

SPONDYLITISPLUS

Questions & Answers



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Question & Answer

Spondylitis Association Educational Program, Chicago 2005

Dr. Elaine Adams • Dr. Muhammad Asim Khan • Dr. Perry Nicassio

Recently, during a sunny spring day in Chicago, several of the SAA staff and Board Members joined with the Chicago support group folks to welcome a packed auditorium of patients, their families and friends to share information about “life with spondyloarthritis (SpA)” and to hear what the experts had to say about the best approaches to treatment and management. In addition, we were deeply grateful to be able to honor Dr. Muhammad Asim Khan as the first recipient of the Greg Field Award which was made possible by the Fallowfield Family.

QUESTION:

If you do not have the radiographic proof or are not showing any fusion and even on MRI (magnetic resonance imaging) is there something such as a pre-AS condition?

ANSWER:

A pre-AS condition would require documentation of those changes on MRI. For treat-

ment with TNF-blockers, the recommendation is that you have to have definite disease; and that recommendation requires that you have to have x-ray evidence of sacroiliac joint inflammation. For the time being, given that these drugs are costly, and that there are a lot of side effects, you don't want to include people with diseases that are not actually ankylosing spondylitis.

There is not yet a set of standards for diagnosis using MRI, but papers are being published where we could probably agree that some patients can be diagnosed as having very early stages of the disease. However, the “gold standard” for the diagnosis of ankylosing spondylitis for the purpose of TNF-blocker treatment is the presence of x-ray evidence of sacroiliac joint inflammation.

QUESTION:

How can I tell if I am getting the best care from my doctor?

ANSWER:

There are some things that a doctor can do to improve the patient experience. From my perspective, I believe that it is important for the doctor to take time with the patient. This means, no clock watching while the patient is telling his/her “story” – and certainly, no interrupting during the history taking. If you let the patient speak, you will be able to make a correct diagnosis of ankylosing spondylitis. One of the problems with how we practice medicine today is that we don't allow adequate time to hear the patient out. It is nice to hear spontaneously from the patient rather than hurrying them and nudging their

“Spondylitis is not just a pain in the back!”





answer. Also, every physician should ask one specific question of every patient at the end of “history taking” and that is, “Is there anything else you want me to know”? You would be surprised how often important aspects come up, and then you address that concern without being in a hurry. I am a patient first and a physician second. [Dr. Kahn]

QUESTION:

How can I approach my doctor with information that I may have found from other sources, such as from the Internet?

ANSWER:

That is a good question since much of this current information is really new, and it takes a while to get new information about an old disease. Hence, patients should just say, “Well, what do you think about this and that?”

QUESTION:

Question: Is spondylitis a rare disease or is it more common than is generally accepted?

ANSWER:

To dispel some of the myths and misconceptions about spondylitis, it is important to know that it is not a disease of “older people”

— everyone get it, and that also it is a very common disease, contracted by 1:200 adults in the United States, alone. However, it is problematic in that so many remain undiagnosed. [Dr. Adams]

QUESTION:

Could you please explain to us the difference between TNF-blockers and other drugs, for example, Immuran, and how they each modify the immune response?

ANSWER:

TNF-blockers actually have been a very big breakthrough because they are much more focused and targeted on a very specific chemical mediator, which we know to be important in the inflammatory process for AS as well as other diseases. Immuran[®] is much more non-specific in that it does sort of a general down regulation of the whole system and is not nearly as specific. As you might imagine, there are more side effects with a drug like that. Even so, it is a good drug, and we find it very useful for many diseases, but TNF-blockers are very targeted.

QUESTION:

I would like to know about the wisdom of using drugs during pregnancy and even



Dr. Muhammad
Asim Khan



Dr. Elaine Adams

“Spondylitis is a common disease, contracted by 1:200 people in the U.S, alone.”

during the period prior to pregnancy where there might be an overlap?

ANSWER:

There is a categorization that is applied to drugs, that is a), b) and c). Most drugs are what we call category c) in pregnancy. This means that we have no controlled trials in which we are actually studying the effects of this drug in pregnancy. The reality is that this is not the kind of study that we would do. However, we can look at animal data. This can be somewhat helpful. Most of the time we are stuck with “natural observation.”

The TNF blockers or so-called biologics do not cause tuberculosis (TB) or make you get TB but if you are somebody who has been previously exposed to TB and have the dormant infection, like some of us have, but don't even know it, then these drugs can reactivate it.

Dr. Elaine Adams



where, for instance, there is a patient who was not intending the consequence of pregnancy, who was on the drug and we follow it along. There is growing data that these drugs are reasonably safe during pregnancy. The emphasis really is on “reasonably,” because we don’t know for sure, but there is growing evidence that there are patients before and during pregnancy who are doing okay. All other things aside, I have to say that it would be safest if you can do without it. However, as the data grows, there may be circumstances in which life is intolerable without it and the risks are small enough that you can go ahead and continue it.

(Reference Dr. Ostensen’s article, Jan/Feb 2005, in S+ which is available to members through the online archive at www.spondylitis.org)

The biggest group of drugs that we have historically used is called non-steroidal anti-inflammatory (NSAIDs). Ibuprofen is the most common, and is one of the oldest available over the counter. These drugs can reduce inflammation and relieve pain. They are not potent enough to turn the disease off but they do help.

Dr. Elaine Adams

QUESTION:

Could you please tell us about heart valve inflammation and whether the rheumatologist is checking for problems in this area?

ANSWER:

The question as it relates to AS is very specific since in AS it is the aortic valve that we are talking about. That is the outflow valve where the heart is pumping the blood into the main blood vessels and into the rest of the body. Heart problems in AS can be detected with a stethoscope, and most of us will listen carefully for aortic valve problems in patients with AS since these are seen more in the AS population than in unaffected people. I don’t think that it is necessary for all AS patients to have screening tests, but, that said, your rheumatologist should listen to your heart for this particular valve problem and pay attention to any symptoms, including shortness of breath. Granted, there are many other causes of shortness of breath, but shortness of breath or fluid retention might raise a question about this valve. The valve involvement is related to the duration of the disease. In the early stages, it is very uncommon for the heart valve to be affected, though it can occur. Some patients may have a “murmur” of the heart. Though not all. With advanced disease, a person may be short of breath. The other problem is associated with “heart block.” In those cases, one of the symptoms will be a low pulse rate. Some of those people will need a pacemaker or valve replacement. It is important not to be too worried about this problem because it is relatively rare, but it is important for your rheumatologist to listen to the heart to make sure that there is not a problem. That said, even when there is a problem, in most cases it is very mild and does not have significant consequences.

QUESTION:

If my children test negative for HLA-B27, does that mean that my grandchildren will not develop AS? How prevalent is the HLA-B27 gene?

ANSWER:

HLA-B27 is associated with AS, but the 90% association that is always cited is true of Northern European extraction, including the Swedes and the northern part of England. They are 90%, but in the South of France, Spain, southern Italy, and the Mediterranean region, the association is much weaker. So, as part of the answer, the association depends upon ethnicity, not just the color of skin. Among Jews, and others, the association is even weaker. Now, if we take Americans of African descent as an example, only 50% of those with AS have the gene. Therefore, we cannot really use the gene as a test. The point that I am making is that this is a healthy, normal gene and that if a patient has AS, he or she doesn’t have to be tested if the diagnosis is obvious because, in fact, testing for B27 has actually led to further delays in diagnosis among B27 negative patients. So, if we have the B27 gene, we do not need to test our children because half of them, roughly, will possess the gene, and even though they have the gene, most of them will never get AS. It is much better as an educated patient to know when to seek help if your child starts getting the kinds of symptoms that would suggest AS. Then, the gene typing can be helpful. If you have no psoriasis, no Crohn’s disease running in the family, no ulcerative colitis running in the family, the chances are that your children and grandchildren will not be afflicted. In addition, it is important to remember that once the test for the gene has been done, there is no need to retest since it cannot be acquired or lost, but is something that a person has present at birth or not.

QUESTION:

How do TNF-blockers differ from other drugs?

ANSWER:

TNF-blockers were a very big breakthrough because they are much more focused and targeted on a very specific chemical mediator that we know to be important in the inflammatory process for AS as well as other diseases. In the past this wasn't possible.

QUESTION:

With the biologics, how long should one wait to find out if they are working if you feel that you aren't getting any positive results?

ANSWER:

First of all, whenever a person doesn't respond the way you think they should, it is important to make sure that we are on the right track and have a correct diagnosis. Assuming that we have the right diagnosis, then there is the possibility that a patient may not respond for some reason. TNF-blockers usually work fairly quickly. Therefore, one should know within three months of treatment whether or not a person is responding. If there is still evidence of active inflammation after a given period of treatment, I may consider switching drugs – for example, we might try one of the other TNF blockers. Sometimes a person may respond to one rather than the other. Even though they all have a similar effect, they do it in a slightly different way. Therefore, we do see patients who respond to one and not to another.

QUESTION:

Does the forward stooping position in the upper part (neck area) of the spine mean that fusion of the spine has already occurred?

ANSWER:

Forward stooping of the spine is a sign that the neck is showing the result of the inflammation. That said, it was interesting for the researchers to observe during the clinical trials of the TNF-blockers that some of the patients, many of whom had 10-15 years of documented disease, were able to see improvements in neck flexibility and chest expansion as a result of taking these drugs, in addition to an improved ability to bend forward, backwards and sideways. It seems that part of the limitation is a direct result of the muscle pain associated with AS, which causes muscle spasms, and because of these, there is an inability to properly use these muscles, which in turn causes fibrous adhesions and so on, even before bony fusion takes place. That is why many patients will show improvement on the TNF-blockers. However, if there is a totally fused spine with no joints left, then we do not expect to see these types of results.

QUESTION:

When are TNF-blockers prescribed to a person with AS?

ANSWER:

TNF-blockers can potentially be prescribed to a person with AS when a diagnosis of active inflammation has been observed and other medicines have been tried and failed, such as non-steroidal anti-inflammatories (NSAIDs). Two or more of these drugs need

“It is not a disease only of men, lots of women out there get it.”

to be tried over a period of three months because people react individually to them, which means that one might work better than another.



The SAA would like to thank Elaine Adams, M.D., Muhammad Asim Khan, M.D., and Perry Nicassio, Ph.D for graciously sharing their time, experience and energy during this program. Many thanks to our supporters in Chicago for assisting with this program, in particular Board Member, Ann Howat and Support Leader, Michelle de Long.

“Our goal in 2005 is not to allow the postural changes of severe AS to happen any more.”

Questions

Answers

QUESTION:

Although we know that non-steroidal anti-inflammatory drugs (NSAIDs) can be really good drugs for AS, what are the downsides of these medications?

ANSWER:

The primary downside of NSAIDs is gastrointestinal distress: 48% on NSAIDs will have dyspepsia or irritated stomach from their NSAIDs, and 2-3% will have serious gastrointestinal complications, such as internal bleeding. The COX-2 inhibitors such as Celebrex, reduce that by half. Another issue is the potential for long-term heart problems. It is important to be very careful with people who have established heart disease or who are at high risk for heart disease because of blood pressure or cholesterol problems. If you can get by with a lower dose, that is probably the best way to do it. The third possible side effect is dizziness. In addition, NSAIDs can affect the liver, although the incidence is low. If you are taking NSAIDs on a regular basis, you need to have your blood checked once or twice a year.

QUESTION:

It has been my experience that every drug stops working after a while. Is there an explanation for that? Is there something beyond TNF blockers? Are there other new treatments that are in the works?

ANSWER:

You are going to see some trials on AS in the next few years. There are chemicals in your blood that cause inflammation. New medications are being developed to potentially mediate these chemicals. Hence, a lot of them are being looked at; they may do an even better job than the TNF blockers.

It is thought that TNF blockers wear off over time at least in part because the body forms antibodies against the medicine. That is why in inflammatory bowel disease when using Remicade, patients are often put on Methotrexate, because it helps to suppress the formation of the antibodies. We see AS patients who have started having breakthroughs where symptoms begin to come back. Sometimes Methotrexate is administered in AS, but unfortunately, it does not do anything for the spinal disease. These issues need further study.

QUESTION:

What are the side effects of Methotrexate?

ANSWER:

Methotrexate is an interesting drug. It is the reason that Leukemia in children suddenly stopped being a universally fatal disease in the 1950s. In high doses, it is a potent anti-cancer drug. They started using it for Hodgkin's disease in the 1970s, and the people with rheumatoid arthritis (RA) along with Hodgkin's had their arthritis go away. By 1985 it was shown to be very effective in RA when given once a week and at relatively low doses. It has also shown to work with the peripheral arthritis of AS, although it has not been well studied. It is a drug that can have liver side effects, although the prevalence is low. It can also affect the blood count, so we monitor that. In addition, it can cause skin rash, mouth ulcers and hair loss. Folic acid, a vitamin, seems to help the hair loss issue, in some.

QUESTION:

I have heard that there is a higher risk of cancer through use of Methotrexate.

ANSWER:

I am not aware of any data in the study of AS that has convincingly shown that. In the study of RA there appears to be a high risk of cancer, but there is a high risk of cancer in RA because of lymphoma, due to chronic stimulation of the lymph system because of the RA itself. So, even if you are not on any drugs at all and you have RA, your chances of contracting lymphoma are twice that of an unaffected person.

QUESTION:

I don't appear to have gastric side effects or at risk for heart disease, so would you say the COX-2 inhibitors would be good for me?

ANSWER:

They can be good drugs for some people. It is important to discuss all issues concerning treatment with your medical team.

QUESTION:

My daughter is 18 and has significant damage to the sacroiliac area. She has had pain for 3-4 years. She has been on Celebrex and everything else. Are the TNF drugs appropriate for use in children and teenagers?

ANSWER:

A TNF-blocker would be necessary in this setting if she is having continuous symptoms. Remember that 50% of people with AS probably don't require a TNF-blocker. There are some data that show that structural change over time is slowed down to a great extent with the use of these drugs, according to data from Europe, where the TNF-blockers have been used for 5 years. If your daughter's disease is active, if she is having a lot of pain and stiffness, if she has not responded to non-steroidal anti-inflammatory drugs, if it's in her knee or hand, or if she took Methotrexate or injections and didn't get better, then she is clearly a candidate for a TNF-blocker. Her doctor can assess this in conjunction with your daughter.

QUESTION:

How long can people be on Enbrel?

ANSWER:

Right now, the long-term data looks good. There is no evidence that this is a major issue over time, but we have a lot to learn; these drugs have only been available since 1999.

QUESTION:

I am 63 years old, and I find that after receiving a pacemaker in 1998 I now require aortic valve replacement surgery due to insufficiency. Since my slow heartbeat was treated utilizing a pacemaker, is it the case that my scarred aortic valve is only treatable through replacement? Or does treatable mean an alternative to surgery?

ANSWER:

The medical management of aortic insufficiency is one of the more daunting challenges to modern cardiology, as is the decision regarding the timing of Aortic Valve Replacement. Medical management can help the heart compensate, but the "hard data" from imaging and catheterization are not as definitive in this setting.

Furthermore, since the US cardiology community is so focused on coronary artery disease, it is not so easy to find a cardiologist/cardiac surgeon team that is truly experienced with aortic insufficiency. That's what you need. With such a specialist you should do well.

QUESTION:

When I was a young man of 22 years (1964), I slipped on ice and injured my back. The following year I developed severe pain in my leg. I made an appointment with an orthopedic doctor, and he confirmed spondylitis in my spine. After being treated with aspirin (12 a day) and special exercise for several months, the symptoms disappeared.

Are the TNF drugs appropriate for use in children and teenagers?

For the next 39 years, I had absolutely no problems with my back or legs. Each morning I would do stretching and light exercise, I would walk 3 to 5 miles each evening during the summer months, play golf, basketball and swim. Then in April 2003, I tripped over a wire and landed on my back. Immediately I felt pain in my back, neck and shoulder.

X-rays and an MRI showed severe spondylitis and disc degeneration. This problem got worse as time progressed, and today I can only walk a short distance. I have pain in my back, legs and neck 24/7. I received epidural injections and have currently taken pain relievers and nonsteroidal anti-inflammatory drugs. Any advice would be appreciated.

ANSWER:

It is likely that there is a small fracture(s) of your syndesmophytes and/or adjacent vertebral structure consequent to the trauma in 4/03. The "disc disease" is probably irrelevant. A specific bone scan called single photon emission computerized tomography scan (SPECT), would help to localize the likeliest lesions and then plain films and an MRI of the "hot" spots would be helpful. Once the fracture(s) are defined, then options can be discussed. Not all are surgical.

Many thanks to the SAA Medical and Scientific Advisory Board for answering these patient questions. If you have questions that are of a universal nature, please email laurie.savage@spondylitis.org. We regret that we cannot respond individually to questions, but selected ones will appear in these pages in future issues.

Questions & Answers

QUESTIONS

QUESTION:

My 18-year-old son, who was diagnosed with AS when he was 10 years old, has been receiving TNF blocker therapy infusions for the past 3 years and doing remarkably well. All pain and symptoms have been greatly reduced. We are pleased that he will be attending college in a few months, which will require him to live in the dorm during his freshman year. The student health services at the University are recommending that all students who will be living in residency halls be vaccinated against meningococcal disease. In order to be sure that this was a safe option for our son, we spoke with both his pediatrician and the physician assistant in the rheumatologist's office. As a result of our inquiry, we now have conflicting advice. The PA says that he should not have the vaccine because it is a live virus, and since he is immune compromised as a result of his TNF therapy, this would be put him at risk. His pediatrician disagrees. She highly recommends the vaccine.

We are now at a loss and do not know where to turn for advice.

ANSWER:

There are two meningococcal vaccines available in the U.S. A polysaccharide vaccine has been available for years, and a conjugate vaccine (MCV4) was released this year. Neither of these is a live vaccine. In addition, meningococcus is a bacterium and not a virus. No one is at risk of infection from either vaccine.

I am aware of no data as to whether infused TNF therapy will blunt the response to this vaccination, and thus, render it less effective. However, there is no reason to think that it would confound the vaccination in any other fashion.

QUESTION:

I have had AS for many years, and my neck is fused and rigid. Sometimes after eating, it feels like the food is stuck in my neck. Can

you please tell me if this is something that I should have my doctor investigate?

ANSWER:

This is a very concerning complaint whether or not a person has spondylitis. It demands a visit with a physician and probably some testing to sort it out. Trouble with swallowing is a "red flag" complaint.

QUESTION:

I have been troubled by AS and what I have come to know as a group of related diseases since I was 15 years old. During the past 40 years, I have been treated for AS, Crohn's disease, iritis and the nastiest of them all, pyoderma gangrenosum. You will have to take my word for it that I am not a hypochondriac! In May 1968, as part of a stress test and physical, I was told that I have a cardiovascular conduction abnormally called a left bundle block. I believe that this is the condition described in a past Spondylitis Plus article, The "Heart in Spondylitis." I never realized until just recently that there was potentially a connection between this and my AS. In 2001, I started on a TNF blocker, and it has been very successful in controlling my pain and other symptoms since then.

My question: "The Heart in Spondylitis" article implies that the conduction abnormality is related to inflammation. Since I no longer seem to have the inflammation since starting the TNF therapy, do I still have the conduction abnormality?

ANSWER:

No one would accuse you of hypochondriasis. To the contrary, you have withstood the onslaught of nearly the entire spectrum of spondylitis with your courage intact.

Thankfully, we now have agents such as TNF blockers to assist you. Left Bundle Branch Block (LBBB) is not one of the conduction defects associated with inflammation of the

aortic root in AS. You have no need to worry on that score. Furthermore, you probably have no need to worry about the implications of LBBB for your cardiac health. LBBB is a relatively common occurrence that usually reflects a microscopic scarring process that reroutes conduction but does not otherwise interfere with cardiac function. There are exceptions that I am sure your physicians have addressed and excluded. Hopefully, your LBBB is just one of those things.

QUESTION:

After a series of unsuccessful treatment protocols for my AS symptoms, I am currently getting a great deal of relief from a combination of Tramadol and Naproxen. These drugs are not very expensive in comparison to others. My rheumatologist says that she finds these drugs to be very effective for many of her AS patients. I would like to know your opinion.

ANSWER:

Tramadol (Ultram) is one of the many non-opioid, nonsteroidal anti-inflammatory drugs. The general experience is that it is no more effective than are most others of that class. In addition, it does not spare one of the gastrointestinal toxicities (and may be more predisposing in that regard) and has frequent side effects, including somnolence, headache and confusion. Therefore, most of us shy away from its use, particularly as a long-term option. I never prescribe it.

However, it is an option, and there are patients for whom it is said to be particularly effective. I cannot fault your doctor, or question your perception. I also cannot support a general recommendation for the use of this agent in the AS patient.

QUESTION:

I am a 77-year-old male. I came down with crippling pain in my lower back and sacroiliac areas in my early 20s, circa 1950. I experienced a serious urinary tract infection at the same time. My diagnosis was rheumatoid arthritis. I was in the military at the time and wound up in an Air Force hospital in St. Johns, Newfoundland. I was to be medically processed out of the service. My doctor there wrote a research lab that I believe was at the University of Wisconsin, and they referred him to a Canadian doctor that happened to be practicing in St. Johns. Their recommendation was that this doctor

claimed a cure for rheumatoid arthritis in a male patient within a certain age group, if the condition was isolated to the lower spine area. At this time, my sed. rate was elevated and the affected area was inflamed. Upon my first visit, the doctor proclaimed he could cure me, in that progression would cease and my sed. rate would normalize and inflammation would disappear. I agreed to treatment that consisted of lying under an X-ray machine for long periods of time. After each treatment he took a blood sample. After the third treatment, he proclaimed success and declared he had cured me of rheumatoid arthritis. My acute pain subsided within 24 hours; my sed. rate has been normal since. However, I have had serious arthritic pain since, increasing with age. My best relief came with a nonsteroidal anti-inflammatory drug that the doctor put me on when it first came out. I have cardiovascular disease and therefore was taken off recently. Since then, I have had excruciating pain in my lower spine and sacroiliac areas. As of yesterday, I put myself back on the anti-inflammatory since I am not able to function without it.

I have yet to get any doctor to believe this story. My concern is whether that radiation treatment may have done some harm to my bones and tissues.

Five years ago, I learned through my grandson that I had spondylitis. He suffered the same as I at about the same age. He went to a rheumatologist and was diagnosed with ankylosing spondylitis. I then asked my doctor, and he verified mine. I suffer from iritis, and this year my eye doctor told me many people with spondylitis have iritis. I suffer with pain in my feet, hands, neck and shoulders. I have a right hand I can't make into a fist.

I would really love to know what you think about all of this.

ANSWER:

I am not able to comment about this gentleman's current circumstance. He is describing back pain and pain elsewhere of a quality that one would not predict 55 years into spondyloarthritis. He should be under the care of an experienced rheumatologist to help sort this out.

His recall of the events in Newfoundland is fascinating. Since he had a coincident "serious urinary tract infection," he may well

have presented with "Reiter's Syndrome," which is one of the forms of spondyloarthritis and which shares many features with ankylosing spondylitis. I am not surprised that the initial diagnosis was "rheumatoid arthritis," as there was a debate as to whether ankylosing spondylitis was a separate entity or a form of rheumatoid arthritis, so-called rheumatoid spondylitis.

In mid-century there was much use of therapeutic radiation therapy for non-malignant diseases. Ankylosing spondylitis was one of the diseases so treated, resulting in what was said to be dramatic relief of low back pain. However, the treatment entailed exposure to high doses of radiation, higher than the ordinary x-ray machine can deliver in 30 minutes. If he was placed in a "cobalt machine" or the like, I would have guessed that this gentleman's memory would be more vivid. It is possible that his acute presentation subsided spontaneously, as is most often the case for acute Reiter's syndrome.

It is perhaps of interest to note that epidemiologists from Oxford University published a very important paper in the 1960s documenting that radiation exposure to the spine of patients with ankylosing spondylitis was associated with an important (though not overwhelming) risk of leukemia. Since that paper, nearly all North American radiation oncologists have been loathe to treat any but patients with malignancy, with rare exception and then with only low doses. Radiation oncologists in Europe feel somewhat less constrained.

Hopefully this response will provide this gentleman with the information he seeks.

We thank Dr. Nortin Hadler for generously sharing his time and expertise in answering these patient questions.

Dear readers, we welcome your questions for this section of Spondylitis Plus. We would ask that questions be of a general nature and hence of potential universal interest to others in that regard. Answers to the questions selected will appear in this column and also on our website, rather than by personal communication. We look forward to your participation.

Questions

Answers

from the
Spondyloarthritis Educational Seminar
San Diego, 2005

QUESTION

Are there any recognized differences seen on magnetic resonance imaging (MRI) when comparing HLA-B27 positive individuals with HLA-B27 negative individuals?

ANSWER

I am not aware of any data addressing this question. A German research group, which is currently studying the usefulness of MRI in AS, is not testing study participants for B27 positivity. When we compare standard (plain) radiographs of people with AS, both B27 positive and B27 negative individuals, we have found no difference between the two groups.



Bruce Clark, RPT

Note: Current scientific knowledge strongly suggests that HLA-B27 probably accounts for about 40% of the overall risk, though there are other genes working in concert with B27 as a causative factor in the disease.

QUESTION

Are people with AS at greater risk for disc lesions?

ANSWER

There is no evidence to suggest that people with AS are at greater risk for disc lesions. In fact, the risk most likely is less in more advanced AS where there is fusing of the spine and the vertebrae have grown together following inflammation due to the AS. People with AS can have herniated discs. If they are not fused, then their chances of this are about the same as unaffected persons would be.

QUESTION

Can the newer biological treatments (TNF- α inhibitors) help those who have long-standing AS? Is there any chance to believe that they can reverse our advanced condition?

ANSWER

No, we are sorry to say that the newer treatments cannot reverse the damage of long-standing AS. Though, if a person with

long-standing AS is still in a lot of pain, the newer drugs potentially could help.

QUESTION

Can a person with undifferentiated spondyloarthritis potentially benefit from the biologics? And if so, can they be prescribed for this condition?

ANSWER

They are approved in Europe for undifferentiated spondyloarthritis, though not in the U.S. The undifferentiated form of spondyloarthritis is coming more and more to the forefront. Everyone starts out as undifferentiated before physiological changes take place, and since it is now recognized that these medicines can do so much good, it is becoming increasingly obvious that we need to use them much earlier on in the disease process in order to make a long-term positive impact.

QUESTION

During the past year or so, I have been working with a personal trainer who is also an RN. We meet for 2 hours per week and I train for 1 hour per day on my own. My range of motion, bone density and strength have all improved. The only trade-off is increased fatigue. I am not sure how to evaluate this problem and can't help but wonder whether it is going to better or worse if I continue to exercise. Also, my disease activity has also increased in recent times.

ANSWER

You are doing all of the right things with your exercise routine in that you are maintaining range of motion, muscle strength and your general fitness level. Since fatigue is a marker of inflammatory disease activity and you are seeing an increase in both, it would be important to obtain improved control of disease activity. It would be helpful for you to consult with your rheumatologist to find

out how you can achieve more control over disease activity with medication. If you can be successful in that regard, you would expect your fatigue level to diminish.

QUESTION

My 19-year-old daughter, who was diagnosed with AS when she was 17, is experiencing severe pain in her ribcage, which is interfering with her sleeping patterns and making it difficult to obtain adequate restorative sleep. Is there anything that can be done to help her?

ANSWER

Inflammation in the ribcage is a well-established symptom of active spondyloarthritis. Some non-steroidal anti-inflammatories can help, somewhat. If that does not provide adequate relief, I inject half a cc of cortisone and half a cc of Markain into the sore spots using an insulin syringe so that there is very limited pain, and the symptoms go away within 24 hours. There aren't any controlled studies of this treatment method, and many doctors don't know about it. It works very, very well.

The SAA acknowledges with great appreciation Dr John Reveille and Mr. Bruce Clark, RPT for volunteering their time to share their expertise at the SpA Educational Program in San Diego. The program was funded by a generous educational grant from Amgen and Wyeth Pharmaceuticals

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Top: Laura Diekman, MS of Houston, TX

Middle: Attendees of the seminar quietly listen.

Bottom: John D. Reveille, MD of Houston, TX

The Experts Answer Your Questions

The Spondylitis Association of America sponsors several Spondyloarthritis Educational Seminars annually. We are pleased to bring you this series of Questions and Answers from our most recent conferences which were held in Washington, D.C.

What is known about juvenile onset spondyloarthritis?

From recent studies, researchers have been able to determine that people with early onset spondyloarthritis have a two-fold risk of needing a total hip replacement later on.

Is there any new data on women and AS?

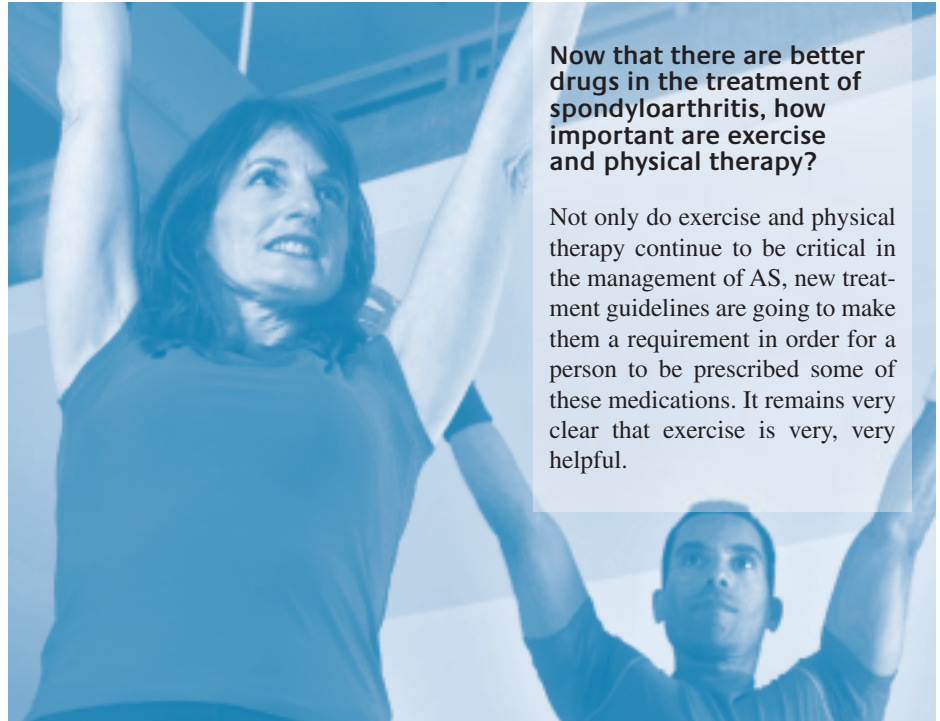
The researchers involved in the PSOAS study have been able to determine that women with AS have a different disease experience than men with AS, and that this possibly points to one of the reasons that doctors have greater difficulty in making a diagnosis in women. The study results showed that women get sacroiliac involvement, then the symptoms sometimes skip the spine, and then involve the neck and peripheral (small) joints much more significantly than in male disease, but can be equally functionally impaired as men with the disease.

Are there any blood markers in AS that can tell us anything about the disease in one person compared to another?

Yes, there are. Dr. Maksymowych from Alberta and his research team have identified a new blood marker called MMP3, which can be an independent predictor of damage progression in patients with AS. (Reported in the Spring issue of Spondylitis Plus, page 6) So, we now have another marker to help in examining AS patients.

Is there anything new that is known with regard to the prevalence of AS in other countries?

It has been recently recognized that the prevalence of spondyloarthritis in China is 1% as apposed to 0.2% in rheumatoid arthritis. So, in China, spondyloarthritis is a much bigger problem than previously thought.



Now that there are better drugs in the treatment of spondyloarthritis, how important are exercise and physical therapy?

Not only do exercise and physical therapy continue to be critical in the management of AS, new treatment guidelines are going to make them a requirement in order for a person to be prescribed some of these medications. It remains very clear that exercise is very, very helpful.

Is there any new information with regard to nonsteroidal anti-inflammatory drugs (NSAIDs) such as Naproxyn and Celebrex?

Yes, it is currently estimated that when taken at a full anti-inflammatory dosage, NSAIDs can provide adequate relief to about 50% of people with AS.

What can be done for a person who cannot take NSAIDs or TNF-blockers?

Sometimes Prednisone (cortisone) can provide some help to this group of people. In addition, even though there is no good data to support the use of sulphasalazine in spinal disease, it can be helpful in some people. Everyone is different, and hence, a very thorough workup by a rheumatologist would be strong advised.

Though most people with ankylosing spondylitis are HLA-B27 positive, what is known about people who have AS who are HLA-B27 negative?

Recent studies have shown that the majority of people with AS who are HLA-B27 negative often have other HLA-B genes that are associated with other types of spondyloarthritis. These include psoriasis. There seems to be about 5% of people with AS who have no HLA-B explanation for their disease whatsoever. Furthermore, this group goes on to develop just as severe spinal disease as the HLA-B positive group over time. The only difference seems to be that these people have less iritis (inflammation of the eye).

I have heard that sometimes the disease “burns itself out” over a period of years to where the symptoms go away.

Could you please explain that phenomena?

Quite often in older patients, once the bones are fused together, the disease activity can completely shut off. Though this phenomenon is not uncommon, it is not true for everyone. Even when this does happen, it is important for physicians to look for other potential complications. These complications can include cauda equina syndrome, where the bony overgrowths can start affecting the nerves in the spine.

What is known about chiropractic care in the AS patient?

It really depends upon the different chiropractic treatments. Though manipulation of a fused spine is contra-indicated, there are sometimes other gentle techniques that can be helpful. In this situation, it is important that the rheumatologist and the chiropractic communicate with each other with regard to the care of the individual with AS. A lot of chiropractors are focused on manipulation and so it is important to differentiate between that and other approaches.

What is known about the benefits of exercise in ankylosing spondylitis?

There are two different types of activity that one could think about. There is any type of exercise, just moving around and being physically active, whether that is sports, running, jogging, tennis or swimming. Then there are specific exercises such as back stretching and strengthening. There is evidence to show that both types of exercise are important in helping to maintain function or even improve function in spondyloarthritis.

Researchers found several years ago that when people were charted for five years to measure how much exercise they did on a regular basis and how that impacted the functioning over time, that those who reported doing back stretching and strengthening exercises at least five days a week had much better outcomes than people who engaged in that activity less often. It was also found that when people engaged in this type of activity for 200 minutes a week, over time, they were able to function much better. That may sound like a lot, but actually, it is only 30

minutes a day and the payoff can be tremendous.

What do you think would be one of the most important daily exercises?

One of the very best exercises is called a “chin tuck.” This can be helpful to just about anyone who sits a lot during the day. You can do this exercise while standing or sitting. What it requires is that you pull your head backwards while pulling your chin in—keeping the eyes as straight ahead as possible. This can be helpful because we all tend to lean forward and this exercise can help to counteract the negative aspects of that type of posture habit.

Another helpful and very simple exercise to do during the day is to raise the arms above the head because it stretches the upper and lower back. It can be helpful to do this exercise with the shoulders against the wall. Sometimes when a person has difficulty with this exercise, it can be helpful to use one hand to support the other arm.

What can I do to help stretch when my sacroiliac joints are fused?

Many people with AS have lower back stiffness even without fusing and hence, it is really important to exercise the pelvis. A “pelvic tilt” exercise can be important

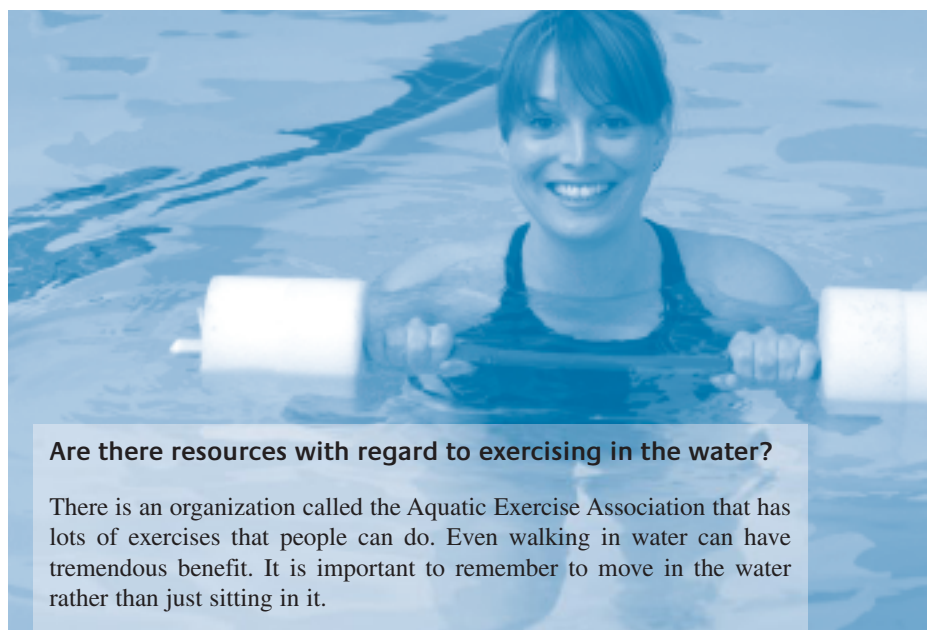
because once the lower back has lost motion; it becomes much more likely that the upper back will also lose motion since everything is connected.

With regard to stretching exercises, I have been told to hold a stretch for 20-30 seconds in order to gain the most benefit. What do you think about that?

It is advised in the sports literature to hold a stretch for that length of time, but for a person with AS, the most important thing is that the stretch is held without bouncing because bouncing stretches the little mechanisms in the muscle, which can cause them to tighten up even more. 20 seconds is a good recommendation, although most people do not hold that long.

Compared to the general population, what are the risks associated with spondyloarthritis with respect to becoming work disabled?

After 30 years of disease, research has shown that relative to the general population, a person with spondyloarthritis is likely to have a three fold risk of becoming work disabled. That said, most people with spondyloarthritis are still working 30 years after disease onset. More physically demanding jobs can cause a higher risk of



Are there resources with regard to exercising in the water?

There is an organization called the Aquatic Exercise Association that has lots of exercises that people can do. Even walking in water can have tremendous benefit. It is important to remember to move in the water rather than just sitting in it.



Doctor John Reveille and attendees of the D.C. seminar share a moment of fun during the break-out sessions.

Osteoporosis medication is commonly used in ankylosing spondylitis. There is no thought that they would promote abnormal bone growth and they certainly do a very good job in maintaining bone density.

becoming work disabled. Lower education seems to also impact work disability, as does arthritis in the hips.

One of my worst symptoms is fatigue. Doctors seem to have difficulty in understanding just how debilitating this can be.

Fatigue is a very important symptom in this group of diseases. When studies are done on

people with spondyloarthritis, fatigue is always brought up as one of the top four symptoms that affect daily living. Pain, stiffness, fatigue and poor sleep are dominant symptoms for most people.

What is known about spontaneous remissions that last for any amount of time from one day to several months? Are there recognized triggers that cause symptoms to be better or worse?

We have very, very poor understanding from a medical research perspective with regard to triggers and particularly what makes symptoms go away, apart from medication. It is really difficult to study these things, mostly because spondyloarthritis is a very individual disease. Sometimes it can be helpful for a person to keep an activity diary to find out if there are triggers that affect how poorly or how well you are doing.

Since it is well recognized that osteoporosis is a very big problem in

spondyloarthritis, are osteoporosis drugs contra-indicated in AS because of the extra bone growth tendencies?

Osteoporosis medication is commonly used in ankylosing spondylitis. There is no thought that they would promote abnormal bone growth and they certainly do a very good job in maintaining bone density. There are no reservations whatsoever in this regard. There are lots of patients using them.

Could you please comment on the use of TNF-blockers in ankylosing spondylitis? If a person takes them for a while, is there any possibility that a short course of these drugs can course the AS to go away permanently?

No. Research has shown that for 100% of patients who go off TNF-blockers, symptoms return. It might take a year, but our current thinking is that there is nothing permanently switched off with short-term use of these medications. What we don't know, is if you use them for 5 years or even 10 years, whether you can withdraw the medicine or not. That data is not yet available.

Are women less likely to fuse than men?

That is a difficult question. The spine involvement in women has historically been thought to be different than in men. The difference is that men tend to have a more uniform involvement in the spine, in general, than women. Women seem to have more of a patchy type of fusing with more neck involvement.

Editor's note: The SAA would like to acknowledge, with great gratitude, Dr. John D. Reveille, Dr. Michael Ward and Ms. Victoria Gall, PT for sharing their time and expertise during this program.

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Questions

Answers

QUESTION

Why is there still such a long delay between the onset of symptoms and the confirmed diagnosis of the disease?

ANSWER

There are many reasons for this. First, the diagnosis is not easy to make early on in the disease and consequently, is often misclassified. Second, the disease presents in many different forms. For instance, sometimes, a person will experience joint pain but no back pain. At other times, an individual may experience just neck pain at the beginning, or even iritis with no back pain. Then again, some people, in more rare situations, will have no pain at all, but rather x-ray evidence of sacroiliitis.

One study, in conjunction with the SAA, is seeking to develop a screening tool to help with earlier diagnosis.

QUESTION

What is the typical pattern of symptoms once the disease is established?

ANSWER

The disease is really very mixed. In the early stages there may be long periods of time



where it is quiet. Onset may take place in the twenties, but even during the teenage years, an individual may already have had something going on that just “didn’t feel right.” At the beginning you can’t see AS on normal x-rays, though researchers do not believe that a pre-spondylitic phase exists for many people.

QUESTION

What is the prevalence of AS and related diseases in the U.S.?

ANSWER

No one really knows. A study was done in 1998 to look at the numbers in the U.S., but the study was flawed since the number of cases that were accounted for was based on x-rays of sacroiliac joints. Since plain x-rays do not show inflammation, but rather take pictures of the bones, you have to have a certain amount of damage to the bone for it to show up. But you can have lots of damage in the joint prior to damage showing up on the plain x-ray. MRI is showing a potential in early diagnosis, but researchers are still trying to develop a validated scoring system that can be used for this purpose.

QUESTION

How much of the risk of getting AS is related to genetics?

ANSWER

Genetics play a very big part in disease susceptibility in AS. When compared to other genetic diseases, the concordance of AS in identical twins is 63% compared to 15% in rheumatoid arthritis and 25% in lupus. Hence, the importance of our conducting genetic research in AS.

QUESTION

Why do the different biologics (TNF-a blockers) work for some people for a period of time and then become less effective?

ANSWER

There is a great deal of variability with regard to how an individual responds to medication. This includes the newer biologics as well as the traditional anti-inflammatory drugs (NSAIDs). Sometimes, the mechanism of action of a given medication will be efficacious or not depending upon the stage of a person's disease. Sometimes it has to do with the individual's make-up. In the case of the biologics, each one has a different mechanism and therefore, one might work better than another at different stages of a person's disease. No one size fits all. The good news is that when one stops working or has a reduced efficacy, one of the others, when prescribed, may be an effective replacement.

QUESTION

What are the main side-effects associated with biologics in AS?

ANSWER

To date, most of the side-effects associated with the biologics have been observed in studies in rheumatoid arthritis (RA). Very few side-effects have been documented in AS. RA is a disease that already predisposes to certain risks such as getting more infections and being more susceptible to certain types of malignancies, like lymphomas. These are the concerns also associated with the biologics. What has been suggested is that if you already have a greater tendency toward a malignancy, then these drugs may tend to bring out the malignancy at a greater frequency. However, the data does not necessarily support this thesis. When we look at the data, with regard to this issue, they do not show an increased frequency of these malignancies in people who are receiving biological therapy.

The one known side-effect in AS patients is the risk that some of the biologics can unmask tuberculosis (TB) in a patient with latent TB. If your doctor discovers that you have latent TB, biologics can still be prescribed along with anti-TB medication. There are no drugs free of side effects. The issues must be weighed carefully.

QUESTION

I was treated for more than 29 years for back pain. After all of those years, it was a

diagnosis of iritis that clued the general practitioner (GP) that I might have AS. Family practitioners were not able to diagnose me. They thought that I had RA. Why can't we create a greater awareness of the disease among GPs?

ANSWER

The diagnosis of AS has always been a big problem, though patients are telling us that there have been improvements in recent years. In part, this is due to the work of SAA, the wide distribution of its educational brochures and the widespread accessibility of www.spondylitis.org. One reason we are developing the screening tool is so that patients can become their own advocates. With the screening tool, you can take the test and if you come up with a 30% likelihood of having the disease, you can go to the doctor and request a B27 test. It will work just like Direct-To-Consumer Advertising, which is very successful at educating the public with regard to drugs available to treat certain diseases.

QUESTION

What can you tell us with regard to prescribing the biologics to someone who suffers from chronic infections? Is it safe?

ANSWER

We are very cautious about prescribing biologics to patients with a history of chronic infections. However, infections can be treated. Hence, we must weigh the decision. The biggest concern here is associated with potentially triggering those infections and/or making them worse.

QUESTION

What about biologics in pregnancy?

ANSWER

They appear to be safe, but there is no data to support that theory. There does not seem to be a higher risk during pregnancy either to the baby or to the mother. Typically we recommend that pregnant women go off the drug and use either no medication at all or other, safer drugs during the nine-month period of gestation.

QUESTION

When should we have our children tested for the marker?

ANSWER

Unless it is for research purposes, doctors do not see any reason to test a child if there are no symptoms. That would potentially just create extra worry, concern and anxiety unnecessarily. If and when symptoms are present, that is when one should be concerned.

QUESTION

Can you tell us anything about the other common symptoms such as fatigue, weight loss and low-grade fever.

ANSWER

Some people with AS experience a systemic or whole body disease. These symptoms sometimes mask the disease in young people. Through our genetic studies, we are trying to identify which genes are associated with the more systemic disease which affects the whole body, and which genes are associated with the type of disease that affects only the peripheral joints and spine. That will be able to help us improve both diagnostically and therapeutically. We are at the forefront of being able to address these issues and thus anticipate better treatments in the future once those genes are identified.

QUESTION

Could disease be triggered by trauma?

ANSWER

We do not know whether trauma is a trigger, but we do know that trauma can be very important once a person has the disease. Proper studies have to be done in order to find out if trauma actually is a trigger.

WE ACKNOWLEDGE with great appreciation Drs. Weisman and Siddique and Professor D. Garnett for volunteering their time to share their expertise at the SAA Spondyloarthritis Educational Seminar in Los Angeles.

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Dear Readers, we welcome your questions with regard to AS or the Related Diseases for inclusion in this section of Spondylitis Plus. We do ask that questions be of potential universal interest to others. Responses by the experts to selected questions will be published in this journal and on our Web site, www.spondylitis.org. We look forward to hearing from you.

Email questions to: Laurie.savage@spondylitis.org

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