



ANKYLOSING SPONDYLITIS

Introduction: While AS is not necessarily a household term, it is a common illness, affecting at least 0.5% of the United States population. The name of this condition comes from the Greek words “ankylos” (bent) and “spondylos” (spine). Symptoms of AS begin before the age of 40, with an average age of onset in the mid 20’s. Men tend to develop AS more commonly than women, some say by as much as 5:1. Some suggest, however, that women with AS may be under-diagnosed or mislabeled as having “seronegative rheumatoid arthritis” due to differences in the way the disease tends to affect women, causing less spinal inflammation and more involvement in other joints.

AS is the prime example of a larger family of arthritis conditions known as *spondyloarthropathies*, all of which involve spinal inflammation in one form or another as well as inflammation of soft tissue structures around the joints such as tendons, ligaments and bursa. Psoriatic arthritis and reactive arthritis are other examples of spondyloarthropathies that share many features with AS (see related sections). In comparison to all of these conditions, however, AS has the greatest potential to cause restricted movement in the spine. The rate of spinal limitation and the extent of damage to other joints varies greatly from patient to patient, but AS has the capacity to introduce significant limitations and disabilities into the lives of young patients.

Features of AS: While the first sign of AS in teenagers may be arthritis in a single joint, such as the knee or hip, lower back pain is the most common initial symptom of AS. The pain is usually present below the waist or in the buttock region, poorly localized, and gradual in onset. The specific areas involved are the *sacroiliac* joints, located at the junction of the pelvis and the *sacrum*, a triangular shaped bone in the lower back. Symptoms often become better with activity and worse with rest, and morning stiffness of > 30 minutes is typical. These features contrast with other causes of chronic back pain (such as muscle strain or injury), which often get better with rest and worse with activity.

As pain moves up the back, the patient may become more bent over and less mobile. In severe cases, the neck also becomes stiff and less able to move. Not all patients progress this far, but AS has the potential to involve the entire spine from top to bottom, creating what is known as a “bamboo spine,” which is completely fused. In such individuals, the spine is also brittle and prone to fracturing after minor injury.

As mentioned above, tendinitis, bursitis, and inflammation of soft tissues around joints is commonly observed in AS (see *Regional Pain Syndromes* section). The shoulders, elbows, hips, and especially the heels are common sites of this type of inflammation. Heel pain can either be located on the back portion of the heel in the region of the “Achilles tendon” or in connective tissue on the bottom of the heel known as the *plantar fascia*. Symptoms in these locations may be so intense that they overshadow the lower back pain and stiffness that are the key features of AS.

Arthritis in joints outside the spine occurs most commonly in the hips, knees, and ankles. Smaller joints in the feet may become inflamed, but joints in the upper part of the body are involved much less commonly. When a joint becomes inflamed in AS, less damage tends to occur than what we see in RA, but a loss of mobility can occur.

While predominantly affecting the spine, other parts of the body are often involved in AS. A form of eye inflammation known as *iritis* can occur in 20-30% of AS patients and may result in loss of vision if left untreated. A rigid chest wall may lead to restriction of lung function and difficulty breathing. Inflammation may also occur at the beginning of the aorta, the large artery leading out of the heart, causing a leaky heart valve and strain on the heart muscle. Inflammatory bowel diseases such as Crohn’s disease seem to develop more commonly in patients with AS and should be investigated if a patient reports chronic diarrhea.

Diagnosis: AS is typically a difficult condition to diagnose due to its slow onset of symptoms, lack of specific laboratory tests, and delay in development of x-ray changes. As with any diagnosis, the best place to start is to review the history of the symptoms. Any lower back pain beginning at a young age and fitting the above description (see *Features of AS*) warrants investigation into possible AS. Because back pain due to other causes such as injury or damage is so common, symptoms are often blamed on heavy lifting or other activities. The physical examination is also very important. An experienced physician can detect subtle limitations in mobility of the spine and expansion of the chest wall using certain measurements and can reproduce tenderness over the sacroiliac joints, both of which further support AS as a possible diagnosis.

X-rays are important to document the presence of inflammation in the sacroiliac joints. While these changes may take several years to be noticeable, an experienced physician is able to detect subtle abnormalities, which can confirm a diagnosis of AS. As the disease progresses, fusion of the vertebrae can also be visualized, the end result being the “bamboo spine” appearance described above. Ideally, the diagnosis of AS should be made before this complication is encountered. In patients early in the course of their disease, magnetic resonance imaging (MRI) can detect changes in the sacroiliac joint and other areas of the spine before they are apparent on x-ray. When encountering inflammation in other joints or tendons, plain x-rays may be unhelpful, but either MRI or

ultrasound can demonstrate inflammation in the joints or soft tissues and give further evidence for the diagnosis.

While laboratory tests may be abnormal in AS, they are less helpful in making the diagnosis. Markers of inflammation may be elevated, but these findings are both nonspecific and not consistently observed even in active AS. Among all of the spondyloarthropathies, AS is mostly strongly associated with a genetic marker known as *HLA-B27*. This marker is seen in about 90% of Caucasian and 50% of Afro-American individuals with AS, but is also found in about 8% of the general population. Testing of every patient for HLA-B27, therefore, is not recommended and can be misleading. Only in cases where the suspicion for AS is high does this test help with the diagnosis.

All of the above investigations can be helpful in distinguishing AS from other more common causes of chronic lower back pain and designing a proper treatment plan. Still, some patients are difficult to diagnose initially and may be labeled as “*undifferentiated spondyloarthropathy*.” Many of these patients will eventually “declare themselves” and demonstrate clear features of ankylosing spondylitis or other related conditions such as psoriatic arthritis. The remainder continues to show incomplete features and designing a treatment plan can be challenging in this group of individuals.

Therapy: Treatment options for patients with AS have improved dramatically in the past few years. Prior to recent advances, therapy focused mainly on reducing symptoms. Now, it may be possible to slow down the progression of the disease, although further studies are needed to confirm this impression.

Non-steroidal anti-inflammatory drugs (NSAIDs) are the first form of medical therapy that should be initiated for AS. These medications work directly on the inflammation of AS, as with other inflammatory diseases, and may be all that is needed for patients with mild disease. Examples of these drugs include ibuprofen and naproxen, but many doctors choose a possibly more powerful drug indomethacin, which may be more effective in the majority of AS patients. Side effects, such as stomach upset or serious bleeding or reduced kidney function may limit the use of these medications in certain individuals. The stomach side effects may be avoided by using the COX-2 selective NSAIDs celecoxib (Celebrex). While NSAID therapy does not appear to prevent joint damage in rheumatoid arthritis, a study performed a few years ago demonstrated that patients with AS have significantly less progression of their spinal disease when taking NSAID therapy routinely rather than intermittently or not at all.

Disease modifying anti-rheumatic drugs (DMARDs) used in rheumatoid arthritis (RA) have also been studied in AS. *Sulfasalazine (SSZ)* has been shown to improve joint pain and swelling in patients who have arthritis in areas outside of the spine. Unfortunately, other DMARDs that are highly effective in RA, such as methotrexate, have not shown convincing benefit in treating arthritis in AS patients. Many of these

drugs, however, as well as SSZ may reduce the frequency or severity of iritis flares in AS patients and may have some value in treating these individuals.

The most promising new therapies for treating more severe AS are known as *tumor necrosis factor (TNF) inhibitors*. All of these medications block the action of tumor necrosis factor, a protein in the body that is involved in many types of inflammation. When used in the treatment of AS, these drugs often dramatically reduce spinal pain and inflammation as well as symptoms in other joints. As impressive as the effects these drugs exert may be, however, it has yet to be determined whether they alter the course of the disease or prevent complications, but studies investigating this issue are ongoing.

Currently, there are four TNF inhibitors approved by the FDA for treating AS. At the present time, patients and physicians can choose between *etanercept* (Enbrel), given as a once weekly injection; *infliximab* (Remicade), given as an every 8 week intra-venous infusion; *adalimumab* (Humira), given as an every two week injection; and the most recently approved *golimumab* (Simponi), given as an every 4 week injection. In patients with iritis or inflammatory bowel disease, Remicade and Humira have documented efficacy for these complications as well, while Enbrel has not shown benefit, and Simponi is yet to be studied. TNF antagonists can increase one's risk for certain infections, and patients beginning such therapies should be screened for tuberculosis before starting.

A single study suggested that *pamidronate*, an intravenous medication used to treat certain bone diseases, can also result in significant reduction in pain and stiffness in AS patients. The role this medication may have in treating AS is unclear, but further investigation is anticipated.

A new drug known as *ustekinumab* (Stelara) is being investigated as a potential therapy for AS. This drug inhibits two chemicals that also appear to be involved in the inflammatory process, interleukin 12 and interleukin 23. While already approved for the treatment of psoriasis, Stelara may be considered as another option in AS if future studies prove favorable.

In addition to medical therapies, *exercise* has been shown to reduce pain and stiffness as well as improving mobility in AS patients. Specific exercises aimed at stretching the back, neck, and chest seem to be the most useful and should be performed under the supervision of a health care professional.

Recently, a panel of international experts got together to form guidelines for treating patients with AS. Their recommendations were that if a patient had spinal involvement alone, to begin with NSAIDs and to try full doses of at least two drugs in this category. If a patient had spinal disease plus arthritis of other joints, beginning

NSAIDs and proceeding to SSZ if the disease is not well enough controlled was suggested. In patients failing these interventions, however, it was recommended that therapy with TNF inhibitors be considered. It is hoped that this aggressive approach will prevent spinal fusion and other complications of AS, as further studies will hopefully soon determine.