EXCALIBUR
MEDICAL EDUCATION

HANDLING THE HARD QUESTIONS:

WHAT OUR PATIENTS ARE ASKING US ABOUT ANKYLOSING SPONDYLITIS

THE PURPOSE OF THIS DOCUMENT

Patients with newly diagnosed ankylosing spondylitis (AS) 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 AS 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 AS. We hope you find this guide useful for your professional development.

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WHY DID I GET ANKYLOSING SPONDYLITIS?

While we have some idea in a general sense why patients develop ankylosing spondylitis (AS), we can't currently pinpoint the precise reason why any individual patient develops the condition. It's likely that there are several different factors at play.

AS affects approximately 0.2-0.5% of the population in the United States.[1] It is the most common form of spondyloarthropathy, a group of chronic inflammatory diseases that largely affect the joints of the spine, the sacroiliac joints (the joints that link the sacrum to the pelvis), and the entheses (the connective tissue within joints that attaches the tendons and ligaments to the bone). It's not clear exactly how this works, but in patients with AS, the immune system becomes overactivated and attacks the healthy tissue of the joints, resulting in inflammation and damage to the bones.[2–4]

Both genetic and environmental factors are thought to contribute to an individual's risk of developing AS. In terms of genetics, a specific human leukocyte antigen (HLA) gene called HLA-B27 appears to play a central role and is present in almost all patients with AS. HLA genes encode proteins that help the immune system identify the presence of foreign material within the body. While approximately 6% of the U.S. population has the HLA-B27 gene, only 1-2% of these individuals will develop AS over the course of their lifetime. However, that percentage increases to 15-20% in individuals who have a first-degree relative who is affected by AS, showing that AS can be a heritable disease.[5-7]

There are also environmental risk factors that may be linked to the development of AS, including cigarette smoking, exposure to certain microbial infections, and high levels of mechanical stress on the joints through, for example, working physically demanding jobs.[2-4,8]

WHY DID I GET ANKYLOSING SPONDYLITIS?

WHAT OUR PATIENTS
ARE ASKING US ABOUT
ANKYLOSING SPONDYLITIS

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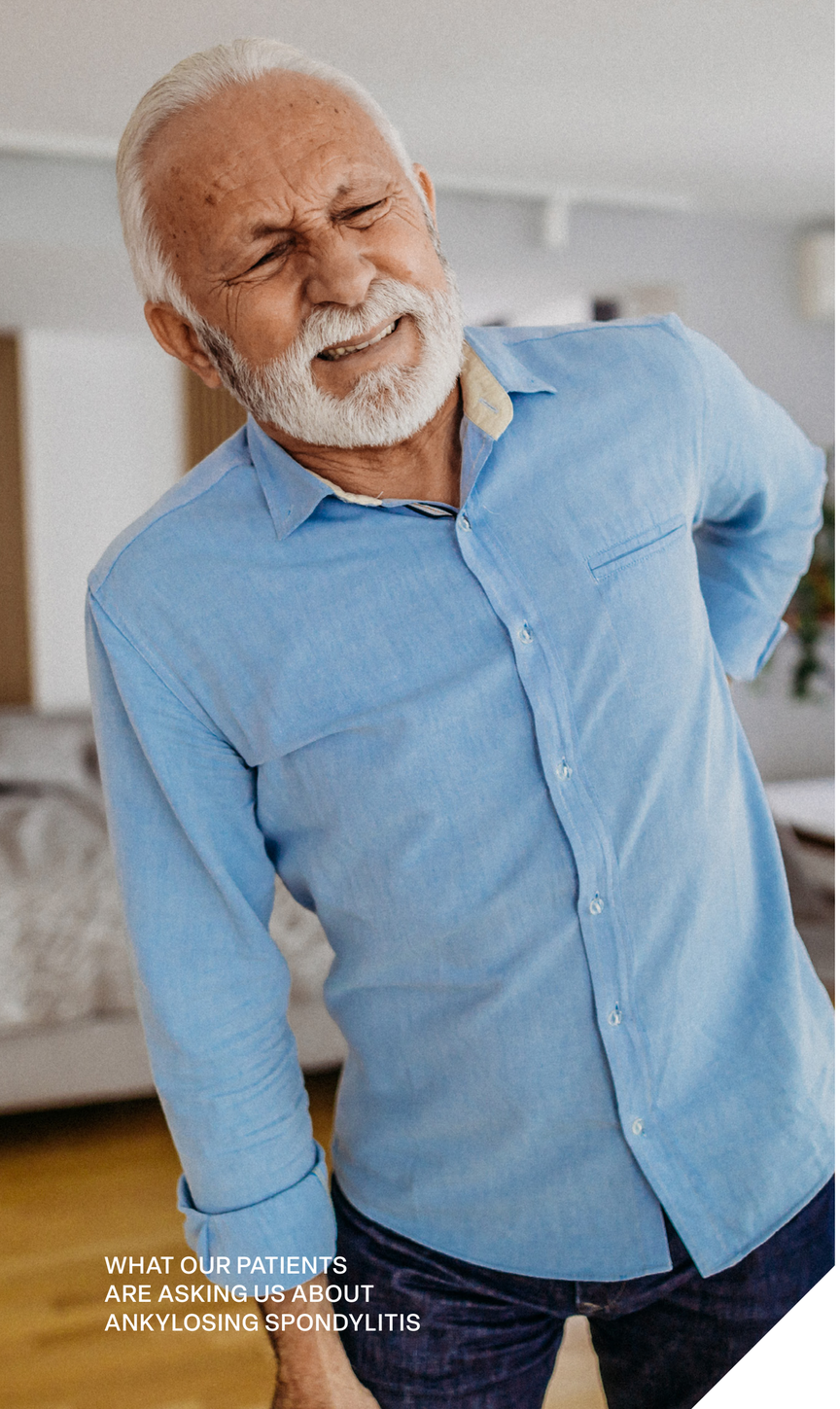

WHAT OUR PATIENTS ARE ASKING US ABOUT ANKYLOSING SPONDYLITIS

HOW DO YOU KNOW I HAVE ANKYLOSING SPONDYLITIS?

AS can be challenging to diagnose as there is no single test that definitively determines that you have the condition.[1] Instead, we base our diagnosis on a combination of a thorough physical exam, X-rays, magnetic resonance imaging (MRI), and blood tests, as well as your medical history—most importantly, whether any of your close relatives have AS or other forms of arthritis. Collectively, the evidence we gather will help us to rule out other conditions with a similar symptom profile.[1–3]

A key characteristic of AS is chronic back pain lasting more than 3 months that is inflammatory in nature. That means that we are looking for back pain that occurs without any obvious cause, in patients who are less than 40 years of age, and that improves with exercise but not with rest.[2,3] This is distinct from back pain that is caused by some kind of mechanical defect in your body, which can occur at any age and improves with rest.

With AS, we also often typically find symptoms outside of the spinal region. Most often, this involves inflammation of the iris at the front of the eye known as acute anterior uveitis, which occurs in up to 50% of patients with AS.[4] Some patients with AS also often experience inflammatory bowel disease (IBD) and cardiovascular disease.[1,2]

Inflammation in the entheses will often manifest as Achilles tendonitis or plantar fasciitis, and the presence of these conditions can provide further evidence of AS. Meanwhile, AS can be distinguished from other types of arthritis based on the pattern of the joints affected, as well as generalized swelling of whole digits (a condition called dactylitis or ‘sausage finger’) rather than localized swelling around a single joint.[1,2]

An MRI can help us to visualize inflammation in the joints that is characteristic of AS, while X-rays help us to identify bone changes. As

HOW DO YOU KNOW I HAVE ANKYLOSING SPONDYLITIS?

AS progresses, persistent inflammation can cause damage to the bones, including bony erosions and calcification of the spine and sacroiliac joints. Over time, AS can cause some of the bones in the spine to fuse, resulting in a distinct “bamboo” shape to the spine that causes patients to maintain a hunched posture and gives them limited flexibility around the spine. AS can also affect the ribs, making it harder to breathe as chest expansion is restricted. Finding evidence of these things on an X-ray or during a patient exam helps to further support our diagnosis of AS.

Finally, blood tests can also aid in our diagnosis. For example, a blood test can determine if you have the HLA-B27 gene, which would be highly suggestive of AS. We can also look for signs of inflammation—for example, a high erythrocyte sedimentation rate (ESR) and elevated levels of serum C-reactive protein (CRP) in the blood are markers of inflammation. A blood test can also reveal the presence of a protein called rheumatoid factor (RF) that is commonly found in the blood of patients with other types of arthritis but is rare in patients with AS. You may hear AS referred to as “seronegative” for this reason.[2]

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HOW DO YOU KNOW I HAVE ANKYLOSING SPONDYLITIS?

WHAT OUR PATIENTS ARE ASKING US ABOUT ANKYLOSING SPONDYLITIS

Diagnostic Features of Ankylosing Spondylitis[3]

Patient with predominant axial manifestations (back pain ≥3 months and age at onset <45 years) with or without peripheral manifestations

Sacroiliitis on imaging

plus

≥1 SpA feature

or

HLA-B27

plus

≥2 other SpA features

AS FEATURES

Inflammatory back pain	Dactylitis	Family history of SpA
Arthritis	Psoriasis	HLA-B27
Enthesitis (heel)	Crohn's disease/colitis	Elevated CRP
Uveitis	Good response to NSAIDs	

ARE THERE ANY SPECIFIC EXERCISES I SHOULD BE DOING?

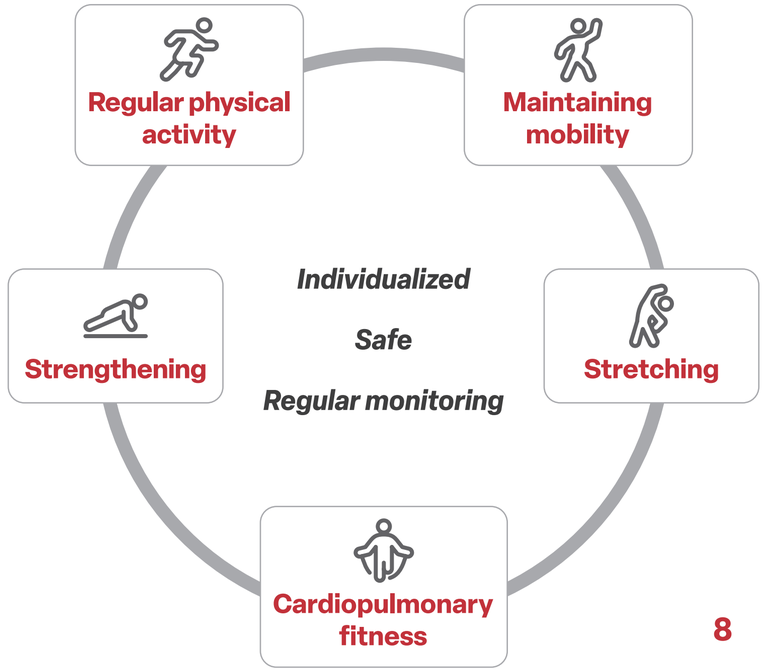
Absolutely. Physical therapy and exercise are an important complement to taking your medications that can help manage your AS. Various guidelines recommend combining pharmacologic and non-pharmacologic treatments, including exercise and physical therapy, as the best way to treat AS.[1,2]

Studies have shown that physical activity and exercise in patients with AS have significant beneficial effects on disease activity, physical functioning, as well as pain and spinal flexibility.[3,4] These benefits also likely extend beyond musculoskeletal symptoms, as exercise could help to reduce the risk of cardiovascular disease and improve respiratory function. Physical activity may also help to reduce depression and anxiety—patients with AS are at increased risk for both of these issues.[5]

Only a few studies have looked at which types of exercise are most beneficial in patients with AS.[6] These studies suggest that supervised group exercise programs are more effective than unsupervised home exercise, although they agree that any kind of exercise is beneficial.[7] Whatever exercise program you choose should be tailored to your specific needs and abilities.

In general, exercise programs should incorporate different types of activities

A Balanced Exercise Program for Ankylosing Spondylitis[9]



ARE THERE ANY SPECIFIC EXERCISES I SHOULD BE DOING?

designed to improve your AS-specific musculoskeletal symptoms, reduce your risk of complications, and promote your general health and well-being (both physical and emotional). These exercises may include stretching exercises designed to improve your flexibility and reduce stiffness and pain, aerobic exercises to improve heart and lung function, and balance exercises to improve your stability and reduce your chance of falling.[8,9]

Most types of exercise are safe for patients with AS, but we would want you to talk to us before engaging in any high-intensity, high-velocity, or high-impact exercise (e.g., contact sports, martial arts), or any exercise that challenges your balance or stability.[9]

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WHY ARE YOU ASKING ME TO GET A BLOOD TEST AND OTHER EXAMS?

Blood tests are a key part of the initial diagnostic workup for patients with suspected AS. When we send your blood to the laboratory, the tests we request may include a test for the human leukocyte antigen (HLA)-B27 gene, a key marker of AS. They may also measure the erythrocyte sedimentation rate (ESR; how quickly the red blood cells in your sample settle at the bottom of a test tube) and the levels of C-reactive protein (CRP) in your blood. Collectively, ESR and CRP are often referred to as acute phase reactants (APRs) and are an indication of inflammation in your body.[1,2]

In conjunction with X-rays and MRI scans, blood tests not only help us to establish a diagnosis of AS, but they can also help us establish a baseline for your disease activity. This will allow us to monitor changes in your disease over time. Disease activity for patients with AS is assessed using either the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) or the Ankylosing Spondylitis Disease Activity Score (ASDAS); both ESR and CRP are included within the ASDAS calculation.[2,3] Several studies suggest that CRP is a reliable biomarker of treatment response in patients with AS, and elevated ESR and CRP levels have both been shown to predict future radiographic disease progression, so monitoring their levels in the blood can give us important information about the course of your disease.[2,4]

It is important to schedule regular follow-up appointments so that we may assess your disease activity, determine your response to therapy, and check for any potential side effects. We may check in with you

WHY ARE YOU ASKING ME TO GET A BLOOD TEST AND OTHER EXAMS?

more regularly at the beginning of any new treatment regimen, but once your disease is stable, you'll be monitored every 3-6 months.[3]

Other rheumatic diseases, such as rheumatoid arthritis, are managed with a treat-to-target (T2T) strategy. This involves identifying a target (for RA that target is disease remission, for AS it has been suggested that ASDAS inactive disease could be used), initiating treatment, regularly monitoring your disease to ensure the target is being met, and then adjusting therapy as necessary to remain on target.[5] There is little direct evidence that a T2T approach is beneficial in patients with AS, but it has been shown to improve outcomes for patients with other rheumatic diseases. Several international organizations recommend using a T2T approach for the management of AS, which require periodic blood tests to monitor your APRs and help calculate an updated ASDAS.[6]

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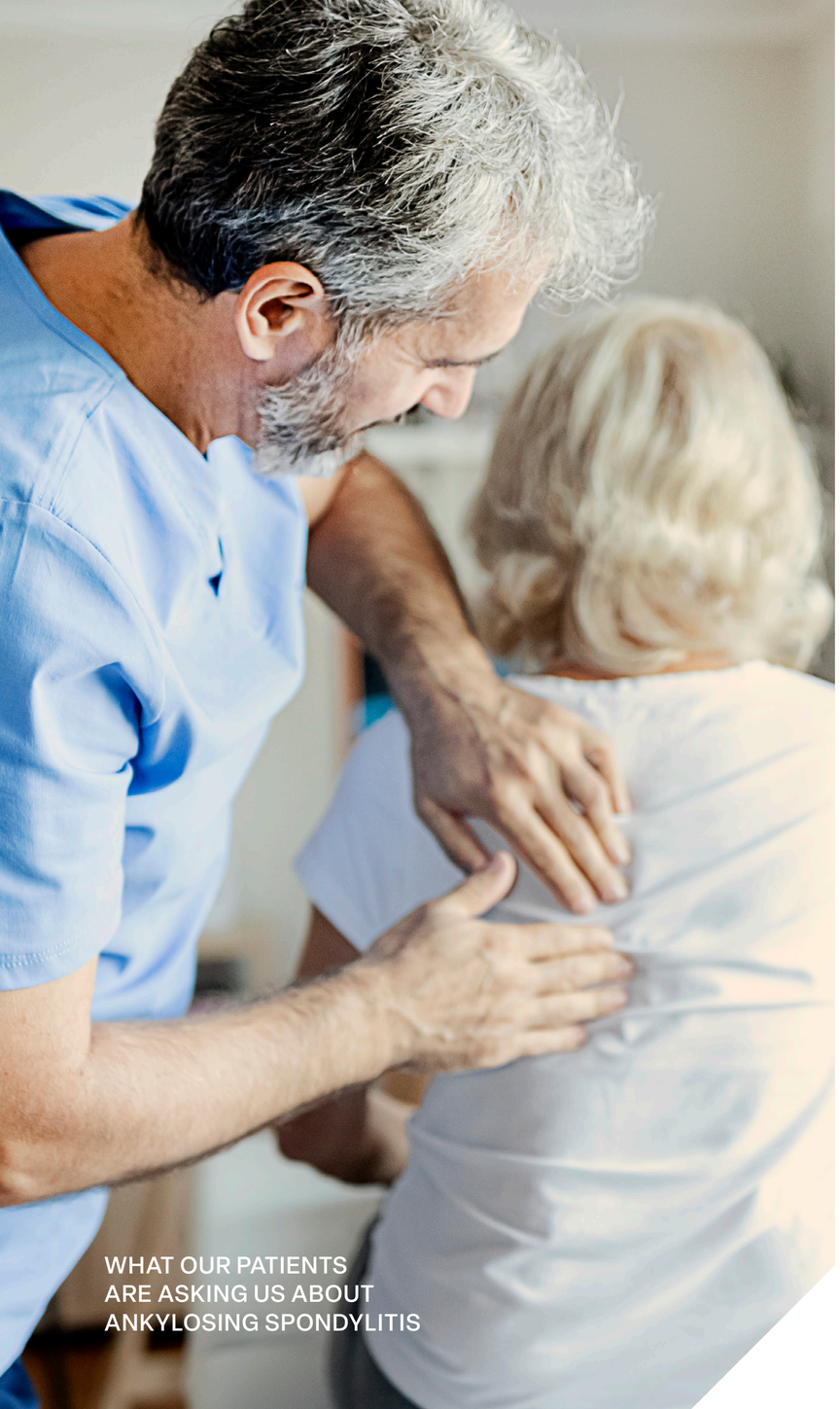

CAN I STILL GET A MASSAGE AND/OR SEE MY CHIROPRACTOR?

Chiropractic manipulation and massage, particularly deep tissue massage, are not typically recommended for patients with AS unless they are specifically prescribed by your healthcare team.[1]

Chiropractic therapy and massage can be helpful for managing general back pain, and more than a quarter of adults with back pain in the United States see a chiropractor.[2] There is some evidence that massage can improve specific symptoms of AS related to pain, stiffness, and fatigue. Chiropractic manipulation may also yield favorable outcomes in the management of some patients with AS.[3–5] However, few studies have been performed to date on these modalities and so we typically err on the side of caution in recommending against their regular use.

In patients with AS, damaged joints and fused spinal vertebrae are highly susceptible to further injury or fracture, and underlying inflammation may be exacerbated with the forceful pressure used in high-velocity chiropractic manipulation.[6,7] Skilled chiropractors and massage therapists who have experience with AS patients could help alleviate symptoms through the use of non-forceful techniques, but it's very important that you talk to your healthcare team and follow their guidance and recommendations if you'd like to receive chiropractic care or massage therapy.[1]

CAN I STILL GET A MASSAGE AND/OR SEE MY CHIROPRACTOR?

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AM I EVENTUALLY GOING TO NEED SURGERY?

Fortunately, most patients with AS do not require surgery as long as they are treated appropriately and adhere to agreed-upon therapeutic regimens. Current treatment options that we have available for the management of AS are designed to halt or delay the progression of disease by reducing inflammation in the joints and avoiding the need for surgery. However, when AS is more advanced either due to delayed diagnosis or ineffective treatment, it can cause significant pain and/or disability due to severe joint damage. In this situation, surgery may be necessary to alleviate the pain and repair damaged joints.[1]

The most common reason for surgery among patients with AS is hip damage, which we see on X-ray in approximately 30% of patients with AS. Between 12-25% of patients with AS will require surgery to repair hip damage—most often involving a total hip replacement that replaces the damaged hip with a prosthetic.[2] Less commonly, we see severe joint damage in the knee that requires a total knee replacement.[3,4]

In rare instances, patients with AS will require spinal surgery. In particularly severe cases of AS, new bone formation (ossification) in the spine can cause the vertebrae to fuse together, resulting in significant deformity and making the spine more rigid. Spinal deformity can also cause the head to be permanently flexed forward in what's known as a "chin-on-chest deformity."

Ossification in the spine can also impact the nerves and cause neurological dysfunction. Because this can significantly impact a patient's quality of life and ability to perform daily tasks, spinal surgery is recommended for patients suffering neurological damage as a result of AS. Patients with AS, particularly those with spinal deformities, are also at increased risk of fractures, even after only

AM I EVENTUALLY GOING TO NEED SURGERY?

minor trauma. Most fractures occur in the cervical spine, and surgery is also the treatment of choice in this case.[1,5-7]

Surgery can take the form of an osteotomy (where the bone is cut to correct the angle of the spine), decompression (which takes pressure off the nerves), or spinal instrumentation and fusion (which involves insertion of medical hardware such as rods, bars, and screws to help hold the spine straight).[7,8]

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AM I GOING TO NEED TO FIND A NEW JOB OR TAKE UP NEW HOBBIES THAT DON'T REQUIRE ME TO LIFT THINGS?

Many patients with AS are able to continue working and participate in active hobbies after their diagnosis, although there may be some modifications you'll need to make depending upon the severity of your condition and the demands of your current physical activities.

Regular physical activity and exercise are important components in the successful management of your AS.[1,2] The inflammatory back pain that occurs with AS is typically worst first thing in the morning and improves upon waking and with activity, so you may even find that keeping active and working helps to alleviate some of your usual discomfort.[3]

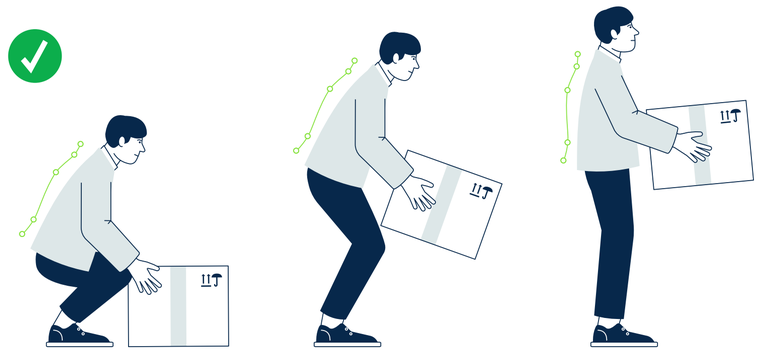
There is, however, some evidence that more physically demanding jobs are associated with greater functional limitations and increased risk of work disability among patients with AS.[4,5] Individuals whose disease is more severe are at greater risk of having their ability to work impaired, of having more difficulty in performing their work, and in having their daily activities negatively impacted.[6] This is one of the reasons why it is so important for us to work as a team to get your AS under control with an effective treatment regimen.

If you work in a physically demanding job and, in fact, even if you work in an office job where you are mostly sitting all day, you should be mindful of the limitations of your disease and take precautions to protect yourself from injury. Consulting an occupational therapist may be helpful to determine your functional capabilities. Under the Americans with Disabilities Act (ADA), you are legally entitled to ask for certain accommodations from your

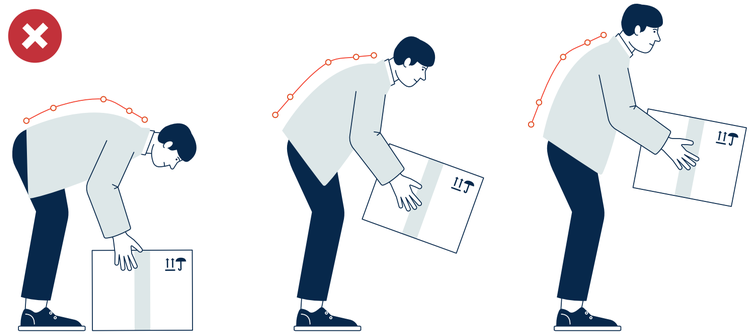
AM I GOING TO NEED TO FIND A NEW JOB OR TAKE UP NEW HOBBIES THAT DON'T REQUIRE ME TO LIFT THINGS?

employer that will allow you to perform your work safely and comfortably.[7]

If your job involves lifting heavy objects, you should use proper lifting technique and avoid twisting or bending your back. It is important to maintain a healthy posture in the workplace no matter your occupation. Outside of work, performing exercise regimens that strengthen your core muscles or getting regular physical therapy can help. If you do find that your regular work or leisure activities cause your spine to become more rigid or worsen your general symptoms, you should consider seeking a less demanding role.[8]



Proper Lifting Technique to Limit Spinal/Joint Damage



Improper Lifting Technique

AM I GOING TO NEED TO FIND A NEW JOB OR TAKE UP NEW HOBBIES THAT DON'T REQUIRE ME TO LIFT THINGS?

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WHAT IS A SAFE AMOUNT OF NSAIDs I CAN TAKE EACH DAY TO HELP WITH THE PAIN?

It is likely that you have tried a combination of over-the-counter NSAIDs to help manage your back pain and stiffness, but our initial treatment step often includes optimizing your daily NSAID usage to find a safe and effective dosage. Most patients with AS rapidly experience significant relief with NSAIDs, although it can take several weeks in some cases.[1,2] While NSAIDs can help to control your symptoms, they are not specifically designed to halt the progression of your AS, although there is some evidence that they may also help in this manner.[3]

A range of NSAIDs are available for the management of pain and inflammation associated with AS. These NSAIDs have a variety of dosages. It is important that you closely follow the instructions on the label, along with any additional instructions that we might give you in our practice, to ensure that you are taking a safe amount of medication. The table that accompanies this response provides information on the most common NSAIDs used to treat AS. We will typically try to start you on the lowest effective dose, but higher doses may be required if your symptoms persist.[1-4]

It is important to bear in mind that higher doses of daily NSAIDs are accompanied by a higher risk of side effects. Although they are generally well tolerated by patients, NSAIDs are associated with some common side effects that vary according to whether the NSAID falls into the specific or non-specific class. These side effects include gastrointestinal (GI) complications such as nausea, heartburn, bloating, and constipation. NSAIDs may also cause stomach ulcers and bleeding in patients who have been taking them continuously

WHAT IS A SAFE AMOUNT OF NSAIDS I CAN TAKE EACH DAY TO HELP WITH THE PAIN?

for a long time. GI issues are usually less of a problem with the specific NSAIDs such as celecoxib that do not block the activity of the COX-1 enzyme, which is found in the stomach. Non-specific NSAIDs are generally not recommended for use if you have a peptic ulcer, GI bleeding, or stomach upset.[1-4]

Patients taking NSAIDs may also experience cardiovascular events such as an increase in blood pressure.[5] NSAIDs should therefore be used with caution in patients with hypertension. NSAID use has also been shown to increase the risk of heart attack or stroke, particularly among individuals with a history of heart disease.[1–4]

NSAIDs are not generally recommended for people with kidney disease and/or patients who have high levels of creatinine in their blood (a biomarker of kidney function) because of their potential to damage the kidneys. NSAIDs can also impact the effectiveness of certain medications used by patients with kidney disease, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and loop diuretics.[6,7]

To determine any specific risk factors, we will perform a thorough medical history and will likely order lab tests before you begin taking regular and/or high-dose NSAIDs. If you have any underlying health conditions such as cardiovascular or kidney disease, it will be important that we monitor you closely, especially in the first few weeks of NSAID use.[4]

WHAT IS A SAFE AMOUNT OF NSAIDS I CAN TAKE EACH DAY TO HELP WITH THE PAIN?

NSAID	Recommended dosage
Diclofenac	• **Oral capsules:** 100-125 mg/day, administered as 25 mg 4 times per day, with an extra 25 mg dose at bedtime if necessary • **Topical gel:** 2 g for each elbow, wrist, or hand and 4 g for each knee, ankle, or foot
Diclofenac-misoprostol	• 100-200 mg daily, administered as 50 mg 2, 3, or 4 times per day
Naproxen	• **Immediate release tablets and suspension:** 250-500 mg (naproxen) or 275-550 mg (naproxen sodium) orally twice daily • **Controlled release:** 750-1000 mg orally once daily • **Delayed release:** 375-500 mg orally twice daily • Dose may be increased to 1500 mg/day for up to 6 months, if needed
Celecoxib	• 200 mg once daily or 100 mg twice daily • If no effect is observed after 6 weeks, a 400 mg daily dose may be tried for up to 6 weeks
Ibuprofen	• Up to 600 mg every 4 hours • Maximum dose of 3200 mg for a 24-hour period
Indomethacin	• **Immediate-release capsules and suspension** – Initial dose: 25 mg orally 2 or 3 times daily – Maintenance dose: adjust dose as needed in increments of 25 mg or 50 mg weekly up to a maximum single dose of 100 mg and maximum daily dose of 200 mg • **Suppository** – Initial dose: 50 mg rectally once daily – Maintenance dose: 50-200 mg rectally daily in divided doses with a maximum single dose of 100 mg and maximum daily dose of 200 mg
Meloxicam	• 15 mg once daily
Piroxicam	• 20 mg once daily
Oxaprozin	• 1200 mg once daily, administered as two 600 mg doses

Recommended Dosing of NSAIDs in Patients with AS[8–17]

WHAT IS A SAFE AMOUNT OF NSAIDS I CAN TAKE EACH DAY TO HELP WITH THE PAIN?

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