Sex Differences In Ankylosing Spondylitis

Clarifying The Social Security Disability Program

Your Stories: Escaping The Opioid Jungle

Spondylitis Association of America™
Dear Readers,

As we come to the end of 2016, we count our blessings here at SAA. First of all, we thank you for your amazing support of our efforts, for your kindness and courage, and for keeping us informed of how we can best serve you. And, rest assured, we do listen.

The very good news coming out of recent scientific meetings informs us that progress is being made on your behalf and that our knowledge base is expanding due to work here in the U.S. and Worldwide. As you most likely are aware, medical science and research advance slowly due to the complexities, diversity of populations, and lack of adequate funding, but still we believe that we can continue to make huge progress with your continued support.

We will have lots to share with you in the upcoming year. We are preparing to launch an exciting awareness campaigns, to unveil additional features on our newly redesigned, interactive, community based website, and are of course sponsoring and hosting the third International Unmet Needs Conference in SpA—informing research for the next decade. This conference will be a two day symposium located on the NIAMS/NIH campus in Bethesda, MD. One of the critical highlights of the meeting is to invite visionaries to present, some of whom are outside of our immediate field. Our goal is to explore intermingling of novel concepts in different specialties not currently immediately connected to our field but that already are supported by bodies of work—and we believe, concepts that potentially could be introduced into AxSpA research that would have a profound effect on our knowledge base and thus advance and improve patient care.

So, here we are, starting a new year with immense hope and excitement for the work that lies ahead.

We do hope to count on your continued support in all ways. Thank you.

Sincerely,

Laurie M. Savage, MS, FLE
Executive Director / CEO
“The article “The Price of Pain Relief” in your most recent issue of Spondylitis Plus resonated with me.

I join the ranks of so many of my fellow spondylitis sufferers in that our days are spent delicately managing just how much pain we can bear and still function, and how many pills from our dwindling supply we absolutely have to take.

In my case, as a geologist, I find when I start making excuses not to bend over to pick up a rock, then I had better take some more temporary relief in pill form.

Thank you.”

~ A.G.

“The article “The Price of Pain Relief” was like reading about my own life. It nearly brought tears to my eyes as I read that someone else has faced the same struggles. Thank you for sharing, for bringing our story to the forefront. Bless you!”

~ Kitty Jones

“Like the entire SAA family, I miss Chris Miller. I know that Chris is resting comfortably knowing that his visions will be continued in how SAA serves people who are suffering.

I remember when Jane and her friends had a vision, and now Laurie, her staff and contributors are growing that vision. Everything that SAA has accomplished these past thirty+ years without advertisers deserves all the praise and rewards you have earned.

I believe your balance of print and electronic information is good, and I also understand the challenge of the cost effectiveness of each. We are comfortable with one foot in print, and one foot in digital, and both feet in this world we call home.

One suggestion: A direct link on the homepage to an archive of all past and present featured articles with an index that would lead new readers to answers to their questions. Grading (Five Star) by readers of featured articles might be helpful to you in planning, and to people who are new to SAA.

Know that the service SAA provides is appreciated by many grateful people.”

~ Russ McDonald

Editor’s Note: Thank you for your kind words and thoughts, Russ! We frequently speak about Chris – whether it’s a story, or a practical joke, or something important he had done. He very much remains a presence here.

And great suggestion on adding a grading feature to our Featured Articles. We will look into the technical aspects of making this work. On this new, redesigned website, you will find a link on the homepage going to our Featured Articles archive. We have not brought over all of the Featured Articles yet as of this writing, but fully intend to do so. You’ll also be happy to find an index to help readers locate articles by content / keyword.

Thank you again!

LETTERS TO THE EDITOR
We want to hear from you! Send your thoughts, questions, opinions, and rebuttals.

Please send letters to:
Elin@spondylitis.org
Letters to the Editor/SAA
P.O. Box 5872, Sherman Oaks, CA 91413

Please note that we reserve the right to edit for space and clarity.
As reported in the On Point column in the last issue of *Spondylitis Plus*, I had the opportunity to travel to Ghent, Belgium to attend the International Congress in Spondyloarthritis. The meeting was very much worth travelling the distance from Los Angeles to Europe for many reasons. First off, it was critical from my perspective to be able to experience, at close quarters, the enthusiasm generated by the advances currently being made in these disease states, which I believe should lead to improved patient care and outcomes over time.

It has been said over the years that the Ghent Spondyloarthritis Congress has become the most important international research meeting focused on all aspects of SpA.

There are only a “handful” of leaders in our field—exceptional individuals who are making a difference, but we need to expand these numbers. That is why SAA has made it part of its mission to further this goal through various means. This includes our annual presentation of the Early Investigator Award in the amount of $20,000 to those who have already demonstrated a body of work in this field. At the meeting it was assuring to learn from various younger colleagues that even a small award had made a difference in encouraging their work. There is a lot more to accomplish, but your SAA is definitely leading the field in this regard.

It has been said over the years that the Ghent Spondyloarthritis Congress has become the most important international research meeting focused on all aspects of SpA. The 2016 meeting, this year in September, was no exception in upholding an already robust tradition. Researchers met with colleagues to discuss and to explore clinical topics including imaging, treatment and outcomes, as well as basic and translational research (taking basic science into the treatment area.) The studies presented explored molecular biology, cellular immunology, and genetics, amongst a broad range of others, equally critical to furthering the knowledge base in SpA. These included but were not limited to epidemiological research, immunology, bone biology, and inflammation in the gut, skin and eyes as well as in the bone and joints.

This year, a new tradition was started which presented a controversial topic in SpA in debate format. Two research colleagues were pitted against one another—in a friendly manner—to argue the fine or not so fine points regarding the potential benefit of genetics using personalized medicine in accelerated diagnosis in axial spondyloarthritis vs. the more traditional approach of personal and family medical history, clinical presentation, as well as X-ray and MRI. The debate is still open for discussion.

Various studies presented reported on the slowing of radiographic progression with IL-17 inhibitors, the effectiveness of IL-17 inhibitors in blocking inflammation, and the new bone formation in HLA-B27 rats. In addition, a well-attended session focused on new insights into the IL-17 / IL-23 pathway.

Further topics in genetics in spondyloarthritis were discussed with a session devoted to better understanding the functional role of HLA-B27, which is considered to be the most important genetic risk factor and is present in the vast majority of Caucasians with ankylosing spondylitis. In addition, results presented from a family-based genome-wide association study of spondyloarthritis will explore whether there is an association between the condition and a polymorphism (genetic variations within a population) in a specific protein encoding a gene called MAPK14.

The latest developments in inflammatory diseases associated with spondyloarthritis, such as inflammatory bowel disease, were also addressed within a presentation on the assessment of disease activity and subsequent challenges in patient-reported outcomes.

In all, more than 200 scientific abstracts were presented during three poster sessions, reporting on the research findings of multidisciplinary teams from around the world.

The highlighted oral abstracts covered a variety of hot topics,
Lack of Information for Patients at Risk for Spondyloarthritis: The APPSPA Study
Karreman MC et al.

Study Aim: The researchers sought to assess whether individuals with Psoriasis (PSO) or Inflammatory Bowel Disease (IBD) are aware of their risk of developing Spondyloarthritis (SpA) and if so, how they became aware.

Method: A cross sectional study included patients with PSO and IBD between 18 and 55 years of age. Individuals were asked to complete a set of questionnaires regarding their disease, the level of awareness about the disease, and the potential presence of musculoskeletal symptoms.

Results: 552 patients completed the questionnaires, of which 43.1% reported to be aware of the possibility of developing a rheumatic condition. Out of this group, 238 or 34% of the patients indicated that they had gained this information through self awareness; 13.5% were informed by a general practitioner, and 24.4% by a specialty physician.

Conclusions: Less than half of the patients with PSO or IBD were aware of the possibility of developing a rheumatic condition associated with their primary presenting condition. Of note, more than 60% of the combined group was not informed by their attending medical professional of the increased risk of developing a rheumatic condition when presenting with either PSO or IBD.

The Prevalence of Axial Spondyloarthritis (AxSpA) with MRI Validation in Patients Presenting with Acute Anterior Uveitis
Sykes M et al.

Study Aim: To examine the estimated prevalence of axial spondyloarthritis (AxSpA) in patients with diagnosed acute anterior uveitis (AAU).

Method: A cohort of 366 patients with AAU were located; 57 of which already had a confirmed diagnosis of AxSpA; 76 others fulfilled the study inclusion criteria, but did not have a previous diagnosis of AxSpA.

Results: Of the 76 previously undiagnosed patients enrolled in the study 22% of these were diagnosed with AxSpA by the end of the study using the ASAS criteria including MRI validation. The median duration of back pain in this newly diagnosed group was 20.5 years with a median of three episodes of AAU per individual.

Conclusion: This study was the first to employ MRI to classify patients with AAU and chronic back pain. The conclusion of the researchers based on this study is that at least one fifth of patients presenting to follow up care with AAU have an underlying diagnosis of AxSpA.

Prevalence of Osteoporosis in an Ankylosing Spondylitis Cohort
Fitzgerald G et al.

Study Aim: It has been recognized and established over time that the prevalence of osteoporosis is higher in individuals affected by AS compared to the general population. This study sought to evaluate the prevalence of low bone mineral density (BMD) — which is an indicator of osteoporosis or osteopenia— in an Irish patient cohort of AS patients.

Method: 416 patients were enrolled in the original cohort of which 103 were involved in the osteoporosis and prevalence of low BMD examination; 78.1% were male with a mean age of 47.95 years, a mean disease duration of 20.9 years, with an average delay in diagnosis of 8.8 years.

Results: The study reported that of the individuals examined for low BMD by a DEXA scan, 39.8% (n=41) had osteopenia and that 10.7% (n=11) showed osteoporosis. Low BMD significantly correlated with men and advancing age, with no evidence of association with disease activity.

Conclusion: Half of the cohort demonstrated low BMD with no association with disease severity. The researchers reported that the majority of affected patients were unaware of their condition.

Lack of Information for Patients at Risk for Spondyloarthritis: The APPSPA Study
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www.stopas.org
Social Security disability benefits are often the final safety net for individuals suffering from medical impairments, such as ankylosing spondylitis, that make it impossible for them to work. For most, struggling through the Social Security Administration’s (SSA) bureaucracy is frustrating, confusing and slow. This article will explain and simplify the Social Security disability program and how it generally applies to claims related to spondyloarthritis (referred to as spondyloarthropathy by the U.S. Social Security Administration).

Q What are Social Security Disability Benefits?

A Social Security Disability Insurance Benefits and Supplemental Security Income disability benefits are the two disability benefit programs administered by the U.S. Social Security Administration. These benefit programs provide monthly benefits and health insurance to those who qualify. There are both medical and non-medical requirements of these programs.

Q How does a claimant prove they are disabled?

A The Social Security Act defines disability as the inability to engage in any substantial gainful activity (SGA) by reason of any medically determinable physical or mental impairment(s) which has lasted or can be expected to last for a continuous period of not less than 12 months, or can be expected to result in death.

Q What is SSA's five-step evaluation process for determining disability?

A Social Security first asks whether a claimant is engaging in SGA, that is working at a substantial level. If work earnings are more than $1,130 per month in 2016, or $1,170 per month in 2017, Social Security can consider those amounts to be substantial and the application for benefits can be denied. There are additional rules for self-employed individuals.
If a claimant is not engaging in SGA (Step 1), then Social Security determines if there is a medically determinable impairment that significantly limits the individual’s physical or mental abilities to do basic work activities (Step 2). If a claimant has at least one severe impairment, then Social Security considers whether the criteria of any of its listed impairments have been satisfied. If so, the claimant can be found disabled (Step 3). If not, then Social Security must establish the claimant’s “residual functional capacity (RFC).” Once that is done, Social Security takes into account the RFC in finding whether the claimant can perform his or her “past relevant work” (Step 4) or any other work (Step 5). At Step 5 SSA considers the claimant’s age, education and transferable skills in ascertaining whether or not the claimant is disabled under the law.

Q What are the Listings of Impairments (Step 3 of the process)?

A The Listing of Impairments describes, for each major body system, impairments considered severe enough to prevent an individual from doing any gainful activity. They do not encompass all possible impairments. Listing 14.00 is titled, “Immune System Disorders – Adult.” It contains a number of illnesses within it, each separately enumerated.

The introductory comments in Listing 14.00 state, “The spectrum of inflammatory arthritis includes a vast array of disorders that differ in cause, course, and outcome. Clinically, inflammation of major peripheral joints may be the dominant manifestation causing difficulties with ambulation (walking) or fine and gross movements; there may be joint pain, swelling, and tenderness. The arthritis may affect other joints, or cause less limitation in ambulation or the performance of fine and gross movements. However, in combination with extra-articular features, including constitutional symptoms or signs (severe fatigue, fever, malaise, involuntary weight loss), inflammatory arthritis may result in an extreme limitation…

Inflammatory arthritis involving the axial spine (spondyloarthropathy) may be associated with disorders such as: (i) Reiter’s syndrome; (ii) ankylosing spondylitis; (iii) psoriatic arthritis; (iv) Whipple’s disease; (v) Behçet’s disease; and (vi) Inflammatory bowel disease. Inflammatory arthritis involving peripheral joints may be associated with disorders such as: (i) rheumatoid arthritis; (ii) Sjögren’s syndrome; (iii) psoriatic arthritis; (iv) crystal deposition disorders (gout and pseudogout); (v) Lyme disease; and (vi) inflammatory bowel disease.”

Listing 14.00 further states that: “Extra-articular features of inflammatory arthritis may involve any body system; for example: Musculoskeletal (heel enthesopathy), ophthalmologic (iritocyclitis, keratoconjunctivitis sicca, uveitis), pulmonary (pleuritis, pulmonary fibrosis or nodules, restrictive lung disease), cardiovascular (aortic valve insufficiency, arrhythmias, coronary arteritis, myocarditis, pericarditis, Raynaud’s phenomenon, systemic vasculitis), renal (amyloidosis of the kidney), hematologic (chronic anemia, thrombocytopenia), neurologic (peripheral neuropathy, radiculopathy, spinal cord or cauda equina compression with sensory and motor loss), mental (cognitive dysfunction, poor memory), and immune system (Felty’s syndrome (hypersplenism with compromised immune competence).”

Within Listing 14.00 is Listing 14.09 - Inflammatory arthritis. There are four sections contained in this Listing:

- Persistent inflammation or persistent deformity of: 1. One or more major peripheral weight-bearing joints resulting in the inability to ambulate effectively…or 2. One or more major peripheral joints in each upper extremity resulting in the inability to perform fine and gross movements effectively.

- Inflammation or deformity in one or more major peripheral joints with: 1. Involvement of two or more organs/body systems with one of the organs/body systems involved to at least a moderate level of severity; and 2. At least two of the constitutional symptoms or signs (severe fatigue, fever, malaise, or involuntary weight loss.)

- Ankylosing spondylitis or other spondyloarthropathies, with: 1. Ankylosis (fixation) of the dorsolumbar or cervical spine as shown by appropriate medically acceptable imaging and measured on physical examination at 45° or more of flexion from the vertical position (zero degrees); or 2. Ankylosis (fixation) of the dorsolumbar or cervical spine as shown by appropriate medically acceptable imaging and measured on physical examination at 30° or more of flexion (but less than 45°) measured from the vertical position (zero degrees), and involvement of two or more organs/body systems with one of the organs/body systems involved to at least a moderate level of severity.

- Repeated manifestations of inflammatory arthritis, with at least two of the constitutional symptoms or signs (severe fatigue, fever, malaise, or involuntary weight loss) and one of the following at the marked level: 1. Limitation of activities of daily living, 2. Limitation in maintaining social functioning, 3. Limitation in completing tasks in a timely manner due to deficiencies in concentration, persistence, or pace.

As used in the above listing, the inability to ambulate effectively means “…an extreme limitation of the ability to walk; i.e., an impairment that interferes very seriously with the individual’s ability to independently initiate, sustain, or complete activities. Ineffective ambulation is defined generally as having insufficient
lower extremity functioning (see 1.00J) to permit independent ambulation without the use of a hand-held assistive device(s) that limits the functioning of both upper extremities. To ambulate effectively, individuals must be capable of sustaining a reasonable walking pace over a sufficient distance to be able to carry out activities of daily living. They must have the ability to travel without companion assistance to and from a place of employment or school. Therefore, examples of ineffective ambulation include, but are not limited to, the inability to walk without the use of a walker, two crutches or two canes, the inability to walk a block at a reasonable pace on rough or uneven surfaces, the inability to use standard public transportation, the inability to carry out routine ambulatory activities, such as shopping and banking, and the inability to climb a few steps at a reasonable pace with the use of a single hand rail. The ability to walk independently about one’s home without the use of assistive devices does not, in and of itself, constitute effective ambulation.

This listing also considers functional impairments in the arms, hands, and fingers. SSA’s regulations state that, “inability to perform fine and gross movements effectively means an extreme loss of function of both upper extremities; i.e., an impairment that interferes very seriously with the individual’s ability to independently initiate, sustain, or complete activities. To use their upper extremities effectively individuals must be capable of sustaining such functions as reaching, pushing, pulling, grasping, and fingering to be able to carry out activities of daily living. Therefore, examples of inability to perform fine and gross movements effectively include, but are not limited to, the inability to prepare a simple meal and feed oneself, the inability to take care of personal hygiene, the inability to sort and handle papers or files, and the inability to place files in a file cabinet at or above waist level.”

“...The focus in all disability claims is upon the medical evidence - that is the physician's clinical findings, office notes, reports, and medical test results. That evidence is primary and is often more important than what the claimant says on SSA forms or in testimony at a hearing.”

Q What if a claimant has a form of spondyloarthritis, but it is not as severe as the listing?

A A claimant can still be found disabled even if the condition does not qualify under the Listings of Impairments (Step 3). As part of Step 4 of their analysis SSA evaluates a claimant’s Residual Functional Capacity (RFC) - what a claimant can still do despite the limitations caused by their impairments. If the claimant’s RFC does not prevent them from performing the duties of their past relevant work, then Social Security will deny the claim. However if a claimant’s RFC prevents the ability to perform their past relevant work, then Social Security will move on to Step 5 and determine whether or not the claimant can perform any other work.

Q What does SSA consider in determining whether a claimant can perform past relevant work?

A As mentioned above, at Step 4 of the 5 step sequential evaluation process, the claimant must prove that he or she cannot perform his or her past relevant work. Generally, past relevant work is work that the claimant has performed in the past 15 years at the SGA (substantial gainful activity) level for a sufficient amount of time for the claimant to have learned the techniques, acquired information, and developed the facility needed for average performance in the job situation. SSA considers the claimant’s RFC (residual functional capacity) and compares it to the physical and mental demands of this work.
past relevant work. If the claimant’s RFC prevents him or her from performing the physical and mental demands of this past work, the SSA should find that the claimant cannot perform his or her past relevant work and the inquiry moves to Step 5: whether the claimant can perform any other work in the regional or national economy. If the claimant cannot perform other work available in significant numbers in the regional and national economy, the claim will be approved. If the claimant can perform other work, the claim will be denied.

Q How important is objective proof of medical symptoms?

A SSA’s regulations require that any impairment must result from anatomical, physiological, or psychological abnormalities which can be shown by medically acceptable clinical and laboratory diagnostic findings. While a claimant’s description of symptoms to the claimant’s doctor and the explanation of a condition’s impact on daily activities must be considered by the SSA, a physical or mental impairment must be established by medical evidence consisting of signs, symptoms, and laboratory findings.

Q How important is it that a claimant obtains medical treatment for the conditions?

A Given the above, this is critical. The focus in all disability claims is upon the medical evidence - that is the physician’s clinical findings, office notes, reports, and medical test results. That evidence is primary and is often more important than what the claimant says on SSA forms or in testimony at a hearing. While a claimant’s description of a condition’s impact on their day-to-day activities is important and must be considered by the SSA, the content of the medical documentation is the primary source of evidence in deciding the claim. SSA generally gives more weight to the findings and opinions of treating specialists, such as orthopedic doctors, rheumatologists, neurologists, and pain specialists, than to family practitioners.

Q What can a claimant expect throughout the application process?

A Unfortunately claims are taking longer to be decided, in large part because fewer claims are being approved prior to a hearing with an Administrative Law Judge. Also, fewer claims are being approved therefore more appeals may be necessary, sometimes to federal court.

Richard I. Feingold is an attorney in the Chicago area who has been practicing in this area of law since 1986. He represents claimants nationwide and is a sustaining member of the National Organization of Social Security Claimants’ Representatives (NOSSCR), as well as a member of the Chicago Bar Association’s Social Security Law Committee. You can find him on Twitter @RichFeingold.

We thank Mr. Feingold for so generously lending his expertise and his time to our readers.
Sex Differences In Ankylosing Spondylitis

“It is evident that sex plays a very important role in AS. The symptomatic burden of AS tends to be higher in females than in males. Progression of spinal changes by X-ray, on the other hand, are more accelerated in males than females. Some inflammatory markers in the blood tend to be higher in males than females with AS. Although there is a male predominance of AS, in that subset of patients without X-ray damage in the sacroiliac joints (“non-radiographic axial spondyloarthritis”) there is a higher representation of females. Finally, in some studies there have been male/female differences in the response to biologic treatments.

To better understand the biologic basis of these sex differences in AS, our research team has just published a study examining the immune profiles in male AS patients vs female AS patients.”

Robert D. Inman MD, FRCPC, FACP, FRCP Edin
Senior study author

The following article is reprinted from The Rheumatologist with permission from The American College of Rheumatology and Wiley.

Sexual Dimorphism In AS: Immunological Sex Differences Identified In Ankylosing Spondylitis
By Kathy L. Holliman, MEd

A study that found distinct *sexual dimorphism in the immunologic profiles of patients with ankylosing spondylitis (AS) suggests that sex is an important variable to address in future research and may eventually lead to more effective sex-specific therapy for patients with the disease.

“AS has long been considered a male-dominated disease, and this assumption often delays the diagnosis in women who may manifest the disease very differently than their male counterparts.”

*Note: Sexual dimorphism relates to the distinct physical differences (beyond sexual organs) between males and females of the same species.

The research, published in the March 2016 issue of Arthritis & Rheumatology, demonstrated that men with AS have elevations of IL-17A and Th17 cells, which are key factors in the inflammatory Th17 axis. These elevations were not found in women with the disease. Men and women with AS had a number of shared gene expression patterns, but the male patients had additional alterations in gene expression that were not seen in the female patients. The sex-related immune profiles were independent of HLA-B27 status, clinical disease activity or treatment.

Robert Inman, MD, senior author of the study and Professor of Medicine and Immunology at the University of Toronto, says there are several clinical indications that a patient’s sex impacts the expression of AS. AS has long been considered a male-dominated disease, and this assumption often delays the diagnosis in women who may manifest the disease very differently than their male counterparts.
Once the disease declares itself, clinical disease expression severity varies depending on whether the patient is male or female. X-rays of the spine and pelvis identify greater radiographic changes in men with the disease than women, specifically erosive damage, and joint fusion is more advanced in men. Women tend to record higher pain symptoms on self-administered questionnaires, “suggesting there are important differences in perception and processing of pain,” Dr. Inman says.

Whereas AS, which involves diagnostic radiographic sacroiliitis, is male dominant, nonradiographic axial spondyloarthritis shows a female predominance.

This dichotomy has given rise to the concept of clinical subsets in the diagnostic classification of axial spondyloarthritis, he explains. “Whereas AS, which involves diagnostic radiographic sacroiliitis, is male dominant, nonradiographic axial spondyloarthritis shows a female predominance in most series,” he explains.

“Fundamentally, it is probably all part of the same spectrum, and the classification differences really hang on radiographic severity. The implication is that erosive radiographic sacroiliitis is more likely to occur earlier and more frequently in males than in females. And then once the disease is established, it looks like the course of radiographic severity and the trajectory of the changes are more accelerated in males than in females,” he says.

Acute phase reactants, such as CRP and ESR, are typically higher in males than in females with the disease, Dr. Inman says. “There is a biological basis for all these differences, including neurobiological differences in processing pain. Large genetic studies have demonstrated that AS is driven by immune-related genes, especially those of the Th17 axis. The question therefore arises if immune profiles, in particular those of the Th17 axis, correlate with sex-related clinical differences in AS patients.”

Inflammatory Signature Differences

Dr. Inman and his colleagues’ research, the first to systematically address the issue of sex differences at the immunologic level in patients with AS, has now demonstrated that there are differences in the inflammatory signature between males and females diagnosed with the disease.

Fifty-three male and 41 female patients with diagnosed AS were included in the study, matched for age and sex with 70 healthy controls. Subsets of the cohort were selected for serum analysis, flow cytometric analysis and gene expression analysis.

Analysis of peripheral blood revealed that the male patients with AS had significantly higher levels of IL-17A and TNF than female patients, whereas men and women had comparable serum levels of IFNγ. The male patients had significantly higher levels of Th17 cells compared with the female patients. The investigators say the Th17 axis is unlikely to be the primary inducer of AS, but that it is possible that “a distinct immunologic event, perhaps one that is mediated by CD8+ T cells and orchestrated by class I MHC, such as HLAB27, precipitates the inflammatory cascade leading to AS, while alterations in the Th17 axis modify disease expression and severity.”

In an effort to define a mechanistic basis for the male sex bias in the Th17 axis, the investigators examined the influence of sex hormones and found that levels of estrogen or testosterone were not significantly different between AS patients and those in the control group.

Study investigator Eric Gracey, BSc, a PhD graduate student in Dr. Inman’s lab at the University of Toronto, says the pathogenic role of IL-17 producing cells in patients with the disease remains unclear. “There is a lot of evidence from in
vitro studies and from animal studies that IL-17 itself, as well as being an inflammatory molecule, actually promotes arthritic changes by promoting osteoclast and osteoblast function. IL-17 producing cells can be found at the sites of inflammation in spondyloarthritis, mainly where the tendons and ligaments insert into the bone.”

“The study looking at gene expression profiles of patients begins to usher in a new era of targeted personalized therapeutics that are based directly on the patient’s own immune profile.”

Cells of the Th17 axis, including TH17 cells, also play important protective roles. They promote healthy gut function and help combat fungal and bacterial infections. “They are a double-edged sword, in that they are absolutely necessary but too much can be a bad thing,” Mr. Gracey says.

Gene expression studies that he and his colleagues have conducted with AS patients indicate the sex bias may exceed the Th17 axis. “In future studies we are going to explore the function of genes differentially expressed in male and female patients and how they may impact on the immune response in male patients,” he says.

Sex is an incredibly important variable in research, he adds. “Often, with sex-dominated diseases, it is hard to balance the sexes in your studies, making it difficult to statistically compare the groups. With RA, for example, most of the studies are centered on female patients, but there may be important differences [when compared with male patients] that researchers are missing. Lessons learned from these studies cannot always be applied to both males and females.”

**Therapeutic Implications**

One aspect of this current study points toward a future that will offer more personalized approaches to therapeutics. “The study looking at gene expression profiles of patients begins to usher in a new era of targeted personalized therapeutics that are based directly on the patient’s own immune profile,” Dr. Inman says.

The research, he explains, has several implications for future research related to therapy. “We are not really thinking of AS as a monolithic single entity anymore. If you factor in genetic diversity, clinical stratifications, and the immune signature of a particular patient, we will more effectively and intelligently be able to develop therapeutic plans that match particular patients. We need to be able to identify the biologic basis of clinical heterogeneity so that we can target that more specifically.”

TNF blockers, he says, have been found to work broadly across a wide range of rheumatologic diseases, including RA, Crohn’s disease and AS. The new generation of biologics includes the IL-17 blockers, such as secukinumab, that are also demonstrating efficacy in patients with AS, Dr. Inman says. “IL-17 seems to be not only a very attractive target in AS but is also a target that differentiates chronic inflammation in AS from RA and inflammatory bowel disease,” he says.

According to Mr. Gracey, the study “suggests that males may respond better to IL-17 blocking than females in light of the sex difference in the Th17–IL-17 pathway.”

There may be some attractive therapeutic targets that arise not only in the microarray profiles that this research group has completed but also in combination with the genome-wide association study, Dr. Inman says. “We may find some candidate genes that pop up in both those screens and some that may seem to fit biologically with what we know about the process—that it is a chronic inflammatory disease associated with new bone growth formation at the site of inflammation. For example, there may be some potential candidates that affect osteoblast function or osteoproliferation.”

Additional research is needed into which differentially regulated genes may serve to identify biomarkers in AS. This research has examined functional gene networks rather than the expression of single genes, a method that has shown shifts in basic metabolic processes such as mitochondrial function and protein translation. “The alteration of genes related to basic cell functions in AS patients likely reflects an altered state of these cells under a state of chronic inflammation,” the researchers say.

Further studies “are required to determine whether these changes represent changes in cell activation, differentiation or proliferation,” they add. “The gene expression pathways shared between male and female patients with AS may represent a base disease profile, with additional gene pathways altered in male patients acting as disease modifiers.”

**Resources**

Two important textbooks have recently been published on axial spondyloarthritis. The first, co-edited by the distinguished Dr. Robert D. Inman, a member of SAA’s Medical and Scientific Advisory Board, includes contributions by over 60 prominent researchers, rheumatologists, and other medical professionals, and features a chapter co-written by our own Laurie Savage, dedicated to patient support and advocacy. The second is authored by Dr. Muhammad Asim Khan, noted rheumatologist, member of SAA’s Medical and Scientific Advisory Board, and AS patient himself.

**Oxford Textbook of Axial Spondyloarthritis**  
Edited by  
Robert D. Inman MD, FRCP, FACP, FRCP Edin  
Joachim Sieper, MD  

“Early in 2014, Oxford University Press (OUP) approached me and Dr. Joachim Sieper, from the Charite Hospital in Berlin, to develop an outline as a possible first step towards a new textbook on ankylosing spondylitis. We responded that this was an important initiative for two reasons:  

- Ankylosing spondylitis is the commonest form of inflammatory arthritis affecting the spine.  
- There are significant advances in the genetics, classification, outcome measures and treatment of this disabling disease which makes this text a timely addition to the medical literature.

OUP then asked us to draft an outline of possible chapter topics with proposed authors. The fact that we had nearly universal agreement from the 55 international authors we approached vindicated our belief in the importance of this textbook. It is interesting to note that in the three years since the project began there have been developments in classification and terminology, such that the final title of the textbook was Axial Spondyloarthritis.

We were particularly pleased to include a chapter devoted to the Spondylitis Association of America (authoring by Laurie Savage) and to the AS International Federation (authored by Seoirse Smith). This is an extremely important section of the textbook, since we were striving to keep individuals with AS the central focus of the project, a goal shared with SAA and ASIF.”

Robert D. Inman MD, FRCP, FACP, FRCP Edin  
Professor of Medicine and Immunology  
University of Toronto  
Director Spondylitis Program  
Toronto Western Hospital

**Ankylosing Spondylitis - Axial Spondyloarthritis**  
By Muhammad Asim Khan, MD, FRCP, MACP  
Professor Emeritus of Medicine  
Case Western Reserve University, Cleveland, OH

“This book provides evidence based, practical information on all aspects of AS-Axial SpA, with emphasis on clinical features, pointers for early diagnosis, and comprehensive coverage of current treatment options, including the latest biologic therapies.”

Dr. Khan’s research interests focus on clinical, genetic, and therapeutic aspects of rheumatic diseases, primarily AS/SpA. He has authored three books on AS, and also authored or co-authored 233 scientific articles and 46 book chapters (including a chapter in the above mentioned Oxford Textbook of Axial Spondyloarthritis.)
The Oxford English Dictionary defines “community” as “a feeling of fellowship with others, as a result of sharing common attitudes, interests and goals.”

When I began working at SAA 12 years ago, we didn’t use the word “community” to refer to the group of people whose interests we serve. For me, the word came into use around 2007, when the organization was transitioning between Co-Founder Jane Bruckel’s leadership and that of our current helmsperson, Laurie Savage.

Our interim Executive Director at the time was a big proponent of the term, and I confess, I didn’t love it. To me, it felt forced, almost kitschy, and I found myself avoiding it wherever possible.

Being new, I didn’t really see a community yet; I saw a patient advocacy organization connecting, one-on-one, with people living with spondylitis and doing what we could to make their lives better by offering information and support, spreading awareness of the disease, and advancing medical research initiatives.

In short, in my view, SAA had a relationship with each of our members and friends, and each of our members and friends had a relationship with us. This made for thousands of relationships, all existing on a two-dimensional plane. I assumed that was how it was supposed to be.

But at the same time, SAA’s program staff was introducing and expanding more and more initiatives designed to connect those people to each other. (And they were getting together on their own on other platforms like Facebook, Twitter, Pinterest, Instagram, etc.)

Some didn’t really take off, while others, such as the Connections Program, which includes SAA Sponsored Educational Support Groups, seminars and webinars featuring leading experts in the field, SAA’s still-growing social media presence, Your Stories, and our popular message boards, were huge successes.

More and more, I began to embrace the word “community” because I could clearly see one where I hadn’t before. And not just a community created by SAA, but an organic one nurtured and furthered by the efforts of its individual members.

Today’s community organizers are numerous and include Health Advocates like Cookie Hopper, who produces Faces of AS; Jenna Visscher, who created An Apple a Day for Spondylitis and now has her own 501c3, “Walk AS One”; Charis Hill, who blogs beautifully about her daily struggles with the disease and Larry Seltzer, who each year puts on a series of concerts in honor of his wife Naomi to support SAA.

And we can go back even further: Michael Smith (Spencer23) who created Spondyville and started the first U.S. online support group with Tom Contrino in 1995; and Rich Feingold, Esq., who has written many articles for Spondylitis Plus (including one in this issue!) to help people navigate the process of applying for, and fighting for, SSDI benefits. These people, and many, many others, are community leaders in the truest sense of the term.

For me, what was once a two-dimensional model is now playing out in an eye-popping, 3-D, surround sound, IMAX, virtual reality experience. I see people from all walks of life, from every continent, young and old, newly diagnosed and seasoned veterans, athletic and disabled, and with a hundred other distinctions, coming together to support each other and learn from each other.

I follow the Facebook posts of people who embrace traditional medicines and the ones who lean toward holistic and complementary remedies; I read the threads where proponents of dietary solutions share their results with others who haven’t yet tried that approach; I watch as people who struggle are propped up by folks they may have never met in person, but who share a common bond and take the time to share a kind word and encouragement.

All of a sudden, those thousands of relationships blossomed into tens, even hundreds, of thousands.
If I ever doubted there was a Spondylitis Community, I no longer do.

In keeping with that community spirit, SAA recently launched a new website that has been a year in the making. As of this writing, I’m not sure which features will be available when this issue hits your mailbox but the finished product will be fully “gamified” and interactive, offering badges and points for participation and allowing community members to connect, in a multitude of ways, with others who share “common attitudes, interests and goals.”

Many of the new features the site will offer are designed to make it easier to connect with others in the community - to ask questions and have them answered in a robust and deeply connected environment, to join groups, follow threads, and so much more.

Points can be earned by sharing posts, commenting on stories, submitting discussion topics, signing up for events, viewing videos, and many other actions, all of which are meant to help foster a feeling of being in a safe place, with like-minded people who share common ground. And, as always, the new site is filled with fully-vetted, up-to-the-minute news and information about all things spondylitis.

We’ve also added new products to our online shop, including cookbooks, baseball caps, backpacks and more. And, we’ve brought back Member Discounts, which will allow our most committed supporters to save a little money while sporting the newest in “spondylitis chic.” The new site is a collaborative effort, and one that will continue to evolve organically as more and more community members chime in and make it their own.

When you get a chance, please take a look around the brand new spondylitis.org. Register or log in by clicking the button on the top right of the screen. If you’re already an SAA member, we’ve started the registration process for you. Simply log in using your email and the computer generated password we emailed you last month. (If you can’t find that email, simply enter your email address and ask for a password reset.)

Once you’re logged in, please be sure to update your Password and Display Name (the name that will appear when you post anything on the site). To do this, click on the pulldown menu where your name appears on the top right of the screen and choose Edit Account.

Be sure to create a unique display name. You can make it as anonymous as you like.

Once your registration is complete, you’ll have access to lots of exclusive content as well as member discounts in our new shop.

Please tell us what you think of the new site and if there are other features you’d like to see. There’s a survey link on the top of each page for you to do just that.

Welcome to the next generation of the Spondylitis Community!
How can I stop using opioids while I still have chronic pain? Sure, the withdrawal is horrible and we always hear about the joy of making it to the other side, but this is different. I’m not addicted to a high. I use these for pain. But now I need them every day just to function. Great. If I make it to the other side, I’ll still be in pain. Now, what the hell am I supposed to do?”

I have ankylosing spondylitis. Like so many others, I noticed symptoms at age 19, but wasn’t diagnosed until age 38 (I’m now 56). I live with chronic pain; inflammation, iritis, IBS, cardiac issues, fibromyalgia and long term complications from four of the five TNF inhibitors. Fusion has limited my range of motion, and fatigue, when it hits, often commands me to stay put. But a few years ago, it became apparent that my biggest challenge had become the narcotics I was using to treat the pain.

“Opioids broke the pain cycle. They made unbearable pain, bearable. In fact, they worked so well that I was able to stretch and strengthen, maintaining some spinal range of motion. I felt good on opioids, until I didn’t.”
It was the 1990s and pain had just been recognized as the fifth vital sign. Physicians began to ask us to rate our pain from 1-10 and pain was aggressively treated. The number of opioid prescriptions rose and those in chronic pain were finally being heard and successfully treated.

Or was it a success? In my case the answer is yes and no. Opioids broke the pain cycle. They made unbearable pain, bearable. In fact, they worked so well that I was able to stretch and strengthen, maintaining some spinal range of motion. I felt good on opioids, until I didn’t.

While in my 20s, a diagnosis of endometriosis was blamed for my lower back pain. In 1994, at age 34, I had a hysterectomy. I had no children and my problem wasn’t endometriosis. The pain continued; this time it was blamed on scar tissue and following several additional surgeries, I found myself using opioids. It was after one of the surgeries that I developed my first bout of iritis. That led to a diagnosis of ankylosing spondylitis in 1998.

Up until that time, I was a successful businesswoman. The pain and stiffness were bad but I was still able to meet my commitments. Meetings, travel, presentations, negotiations; I kept going, by using painkillers.

By 2000, I had been on so many narcotics, I realized it was time to go to a pain management clinic to investigate available alternatives. The pain management doc warned me about pain cycles. “We need to avoid pain,” he’d say. I was prescribed daily doses of fentanyl patches and suckers. For a while, it worked. The fentanyl numbed my pain, but it also seemed to numb my spirit. In 2003 I tried to discontinue it and ended up in the ER, severely dehydrated, malnourished and in withdrawal. The fentanyl numbed my pain, but it also seemed to numb my spirit. In 2003 I tried to discontinue it and ended up in the ER, severely dehydrated, malnourished and in withdrawal. I was given fluids, fentanyl and discharged. Three more times that Spring I went to the ER, with the same results. By this time, I had weaned myself down to a lower, albeit large, dose of 100 mcg/day of fentanyl.

The fifth time I tried to stop, I went to another ER. This time I was admitted and soon the pain management group was in my room, offering their help. I was placed on methadone and within months, I was off both the fentanyl and methadone. I was then placed on daily morphine tablets to manage my pain.

A decade later, I realized that my new problem had become the morphine. Constipation, forgetfulness, insomnia, drowsiness, needing pills with me all the time, that look I’d see on a doctor’s face when he’d learn of my opioid use, the weaning up and down, the GI symptoms; I was just tired of it. I needed an alternative.

It was during a consultation with Integrative Medicine at Mayo Clinic, Phoenix, AZ that I was introduced to relaxation techniques, herbal remedies, breathing techniques, yoga, mindfulness, acupuncture and anti-inflammatory diets. Some topics were new to me, others a refresher. But, there were alternatives out there. I wondered if they’d work for me. What if I stopped the opioids? Will some breathing technique really help? I didn’t know, but I was sure that the path I was on was no longer working for me. I weaned myself down to a low dose of morphine, then prepared to stop.

Although the doctors congratulated me on “virtually ceasing use of narcotics,” I knew it was not over. That last step is so difficult.

In March of 2016, I stopped using opioids.

I had some withdrawal experience under my belt, so I knew what to expect. I also kept my Primary Care Physician informed and in the loop. Still, it didn’t make the process any easier. Below I’ve listed some symptoms I experienced followed by what helped me:
Nausea – Cannabis suckers and ice chips (Medical Marijuana is legal in Arizona)

Diarrhea – Apple sauce and also coconut water to prevent dehydration

Itching – Epsom salt baths

Insomnia – Lavender or peppermint oil, soothing music and a dark room, helped somewhat

Hyperosmia (sensitivity to smell) – No fragrance on me, my husband or laundry

No appetite – Cannabis suckers and spoonfuls of nut butter and bland wheat crackers

Cold sweats – Slept in layers and changed clothing frequently

Skin sensitivity – Wore soft clothing and avoided touch during that time

Body jerking and twitching – Dealt with it. It’s horrible but does let up

Pain flare – Medrol pack, ice, heating pad, Thermacare pads, Epsom Salt baths, Cannabis topical oil, Lidocaine patches for costochondritis, paced breathing, stretching, stretching and stretching.

These symptoms lasted from three weeks to four months.

As soon as the nausea subsided, I began taking the suggested alternative supplements in an effort to regain my health, calm my gut, and help manage inflammation. I also implemented many relaxation techniques. Those listed below work for me:

**Supplements** – such as Turmeric, Curcumin, Vitamin D3, Zyflamend, and Boswellia among others.

**Pain Management and Relaxation Techniques**

**Paced Breathing** – When someone is upset, they’re often encouraged to take a deep breath. This is based on science, so I tried it. Much to my own amazement, paced deep breathing reduced my blood pressure, pulse, and even reduced pain. This was the one technique I used while in withdrawal and it helped, especially when my pulse began to race and the pain became unbearable. The idea is to breathe in slowly, hold, then slowly release your breath. Suggested timing translates to 5-6 breaths a minute. I use the free app by Paced Breathing Trex LLC. You can plug in your own times or use their default. It’s a good guide and I’ve come to rely on it every day, much like I did my pain meds.

**Soft Yoga** – Excellent method to strengthen body, enhance balance and clear the mind.

**Mindfulness** – Initially this technique of focusing on the present sounded a little “woo woo” to me but it works. When I’m laughing with a friend, at that moment, I rarely feel pain. Mindfulness uses the same principle. Focus on the activity. I enjoy gardening and sometimes just trimming a plant puts me in a place far away from the chronic pain. Bread baking works. Or even a walk. If I focus on the outside world, it can sometimes take me away from my inner world of pain.

**Acupuncture** – Based on the principle of the whole body and enabling the energy life force to flow, this technique has been used for centuries. Years ago I used acupuncture with some success and I’ve once again begun treatments. No, there is no pain when acupuncture is done properly.

**Anti-Inflammatory Diet** – Although I’d read about anti-inflammatory diets, I had always assumed that my pain was so severe that a simple diet change wouldn’t make a difference. But it did. A gluten test revealed no sensitivity so I keep whole grains in my diet but I’ve eliminated virtually all white processed foods. My diet now mainly consists of whole grains, nuts, veggies, fruits, beans, seafood, tofu and water. When I stay true to this diet, I feel better. Pizza or a bagel is fine once in a while, but a few days of white foods bring on a flare. No, this diet hasn’t made me inflammation free, but I do feel so much better when I follow it.

**Stretching and Strengthening** – It hurts. It burns. There’s sharp pain and often fatigue, but I work through it. Every day that I am able to get out of bed, I stretch and every other day I stretch and strengthen. No impact, I use weights and it’s sometimes grueling, but I carry on. Through all the pain, throughout all the years, I’ve kept this up and my reward is my current range of motion. The changes I’ve made in 2016, from elimination of opioids to new methods of inflammation management, have made a big difference in my life. It’s almost as if I’ve woken up from a bad dream. I have chronic pain, but after a few months, the chronic pain off the opioids was about the same as when I was on them. Pain flares are my biggest challenge. No pills to help. Pain management now requires more time and rest and that’s what I do. Not once, since being off opioids, have I reached for one of the few pills I keep in the house just in case."

Pain flares are my biggest challenge. No pills to help. Pain management now requires more time and rest and that’s what I do. Not once, since being off opioids, have I reached for one of the few pills I keep in the house just in case.‘”
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