-predominant arthritis is present despite NSAID use, sulfasalazine is recommended
Corticosteroids	--	2019 ACR/SAA/SPARTAN guidelines strongly recommend against systemic corticosteroid use to treat AS, but recent research shows short-term use may improve outcomes
JAK inhibitors	Tofacitinib	Third-line treatment (but an IL-17A inhibitor receives a stronger recommendation)
	Upadacitinib	Not yet FDA approved for the treatment of AS

Table 2 *Helpful Questions in Diagnosing AS in Patients Presenting with Back Pain*[4]

Question	Answer supporting an AS diagnosis
1. Did your symptoms start before age 40 years?	Yes
2. Did your symptoms develop suddenly?	Yes
3. Do your symptoms improve with exercise?	Yes
4. Do your symptoms improve with rest?	No
5. Do you experience pain at night that improves upon getting out of bed?	Yes

2019 ACR/SAA/SPARTAN Treatment Guidelines

In 2019, the American College of Rheumatology (ACR), Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) updated their guidelines for the treatment of AS (see Figure 1).[1] This update was based on an expert panel's systematic review of the AS literature since 2015, when the last set of AS treatment guidelines was published. Here, we explore the treatment guidelines for patients with active AS as well as those with stable disease.

Pathways for patients with active AS

The 2019 ACR/SAA/SPARTAN treatment guidelines define active disease as disease that causes symptoms at an unacceptably bothersome level to the patient and that is judged by the examining clinician to be due to inflammation.[1]

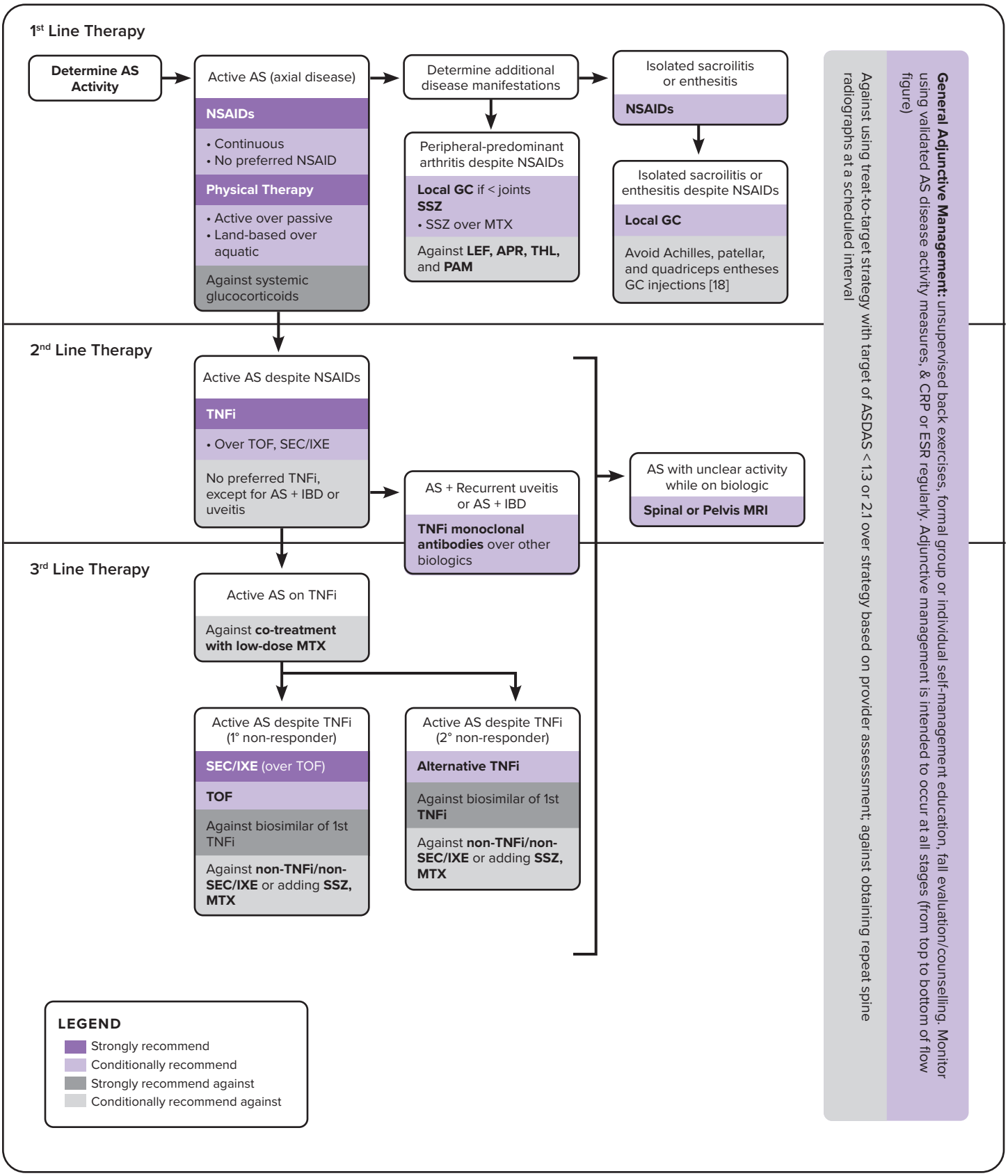
For these patients, NSAIDs are the recommended first-line treatment.[1] NSAIDs are inexpensive, well-tolerated, and effective for some patients with AS. For example, in a trial of patients with early, active axial spondyloarthritis, roughly one-third of patients were able to achieve partial remission on NSAIDs alone (vs. 62% on NSAIDs plus the TNF inhibitor infliximab).[9] The evidence supporting continuous vs. on-demand (ie, as needed) NSAID use is inconsistent; therefore, the guidelines only conditionally recommend continuous treatment over on-demand treatment.[1] Although continuous NSAID treatment may help control disease activity, patient preference, gastrointestinal and kidney comorbidities, or cardiovascular disease may make on-demand treatment of NSAIDs preferable for some individuals with active AS. NSAID treatment may also be helpful once AS has been diagnosed (or is suspected) while a patient is waiting to see a rheumatology specialist for the first time.

What about when NSAIDs don't work? According to the ACR/SAA/SPARTAN guidelines, clinicians should allow for an adequate trial of NSAIDs before dismissing this treatment option for a patient. They define treatment failure as a lack of response (or intolerance) to at least two different NSAIDs at maximal doses over 1 month, or incomplete responses to at least two different NSAIDs over 2 months.[1] Once NSAID failure has been established, the next treatment decision should be made carefully. Choosing an inappropriate AS treatment can prolong the time during which a patient's disease is active and they are in pain.

In adults with active AS despite NSAID treatment, the guidelines recommend treatment with a TNF inhibitor.[1] No particular TNF inhibitor is recommended over another, though patient preferences regarding dosing frequency and route of administration should be considered. The guidelines recommend treatment with a TNF inhibitor over treatment with secukinumab or ixekizumab because of the field's longer experience with TNF inhibitors and greater familiarity with their long-term safety and toxicity profiles. The expert panel that created the guidelines recommend treatment with the IL-17A inhibitors secukinumab or ixekizumab over the JAK inhibitor tofacitinib for the same reasons. For patients with contraindications to a TNF inhibitor such as heart failure or demyelinating disease, the guidelines recommend secukinumab or ixekizumab over tofacitinib or the conventional synthetic disease modifying anti-rheumatic drugs (DMARDs) sulfasalazine or methotrexate. However, if a patient's contraindication to a TNF inhibitor is due to tuberculosis, another chronic infection, or a high risk of recurrent infection, sulfasalazine is the preferred treatment option.

Some patients with AS will not respond to the first DMARD they try, necessitating a switch to another therapy. In one recent study, approximately 20% of patients with AS who initiated their first biologic or conventional synthetic

Figure 1 *Summary of ACR/SAA/SPARTAN 2019 Guidelines*



Abbreviations: *NSAIDs = nonsteroidal antiinflammatory drugs; GC = glucocorticoid; SSZ = sulfasalazine; MTX = methotrexate; LEF = leflunomide; APR = apremilast; THL = thalidomide; PAM = pamidronate; TNFi = tumor necrosis factor inhibitor; TOF = tofacitinib; SEC = secukinumab; IXE = ixekizumab; IBD = inflammatory bowel disease; csARD = conventional synthetic antirheumatic drugs; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein level; ASDAS = Ankylosing Spondylitis Disease Activity Score; MRI = magnetic resonance imaging; PICO = population, intervention, comparison, and outcomes.*

DMARD failed to respond to it.[10] In another study of patients with AS who were initiating a biologic for the first time, 15% ended up switching to another biologic while 32% discontinued their initial biologic during the 1-year follow-up period.[8] Nevertheless, patients with AS tend to remain on a given biologic longer than patients with RA or psoriatic arthritis (PsA).[11,12]

The switch and discontinuation rates for AS reflect the somewhat low response rates for key therapies. In clinical trials of TNF inhibitors, only 53–59% of TNF-naïve patients achieved 20% improvement according to the Assessments in Ankylosing Spondylitis tool (ASAS20) by week 12.[13-15] This compares to 20% improvement rates of 52–73% for TNF-naïve patients with PsA[16-19] and 53–72% for TNF naïve patients with RA.[20-22] For IL-17A inhibitors, ASAS20 rates have been in the 58–61% range at 16 weeks, whereas ASAS40 rates have been in the 48–52% range.[23-26] This is comparable to 20% improvement rates of 50–63% in patients with PsA treated with IL-17A inhibitors.[27,28]

Finally, in a phase 3 trial of tofacitinib in AS, the ASAS20 rate at week 16 was 45%, and the ASAS40 rate was 41%.[29] This compares to 20% improvement rates of 47–61%[18,30] in patients with PsA treated with tofacitinib and 60–66% in patients with RA.[31,32] Because a sizable pool of patients will not respond to any one class of agent, a process of trial and error may be necessary before an effective treatment plan is found.

For patients who fail to respond to their first TNF inhibitor, guidelines recommend treatment with secukinumab or ixekizumab over tofacitinib, again because more safety and efficacy data are available for IL-17A inhibitors.[1] Switching to a new class of biologic is recommended based on the assumption that a patient's failure to respond to their first TNF inhibitor indicates that TNF is not the key inflammatory mediator for these patients. The guidelines recommend against adding low-dose sulfasalazine or methotrexate to the original TNF inhibitor or whatever new biologic/small-molecule agent has been selected. Unlike in RA, it is not clear whether combination treatment with these conventional DMARDs improves efficacy. The guidelines also recommend against switching to a biosimilar of the first TNF inhibitor.

For patients who initially respond to their first TNF inhibitor only to have it lose effectiveness, the guidelines recommend switching to an alternate TNF inhibitor. The expert panel that created the guidelines concluded that these patients have a reasonable chance of responding to a different TNF inhibitor and that this option is worth trying given the limited biologic options currently available for the treatment of AS. For example, in a study of patients with AS who had already used a TNF inhibitor (etanercept or infliximab), ASAS40 rates for adalimumab were 43% in individuals who had experienced loss of response on their prior therapy vs. only 26% for those who had never shown a response.[33] If the second TNF inhibitor does not elicit a response, the patient can be switched to a different class of drugs. As with primary non-responders, the guidelines state that patients should not be switched to a biosimilar of a drug that did not work for them in the past.

Glucocorticoid use

The 2019 ACR/SAA/SPARTAN guidelines strongly recommend against treating patients with AS with systemic glucocorticoids.[1] Despite this recommendation, the use of systemic glucocorticoids to treat AS remains common. In one recent study of patients with AS who were initiating biologics, 56% had used systemic glucocorticoids in the 12 months prior to the data collection date and 42% used them in the 12 months after it.[34] Despite the guideline recommendation against this type of treatment, glucocorticoids may be helpful for some patients with AS. A recent systematic review reported good evidence of efficacy for the short-term (≤6 months) with use of high-dose systemic glucocorticoids in patients with spondylarthritis (including AS), measured in terms of achieving a 50% improvement in BASDAI and ASAS20.[35] The 2019 ACR/SAA/SPARTAN treatment guidelines note that the recommendation against systemic glucocorticoid use comes from the 2015 recommendations and was not reviewed in the latest update.[1] Thus, short-term systemic glucocorticoid use may be considered as a component of AS treatment plans for some patients.

Emerging AS treatments: JAK inhibitors

Two JAK inhibitors, tofacitinib and upadacitinib, have been researched for the treatment for AS. Tofacitinib is already approved to treat other rheumatologic conditions such as RA and PsA, and in December 2021, the FDA approved its use in patients with active AS who have had an inadequate response or intolerance to one or more TNF inhibitors.[36] As described in the 2019 ACR/SAA/SPARTAN guidelines, sufficient trial data were already available at the time the recommendations were written to begin to assess tofacitinib's use in the treatment of AS. However, as more safety and efficacy data become available, tofacitinib's status in AS treatment guidelines may well change. Although the current guidelines minimize the role of tofacitinib in the treatment of AS due to a lack of data relative to other treatment options, it wasn't until 2021 that phase 3 trial results for tofacitinib in AS were published.[29] The week 16 ASAS20 rate of 56% found in this trial appears comparable to the rates documented in trials of TNF and IL-17A inhibitors, and many patients may prefer an oral treatment option over available biologics that require injections or infusions.

Upadacitinib is another JAK inhibitor being investigated for the treatment of AS. In a phase 2/3 trial, 52% of patients taking upadacitinib had achieved ASAS40 at week 14 vs. only 26% of patients on placebo.[37] In a 1-year extension study, the agent continued to show sustained and consistent efficacy.[29] As with tofacitinib, upadacitinib is currently under FDA review for the treatment of AS at the time of this writing.

Both JAK inhibitors have good tolerability and are not associated with the increased infection rates seen for biologics. Thus, they are likely to play an increasingly prominent role in AS treatment in the future. However, it should be noted that the FDA recently announced black box warnings for tofacitinib and upadacitinib (as well as the JAK inhibitor baricitinib) describing the

increased risk of serious cardiac events with use of these medications.[38] In addition, the FDA recently announced that JAK inhibitors should be limited to patients who have not responded well to TNF inhibitors or cannot tolerate them.

Assessing Treatment Effectiveness and Promoting Adherence

AS often emerges in early adulthood.[4,5] Patients of this age may downplay their symptoms out of embarrassment. Younger patients may also experience more difficulty adhering to AS treatment plans for a variety of factors, including a lack of insurance with good coverage for expensive medications and more frequent switching between insurance plans, requiring more frequent authorizations for expensive AS medications. Although AS treatment is intended to help patients live a "normal" life, young patients can also perceive treatment as a threat to their social structure—something that negatively sets them apart from their peers.[39] Research shows that young adult patients are also more likely to value short-term concerns regarding treatment, such as inconvenience, over longer-term concerns, such as permanent damage or changes in mobility.[39]

For all of these reasons, it is particularly important to engage younger patients with AS in discussions of their condition and treatment plans. It may be necessary to carefully probe to get an accurate description of patients' pain levels to help manage their symptoms appropriately. Because short-term benefits and drawbacks of treatment are especially important to younger patients, these considerations should be addressed during these conversations.[39] In addition, creating a strong rapport with these patients is key so they will be forthcoming about current and future challenges such as side effects or life circumstances that make adhering to their treatment plan difficult. Clinicians can then help brainstorm solutions to support adherence.

Managing Biologic Side Effects

Research shows that biologic side effects are the most common cause of treatment discontinuation, even moreso than lack of efficacy.[40] Many times, it is better to manage the side effects of an effective biologic rather than discontinue it altogether.[41] Letting patients know which side effects are most likely to occur—and also that they can be managed—is one of the best ways to lay the foundation for AS treatment success. Patients may also be reassured to learn that the risk of new side effects declines over time with continued use of a biologic.[42]

Injection and infusion reactions are common side effects of many biologics used to treat AS. For patients with an injectable biologic, it may be helpful to leave the medication out for 30-60 minutes prior to injection so it is not as cold and potentially less painful.[41] Taking a pain reliever before injection and icing the skin at the injection site may also minimize pain.[41] Varying the site of injection can be effective as well.[43]

If a patient experiences an infusion reaction when using their biologic, they may be able to prevent future infusion reactions through pre-treatment with pain medication, antihistamines, and steroids.[43] Slower infusion rates may also be useful.

Prior to initiating a patient on a biologic therapy, clinicians should discuss the possibility of allergic reactions, including symptoms and timelines. This way, patients can recognize such reactions promptly, report them, and get help as needed.[41] Clinicians can also review strategies for managing headaches and nausea with their patients, since these side effects are both common among biologics users.[42] For a patient, knowing how to deal with these problems at home can make a big difference in treatment tolerability.

Because biologics suppress the immune system, they can make patients more susceptible to infections. One simple way to minimize the threat of serious infection is to screen patients for latent tuberculosis, hepatitis B virus, and hepatitis C virus prior to initiating biologic therapy. Currently, only approximately 25% of AS patients receive this type of screening,[44] so ruling out these infections prior to treatment initiation represents an easy step toward improving patient care. Helping patients stay on top of their flu and pneumococcal vaccinations is also important.[41] Finally, reviewing basic infection prevention strategies, such as frequent handwashing and avoiding crowded places during flu season, may be helpful.[42] In terms of AS treatment, it is important to recall that in patients with tuberculosis or other chronic infections, or those at high risk of recurrent infections, the 2019 ACR/SAA/SPARTAN guidelines recommend sulfasalazine over biologics.[1]

Exercise for Patients with AS

Exercise is considered a cornerstone of AS treatment.[7] Systematic reviews and meta-analyses of randomized controlled trials have found that, compared with no intervention, exercise improves physical function and reduces pain and disease activity in patients with AS.[45,46] Current evidence favors a combination of endurance and strength training for patients with AS.[7] However, a given patient's exercise regimen should be personalized to suit their preferences and limitations. Referring patients to a physical therapist may be helpful.[47] Common exercise recommendations include stretching, tai chi, yoga, swimming, and alternating between sitting and standing at work.[4,48] Of note, the 2019 ACR/SAA/SPARTAN treatment guidelines recommend physical therapy for patients with AS, with a conditional recommendation of active interventions (i.e., supervised exercise) over passive interventions such as massage, ultrasound, or heat.[1] The guidelines also conditionally recommend land-based interventions over aquatic interventions.

Pathways for Patients with Stable AS

The 2019 ACR/SAA/SPARTAN treatment guidelines define stable disease as "disease that is asymptomatic or causing symptoms, but at an acceptable level as reported by the patient." A minimum of 6 months of this state is required to qualify as clinically stable.[1]

So then what sort of adjustments should these patients receive? The answer depends on their current treatment. If a patient with stable AS is not receiving any pharmacologic treatment, the guidelines recommend on-demand NSAID treatment to manage short-term symptom recurrences or disease flares. If a patient with stable AS is taking a biologic, the guidelines recommend against discontinuing biologic therapy while also conditionally recommending against tapering the dose as a standard approach. A variety of evidence supports this recommendation. Research shows that when patients with AS discontinue a TNF inhibitor after achieving remission or low disease activity, 60–74% will relapse, sometimes within just weeks of discontinuation.[1] Even worse, a study of infliximab treatment in AS found that when the TNF inhibitor was withdrawn and patients with AS experienced relapse, approximately half did not achieve the same clinical response following drug reinitiation than they had before treatment was withdrawn.[49] In 10% of patients in this study, reintroducing infliximab was ineffective and clinicians had to use a new TNF inhibitor entirely. The 2019 ACR/SAA/SPARTAN guidelines do indicate that tapering can be considered in patients with prolonged stable AS if the patient and provider engage in shared decision-making around the issue. However, patients should be counseled regarding the potential for increased disease activity that accompanies discontinuation.

The 2019 ACR/SAA/SPARTAN guidelines also contain recommendations about several other important treatment choices regarding patients with stable AS. If a patient has achieved stable AS on a TNF inhibitor, they strongly recommend continuing with that TNF inhibitor over switching to its biosimilar. In the absence of evidence of interchangeability, the expert panel that created the recommendations judged that a compelling rationale for switching medications should be present. In addition, if a patient has achieved stable AS on a TNF inhibitor in combination with NSAIDs or a conventional synthetic DMARD, the guidelines recommend continuing treatment with the TNF inhibitor alone.

Patients with AS extra-articular manifestations and comorbidities

Extra-articular manifestations and comorbidities are common among patients with AS (see Table 3). In fact, the presence of uveitis, IBD, and psoriasis in patients with back pain can be an important diagnostic clue. All clinicians who treat patients with AS should be aware of how to manage common extra-articular manifestations and comorbidities so they can ensure that patients receive treatment for all problems that may compromise their health and wellbeing.

Table 3 *Common AS Extra-articular Manifestations and Comorbidities*[1,7,35,38]

Condition	Approximate Prevalence in Patients with AS	Special Considerations
Uveitis	17%	• TNF inhibitors recommended over other biologics • Ophthalmologist should treat acute iritis • Topical glucocorticoids recommended for patients with recurrent iritis
Psoriasis	10%	• No specific recommendations in 2019 ACR/SAA/SPARTAN treatment guidelines
Cardiovascular disease	10%	• No specific recommendations in 2019 ACR/SAA/SPARTAN treatment guidelines • 2016 EULAR guidelines recommend that all patients with AS be monitored for signs of cardiovascular disease • Patients with conditions such as hypertension or dyslipidemia should be treated for these conditions • Patients should be educated about strategies for preventing cardiovascular disease
Inflammatory bowel disease	7%	• TNF inhibitors recommended over other biologics

In one cross-sectional study, roughly 17% of patients with AS exhibited uveitis.[6] The 2019 ACR/SAA/SPARTAN guidelines strongly recommend that an ophthalmologist treat patients with acute iritis in order to decrease the severity, duration, or complications associated with these episodes.[1] For patients with recurrent iritis, the guidelines conditionally recommend a prescription for topical glucorticoids. In patients with AS and uveitis, the guidelines recommend treatment with a TNF inhibitor over treatment with other biologics.[1]

Gastrointestinal problems are also common among patients with AS. Gut mucosal inflammation is present in approximately 70% of patients with AS.[5] Some researchers have hypothesized that the origin of AS can even be found in the gut.[5] In one cross-sectional study, roughly 7% of patients with AS also had Crohn's disease or colitis.[6] In patients with AS and IBD, the guidelines recommend treatment with a TNF inhibitor over treatment with other biologics.[1]

Approximately 10% of AS patients also have psoriasis.[50] This seems to be a separate condition than axial PsA: patients with AS and psoriasis tend to be younger (experiencing their first manifestations of arthritis 15 years sooner than patients with axial PsA and presenting to the clinic for the first time 7 years sooner) and are more likely to be male.[50] In addition, patients with AS tend to experience more axial arthritis, less peripheral arthritis, and more back pain than patients with axial PsA. At presentation, they have worse back pain, disease activity scores, and physician global assessments. These characteristics may help clinicians distinguish between the two rheumatic conditions. The 2019 ACR/SAA/SPARTAN treatment guidelines have no specific recommendations about treating patients with AS and psoriasis. However, TNF and IL-17A inhibitors are both approved for the treatment of psoriasis as well as AS.[51]

Finally, patients with AS have a higher risk of experiencing cardiovascular events than the general population.[52] In one cross-sectional study, roughly 10% of patients with AS also had cardiovascular disease (CVD).[6] Therefore, it is important to provide timely and effective management for AS patients at high risk of CVD. The 2019 ACR/SAA/SPARTAN treatment guidelines do not address CVD management.[1] However, the 2016 European League Against Rheumatism recommendations for CVD risk management in patients with RA and other forms of inflammatory joint disorders state that all patients with AS should be monitored for signs of cardiovascular involvement.[53] Ideally, a cardiologist should evaluate patients for CVD risk within a week of AS diagnosis and before AS treatment begins as the presence of CVD may affect treatment decisions.[54] For example, patients with CVD may not want to use NSAIDs continuously.[1] Cardiovascular risk should then be assessed at least every 5 years.[53] Patients with hypertension or dyslipidemia should be treated with anti-hypertensive agents and/or statins.[54] TNF inhibitors have also been shown to reduce inflammation and sub-clinical atherosclerosis in patients with AS.[54] In addition, clinicians can make a difference in their patients' cardiovascular fitness by educating them about the benefits of a healthy diet and smoking cessation, as well as maintenance of healthy blood pressure, LDL cholesterol, and glucose levels for preventing CVD.[53,54]

Conclusion

With more AS treatment options available than ever before, clinicians have an unprecedented opportunity to prevent the progression of this disease in their patients, ensuring that they get to enjoy the best quality of life possible. Because treatment for AS often lasts decades, finding an optimal and sustainable treatment plan for each patient is especially important. Although managing AS can involve complex decisions, the 2019 ACR/SAA/SPARTAN treatment guidelines are a helpful tool as a framework for providing quality care. The evidence-based recommendations in these guidelines have the potential to preserve patients' mobility and ability to function in everyday life. Whether patients have active or stable AS, making sure that they are receiving appropriate treatment is key to optimizing outcomes, from minimizing disease activity to maximizing flexibility.

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Remembering the Worst of the Worst

by Carrie Beach, BSN, RN-BC

Those of us who have been in clinical practice for a while all have those individual patients we remember who represent the worst of the worst in a given disease state. It's that patient with rheumatoid arthritis who has such severe hand deformity that they can no longer perform basic motor skills, or that psoriatic arthritis patient whose skin is covered from head to toe with psoriasis and whose hands are so swollen that they look like baseball mitts.

When I think of the "worst of the worst" among my patients with ankylosing spondylitis (AS), I always come back to James. He came to us as a 39-year-old, which is a typical age when we get a lot of patients with AS referred our way. James' physical limitations, however, were far from typical. At our initial visit, his cervical spine was completely fused and he had zero range of motion (ROM) in his neck. Certainly, that level of physical deformity stood out, but what was perhaps even more remarkable was that James had historically treated his condition with nothing more than NSAIDs.

James was diagnosed with AS 10 years before arriving in our practice. His symptoms began after a motor vehicle accident in his mid-20s. For several years, James attributed his chronic neck pain to the aftermath of the accident and didn't seek professional treatment. When the pain began to migrate to his lower spine, he tried massage therapy, which helped stabilize the symptoms for a short time. When the massages began having less and less effect, James said his massage therapist told him that he had seen patients with issues such as James who were eventually diagnosed with AS. He recommended that he consider seeing a rheumatologist for an evaluation. While not the point of this essay, I should take a moment to commend the massage therapist for observing this pattern and looking out for the wellbeing of his client.

James' initial rheumatology visit and X-rays confirmed the diagnosis of AS. James was referred to physical therapy, which unfortunately made his symptoms worse. He therefore went back to his massage therapist and failed to follow up for additional care with his rheumatologist.

Over the course of the next few years, James was involved in two more car accidents and noticed that he continued to lose ROM in his neck. He attributed these issues to the car accidents and not to a chronic condition such as AS, so he simply continued to self-treat with over-the-counter ibuprofen.

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Four years later, at the age of 33 years, James' neck was completely fused. He decided to try a second rheumatologist after moving to a different state. X-rays confirmed that James now had advanced AS, with fusion of his sacroiliac joints along with the cervical spine. He was prescribed naproxen 500 mg and sent home with information about etanercept. Despite the need for something stronger than an NSAID, James reiterated that he was not interested in biologic therapy and was able to manage OK with naproxen alone. That pattern continued for the next 3 years despite his rapidly deteriorating condition. James had a total hip replacement after experiencing pain in his left hip and shortly thereafter moved again to another state. This is what finally brought him to our practice.

During our initial meeting, I began as I often do by having James walk me through an oral history of his disease. I was stunned at how severe his disease had become in such a short time and perhaps even more shocked by how well—at least outwardly—James thought he was doing. He rated his pain as only a "2" on a 10-point scale (1=no pain and 10=worst pain imaginable) and said his overall health was a "3" on a 10-point scale (0=very well and 10=very poorly). While his physical limitations and X-rays told otherwise, James truly thought he was doing just fine. He explained to me that the main reason he came to our practice was for a simple refill on his naproxen and not because he wanted us to help in any significant additional manner. In his mind, the numerous car accidents were the root cause of his problems and the "damage was already done." There was nothing, James told me, that biologics would be able to do to help, so he was fine sticking with NSAIDs.

There was one small window of opportunity that arose from this meeting—James told me that his wife was expecting their first child, and he was a bit concerned about his ability to help care for the baby. I told him that we could offer infliximab or adalimumab injections to prevent further ossification of his spine, but after thinking about it, James declined and said he would stick with naproxen. I still see him annually for his naproxen refills and always inquire about his condition and willingness to try something else, but at least so far, James won't budge.

During one of our recent conversations when I urged James once again to consider biologic therapy, he told me that one of his previous rheumatologists concurred with him that there was nothing that could be done to reverse his current damage. This was a primary reason why he felt biologic therapy would not be helpful. At this point, James is simply comfortable having adapted to his disabilities. He functions as best he can. As part of his team of healthcare providers, it's a harsh reality for me to accept because I know there are lots of things James could try that might help, but we can't force our opinions onto our patients. Ultimately, it's his life and his choice.

I often wonder whether biologic therapy earlier in James' disease course would have prevented such devastating damage to his spine, or if his previous rheumatologist was right and that his condition had deteriorated so much by the time he sought medical help that the "damage was done." Many of our newly diagnosed patients with AS are young men who attribute their chronic back pain to a certain activity or sport, and they forego medical care for years while self-treating with ever-increasing dosages of NSAID. They often have a "I'll tough it out" mentality until things become serious, at which point they land in our office. James' issues are certainly on the extreme end, which is why I associate him with the "worst of the worst" among my patients with AS.

Win, Lose, or Draw

by Joni Fontenot, RN

The world loves sports analogies. It's pretty easy to understand why. You step on the field/court/rink and, a certain amount of time later, you either win or lose (or, in some sports, tie/draw). It's clean and precise—there are no grey areas.

Perhaps because I am such a big sports fan, I can't help but sometimes think about my patients in the common win/lose/draw frame of mine as I review their history within our practice.

Patients with ankylosing spondylitis (AS)—and the providers who manage their care—face a host of challenges related to their diagnosis, treatment, and overall management. As with many patients with autoimmune diseases, the journey of patients with AS within our practices aren't limited to one or two visits to fix a specific problem. We see many patients for years and years, frequently assessing their condition and modifying their treatment as needed.

Mr. L is a patient in our practice who was first diagnosed with AS about 20 years ago. He came from another rheumatology practice where he was initially prescribed escalating courses of NSAIDs. While these regimens were effective at managing his pain, his lab results remained consistently elevated. Methotrexate (MTX) was eventually added to Mr. L's regimen, which was mildly effective at resolving his neck stiffness but still left him struggling to get through his day-to-day routine.

Two years later, Mr. L's disease had worsened significantly. His neck stiffness, which had always been his primary complaint, had progressed to the point where he had trouble moving his neck at all. In addition, Mr. L developed a gastrointestinal (GI) bleed, which forced him to discontinue use of NSAIDs. Due to the severity of the GI bleed, Mr. L was placed on infliximab, a biologic that has shown some ability to stop GI bleeding in other inflammatory diseases.[1]

There again was mild improvement—Mr. L's GI bleed healed and his neck stiffness improved, but his range of motion was still significantly impaired. He later told me that his previous rheumatologist hadn't given him much hope—"it's just part of the disease process"—which is what prompted him to switch to our practice. Mr. L told me that he never felt like his previous practice took the time to dig deeper into his symptoms, and they therefore continued to prescribe treatment that only scratched the surface of his issues.

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"I encourage every healthcare professional, especially those of us in rheumatology, never to lose sight of our patients' goals, remember why we do what we do, and who we are ultimately here to serve."

He admitted that he stuck with the practice longer than he probably should have, but he didn't want to go through the hassle of finding a new provider. We hear that a lot.

Once Mr. L landed in our practice, we ordered a series of radiologic studies and labs to try and get to the root of his issues. We learned that his cervical spine was nearly completely fused. Our team was a bit shellshocked. Why hadn't his previous practice ordered more frequent radiologic studies to gauge the progression of his disease? Why had they waited so long to change medications and/or modify dosages? We'll likely never find out the answers to those two questions, but they both pointed us toward the bigger issue—what do we do now?

Mr. L's current use of infliximab was a win/lose split—his GI issues had resolved and his neck stiffness indeed was better (a win), but the fusion in his cervical spine meant that he had to turn his torso at the waist to look from side to side (a loss).

We see this so often in rheumatology. If patients either aren't diagnosed quickly or are treated too conservatively for too long, the damage is already so significant by the time they land in our practice that it's hard to reverse. For patients like Mr. L, I can't help but wonder how his story might have been different if he has been treated more aggressively sooner, perhaps by giving him an intravenous or infusible biologic instead of keeping him on NSAIDs for so many years. Would that have prevented his neck fusion? It's impossible to know.

I encourage every healthcare professional, especially those of us in rheumatology, never to lose sight of our patients' goals, remember why we do what we do, and who we are ultimately here to serve (ie, our patients). Continue to listen, especially in these days of ups and downs with the COVID-19 pandemic, and be there when we're needed as a sympathetic ear. So many of our patients have issues that are neither black nor white but various shades of grey. Only by going beyond scratching the surface with our questions can we get those sought-after wins instead of irreversible losses.

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Shaking Up Our Educational Approach

by April Johnson, MSN, APRN, CNP

Dennis loved his Diet Coke®. He couldn't make it to his appointment without lugging along two 32-ounce Diet Cokes from a local fast-food restaurant. He would finish the first one and start on the second by the time his visit to our office was over.

Until a few months ago, Dennis drank approximately 30-40 Diet Cokes a week. It sounds like an extraordinary amount, I know, but it's absolutely true. Dennis said it's not even because he couldn't function with it, but rather because someone (he can't recall who) once told him that drinking Diet Coke would help his bones stay healthy. For whatever reason, that tidbit of information stuck.

At age 40, Dennis was diagnosed with ankylosing spondylitis (AS), and 10 years later, the disease had taken quite a toll on his quality of life. He had been on etanercept 50 mg weekly for several years but had substantial breakthrough pain, for which he used hydrocodone regularly. He also suffered from anxiety, depression, and neurofibromatosis, which he developed as a child.

For more than a decade, Dennis had been coming to see me every 3 months for his standard follow-up visit. These became rather routine at some point, but a visit approximately 1 year ago raised some unexpected alarm bells for me.

Dennis arrived at our practice looking very anxious and relayed a number of concerns to me. He said he was struggling more than usual with extreme back stiffness, pain, and reduced range of motion. He missed fishing, one of his greatest pleasures, which he had been unable to enjoy for several years due to an inability to sit for a prolonged period of time on a boat. He expressed concern about his increased need for opioids to manage his pain, worrying specifically about opioid addiction (he had also recently developed significant constipation).

At this visit, Dennis also informed me that he had stopped taking etanercept on a weekly basis and had instead extended the dose frequency to once a month. The reason? He felt that the drug was affecting the severity of his neurofibromatosis. For those of you not familiar with neurofibromatosis, it is associated with chronic pain, bone deformities, low bone mass (remember the Diet Coke?), and learning disabilities.[1]

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"Patients like Dennis test all of our skills as healthcare providers. Traditional approaches that we use to educate don't work with everyone."

I sympathized with Dennis. He was clearly struggling both physically and psychologically due to the impact that his AS and other comorbidities were having on his quality of life. After hearing of his current struggles, I gently asked Dennis if he had ever been diagnosed with a learning disability because of his neurofibromatosis (a common issue with this disease).[1] Dennis told me that he remembered seeing a psychologist when he was in grade school and being told that he needed to take special classes because he wasn't able to understand instructions like the rest of his peers. This made sense, and led me to believe that perhaps his learning disability was interfering with the treatment of his AS. I probed a bit more into Dennis' educational background and asked him how he learns best. If I was going to help him overcome some of his current issues, I was going to need to find a way to get him to better understand his disease and how some of his behaviors and habits were impacting his symptoms.

As our conversation continued, I realized that Dennis learns best by watching videos. I didn't have a lot of the right resources at my fingertips, but I vowed that I would have materials ready for Dennis at his next visit—scheduled for 1 month out to maintain our momentum—that we could watch together to educate him on his disease and current treatments. We also jointly decided that a referral to a therapist would be wise so that Dennis could have another outlet to discuss his fears and anxieties related to his health struggles.

When Dennis returned for our scheduled educational visit, he clearly appeared less anxious than at our last visit. He had seen a new therapist twice in the last month and was starting to feel a bit more confident about the rationale behind weekly etanercept. One of our nurses had helped me research appropriate YouTube videos about AS and osteoporosis. We also found good, patient-level videos about the way in which etanercept works, along with current treatment options for osteoporosis. Each of these videos was approximately 2-4 minutes long, and I paused between each one to answer any questions that Dennis had based on what we had just watched.

After watching all of the videos and answering Dennis' questions, we talked more about appropriate treatment goals and his expectations. Now that Dennis seemed more in control psychologically and at least had some grounding on the basic ABCs of his disease and current treatment regimens, I encouraged him to take etanercept each week for the next 8 weeks to see what impact that might have on his quality of life. For additional support, I helped Dennis enroll in a nurse partner program through which he receives regular reminders to help him adhere to his weekly medication regimen. This program also allows Dennis to request a conversation as needed to discuss any questions, complications,

or side effects he had regarding his drug regimen. Finally, I set up an appointment for Dennis to have a new bone density scan completed. We agreed that we would discuss a new treatment goal and short-term expectations on each visit until his disease became better controlled.

Over the course of the next few months, Dennis began noticing significant improvement in his disease activity, thanks in no small part to his adherence to weekly etanercept. His bone density scan showed a T-score of -2.7 in the femoral neck, confirming an additional diagnosis of osteoporosis.

Dennis' anxiety and depression have been under much better control thanks to his regular appointments with a therapist as well as medical management (fluoxetine 20 mg/day). With so much positive progress being made, Dennis and I agreed a few months ago that it was the right time to wean him off of opioids. We knew it would be a slow process, but I was hopeful that Dennis had the right support system in place to help him through this difficult adjustment. We put a pain management specialist in place to provide additional support.

I last saw Dennis 3 months ago. He was doing great. He told me he had gone fishing the previous weekend for the first time in nearly 10 years. He had successfully weaned himself off of opioids completely and no longer suffered from chronic constipation. The support system we had put in place seemed to be working as Dennis was taking the etanercept on his weekly schedule and had finally quit drinking so much Diet Coke since he was taking alendronate to protect his bones.

Patients like Dennis test all of our skills as healthcare providers. Traditional approaches that we use to educate don't work with everyone. Some patients who continually veer from their treatment regimens may simply need a different sort of direction or additional resources to better understand the hows and whys of their disease and treatment options. These patients can initially be labor intensive, but the rewards once the right pieces are put in place are substantial. That's something we can all drink to—just no Diet Coke, please!

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AUTHOR BIO

Ali Cornish

Ali Cornish is a freelance writer who lives in northern Colorado with her husband and two young sons. She was diagnosed with AS in 2016 but has been living with its symptoms since 2011. She is the founder of Everthrive, a website dedicated to simple and essential living.

Taking a Different Approach to the Care of Ankylosing Spondylitis

by Ali Cornish

I was raised in the traditional Western system of medicine. If anyone in our family became ill, a doctor would prescribe us medication, which we would take until we became better. This routine was normal, and it seemed to work every time. Prescription drugs or over-the-counter medicines were the only method I knew for treating illnesses.

But as I grew older, I became aware that many drugs do not actually cure illnesses themselves, but rather help to manage specific symptoms. Drugs also cause side effects—some as benign as nausea, dry mouth, or heartburn, as well as others that are much more serious, like cancer, tuberculosis, or even death.

I've dealt with all of those benign side effects (but fortunately none of the more serious ones) during the course of my treatment for ankylosing spondylitis (AS) since being diagnosed in 2017. Each time I started on a new therapy and read through the potential side effects, I couldn't help but wonder, "What if there is a way to treat my condition without drugs?" After speaking with many other AS patients over the course of the last 5 years, I'm fairly certain I am not alone.

My journey to a diagnosis of AS is not particularly unique. As with many patients, it took too long—6 years in my case—to get a proper diagnosis. This was partially my fault. I ignored many signs that something was wrong. My symptoms came on gradually, one after the other, until they began to affect my quality of life in an undeniable way. There were times when I couldn't walk, sit, or lay down without intense pain. I used to wake up paralyzed with stiffness. I'll never forget those days when I felt truly unable to do anything for myself. Looking back, I often think that my doctors could have done a better job directing my care, but I also know that I could also have done a better job of self-advocating. Nevertheless, there's no use in blaming anyone. I have AS, a disease without a cure, and I'll be living with it for the rest of my life.

Once I was diagnosed with AS, I remember discussing treatment options with my rheumatologist. I initially settled on meloxicam, an NSAID with fewer side effects than most drugs. As long as I took it consistently, meloxicam seemed to work well for me, but in late 2017, I had to switch medications because I wanted to have a baby. In order to have the safest pregnancy possible, I was prescribed adalimumab, an immunosuppressant delivered to my home in a Styrofoam crate accompanied by many colorful pamphlets.

I had to inject adalimumab into my thigh. The first time I tried this, I was at my rheumatologist's office. The nurse showed me how to use the mechanism, but when I clicked it, nothing happened. She was confused and decided it was defective.

"Fortunately, I had enough self-awareness to know that feelings of loneliness and hopelessness require a bit of self-reflection."

She went to get another dose from the refrigerator and readied it for injection. I was worried—isn't adalimumab supposed to be at room temperature before it is injected? But the nurse seemed to think it was fine to use it cold, so I thought, OK, maybe you don't have to let it warm up… (Editor's note: The manufacturer of adalimumab notes that, for potential patient comfort, the injection pen can be taken out of the refrigerator for 15-30 minutes before injecting to allow the liquid to reach room temperature, though this is not a requirement).[1]

After the nurse clicked the mechanism, ice-cold liquid coursed through my thigh and into the rest of my body. The injection site tingled and then numbed. *Was that it?*

The way adalimumab entered my body that day was a physical manifestation of all my unspoken concerns: the side effects, my limited treatment options, the implications of problems I'd face in the future, the slight chance it would harm my unborn baby, the possible incompetence of the nurse, and my failure to advocate for myself.

I sat back, feeling a bit odd. My vision became fuzzy, and I slowly lost touch with my surroundings. The nurse, the chair, and the paintings on the wall gradually pixelated into a white oblivion. I almost passed out. The paramedics were called. They thought I was going into anaphylactic shock, and so did I. Fortunately, the episode passed. The rheumatology team and the paramedics told me it must have been a panic attack.

After the incident, I was too afraid to inject adalimumab myself, so my husband did my injections while playing soothing music and simulating a spa-like atmosphere. I don't remember my rheumatologist following up in any meaningful way after my initial episode. I would have appreciated someone reaching out to provide support, but none was offered. This made me feel very alone and hopeless.

Fortunately, I had enough self-awareness to know that feelings of loneliness and hopelessness require a bit of self-reflection. I was clearly uncomfortable with both adalimumab itself and the manner in which it is administered. If I was going to live with AS and face situations like this for the rest of my life, I had to make sure both my mind and body were aligned. In addition, I needed to feel supported along the way. Consequently, I decided to seek out alternative methods to manage my disease.

I don't remember how I heard about naturopathic medicine, but once I did, I was immediately intrigued. The naturopathic method treats the whole person—mind, body, and spirit—and it was exactly what I was looking for.

My naturopath made it clear that I had to help my body reduce the inflammation. With her assistance, I began to understand the link between gut health and body health. I isolated trigger foods via food sensitivity testing and comprehensive stool analysis. Additionally, I began seeing a therapist so I could heal my mind alongside my body. By maintaining a moderate activity level

and adhering to a low-stress lifestyle, I've kept my AS in remission since 2017 without needing additional biologic therapy.

Not surprisingly, naturopathic care never came up in conversations I've ever had with any of my rheumatologists. I had to seek out information on my own. As it's rarely been studied in a formal manner, there is little evidence-based data out there in support of the naturopathic approach, but pursuing a more natural path to wellness is something that I felt obligated to try after my initial scary experience with adalimumab. And it's worked for me—it's been 5 years since I made the switch and I've been able to keep my AS in check during that time.

I may not be in remission forever, and I'm not completely opposed to medication. I have two small children, and I can't afford to be in pain while caring for them. I'm so thankful I currently only occasionally need NSAIDs for pain relief, but I'm mentally prepared to need something more substantial in the future. I still have a rheumatologist who I see when I feel a flare coming on, but our relationship is admittedly a bit strained. I would like to be able to find a warm, supportive practice where I feel comfortable verbalizing my concerns about treatment in the future, but it's not something I've felt the need to aggressively seek out for the time being.

I understand that I've been privileged in my healthcare journey. Not everyone has the option to pursue naturopathic care since it usually isn't covered by insurance. I also made the difficult decision several years ago to move from the Chicago area to Fort Collins, CO, in order to pursue a lower-stress, more active lifestyle. After much internal struggle, I left my full-time job as a high school English teacher to pursue freelance writing work from home. Part privilege, part proactivity, my choices gave me the opportunity to make some very positive changes in my life. For several years now, I've been able to focus on my whole-body health.

My disease has taught me so much about the power of my mind over my body. Our bodies are blueprints of our lives—everything we go through is held deep within our cells and tissues. If we don't address the causes of stress or trauma, we will quite literally burst into pain. For these reasons, AS has taught me never to bury my emotions or live falsely. AS has taught me to seek support when I need it and not to be a martyr without a cause.

AS has also taught me to be a vocal advocate for both my body and my mind. My fellow sufferers with rheumatic disease and I need to take care of ourselves at all costs. We need to speak up and let others know what we're going through. It isn't enough to pursue an active lifestyle, eat healthy, and visit our healthcare providers on a regular basis. We also have to make sure to do things for the health of our spirits and connect with fellow humans. We must do these things for the longevity of our bodies, minds, and spirits. After all, we identify as people, and not a disease.

Reference

1. AbbVie. Frequently Asked Questions About HUMIRA. Available at www.humira.com/global/frequently-asked-questions. Accessed December 18, 2021.

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