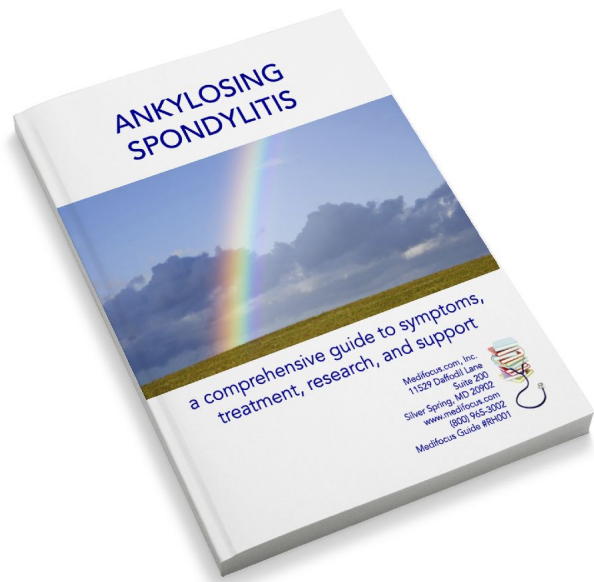


Preview of the Medifocus Guidebook on: Ankylosing Spondylitis

Updated June 20, 2017



This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Ankylosing Spondylitis**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

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Table of Contents

Background Information	8
Introduction	8
About Your Medifocus Guidebook	10
Ordering Full-Text Articles	13
The Intelligent Patient Overview	15
Guide to the Medical Literature	56
Introduction	56
Recent Literature: What Your Doctor Reads	57
Review Articles	57
General Interest Articles	68
Drug Therapy Articles	83
Clinical Trials Articles	92
Centers of Research	107
United States	109
Other Countries	114
Tips on Finding and Choosing a Doctor	140
Directory of Organizations	146

1 - Background Information

Introduction

Chronic or life-threatening illnesses can have a devastating impact on both the patient and the family. In today's new world of medicine, many consumers have come to realize that they are the ones who are primarily responsible for their own health care as well as for the health care of their loved ones.

When facing a chronic or life-threatening illness, you need to become an educated consumer in order to make an informed health care decision. Essentially that means finding out everything about the illness - the treatment options, the doctors, and the hospitals - so that you can become an educated health care consumer and make the tough decisions. In the past, consumers would go to a library and read everything available about a particular illness or medical condition. In today's world, many turn to the Internet for their medical information needs.

The first sites visited are usually the well known health "portals" or disease organizations and support groups which contain a general overview of the condition for the layperson. That's a good start but soon all of the basic information is exhausted and the need for more advanced information still exists. What are the latest "cutting-edge" treatment options? What are the results of the most up-to-date clinical trials? Who are the most notable experts? Where are the top-ranked medical institutions and hospitals?

The best source for authoritative medical information in the United States is the National Library of Medicine's medical database called PubMed®, that indexes citations and abstracts (brief summaries) of over 7 million articles from more than 3,800 medical journals published worldwide. PubMed® was developed for medical professionals and is the primary source utilized by health care providers for keeping up with the latest advances in clinical medicine.

A typical PubMed® search for a specific disease or condition, however, usually retrieves hundreds or even thousands of "hits" of journal article citations. That's an avalanche of information that needs to be evaluated and transformed into truly useful knowledge. What are the most relevant journal articles? Which ones apply to your specific situation? Which articles are considered to be the most authoritative - the ones your physician would rely on in making clinical decisions? This is where *Medifocus.com* provides an effective solution.

Medifocus.com has developed an extensive library of *MediFocus Guidebooks* covering a wide spectrum of chronic and life threatening diseases. Each *MediFocus Guidebook* is a

high quality, up- to-date digest of "professional-level" medical information consisting of the most relevant citations and abstracts of journal articles published in authoritative, trustworthy medical journals. This information represents the latest advances known to modern medicine for the treatment and management of the condition, including published results from clinical trials. Each *Guidebook* also includes a valuable index of leading authors and medical institutions as well as a directory of disease organizations and support groups. *MediFocus Guidebooks* are reviewed, revised and updated every 4-months to ensure that you receive the latest and most up-to-date information about the specific condition.

About Your MediFocus Guidebook

Introduction

Your *MediFocus Guidebook* is a valuable resource that represents a comprehensive synthesis of the most up-to-date, advanced medical information published about the condition in well-respected, trustworthy medical journals. It is the same type of professional-level information used by physicians and other health-care professionals to keep abreast of the latest developments in biomedical research and clinical medicine. The *Guidebook* is intended for patients who have a need for more advanced, in-depth medical information than is generally available to consumers from a variety of other resources. The primary goal of a *MediFocus Guidebook* is to educate patients and their families about their treatment options so that they can make informed health-care decisions and become active participants in the medical decision making process.

The *Guidebook* production process involves a team of experienced medical research professionals with vast experience in researching the published medical literature. This team approach to the development and production of the *MediFocus Guidebooks* is designed to ensure the accuracy, completeness, and clinical relevance of the information. The *Guidebook* is intended to serve as a basis for a more meaningful discussion between patients and their health-care providers in a joint effort to seek the most appropriate course of treatment for the disease.

Guidebook Organization and Content

Section 1 - Background Information

This section provides detailed information about the organization and content of the *Guidebook* including tips and suggestions for conducting additional research about the condition.

Section 2 - The Intelligent Patient Overview

This section of your *MediFocus Guidebook* represents a detailed overview of the disease or condition specifically written from the patient's perspective. It is designed to satisfy the basic informational needs of consumers and their families who are confronted with the illness and are facing difficult choices. Important aspects which are addressed in "The Intelligent Patient" section include:

- The etiology or cause of the disease
- Signs and symptoms
- How the condition is diagnosed
- The current standard of care for the disease
- Treatment options

- New developments
- Important questions to ask your health care provider

Section 3 - Guide to the Medical Literature

This is a roadmap to important and up-to-date medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest developments and breakthroughs in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new clinical developments, and advances in research. To facilitate your review and analysis of this information, the articles are grouped by specific categories. A typical *MediFocus Guidebook* usually contains one or more of the following article groupings:

- *Review Articles*: Articles included in this category are broad in scope and are intended to provide the reader with a detailed overview of the condition including such important aspects as its cause, diagnosis, treatment, and new advances.
- *General Interest Articles*: These articles are broad in scope and contain supplementary information about the condition that may be of interest to select groups of patients.
- *Drug Therapy*: Articles that provide information about the effectiveness of specific drugs or other biological agents for the treatment of the condition.
- *Surgical Therapy*: Articles that provide information about specific surgical treatments for the condition.
- *Clinical Trials*: Articles in this category summarize studies which compare the safety and efficacy of a new, experimental treatment modality to currently available standard treatments for the condition. In many cases, clinical trials represent the latest advances in the field and may be considered as being on the "cutting edge" of medicine. Some of these experimental treatments may have already been incorporated into clinical practice.

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Article title
- Author Name(s)
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)

- Link to Abstract (brief summary of the actual article)

Linking to Abstracts: Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the corresponding URL address that is provided for each cited article. If you purchased a printed copy of a *MediFocus Guidebook*, you can still access the article abstracts online by entering the individual URL address for a particular article into your web browser.

Section 4 - Centers of Research

We've compiled a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of the specific medical condition. The "Centers of Research" directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of the condition.

Inclusion of the names of specific doctors, researchers, hospitals, medical centers, or research institutions in this *Guidebook* does not imply endorsement by Medifocus.com, Inc. or any of its affiliates. Consumers are encouraged to conduct additional research to identify health-care professionals, hospitals, and medical institutions with expertise in providing specific medical advice, guidance, and treatment for this condition.

Section 5 - Tips on Finding and Choosing a Doctor

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver high-level, quality medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it. This section of your *Guidebook* offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

Section 6 - Directory of Organizations

This section of your *Guidebook* is a directory of select disease organizations and support groups that are in the business of helping patients and their families by providing access to information, resources, and services. Many of these organizations can answer your questions, enable you to network with other patients, and help you find a doctor in your geographical area who specializes in managing your condition.

2 - The Intelligent Patient Overview

ANKYLOSING SPONDYLITIS

Introduction to Ankylosing Spondylitis

Ankylosing spondylitis (AS), "stiffening of the spinal joints", is a chronic rheumatoid, inflammatory condition which causes arthritic changes in the sacroiliac joint at the junction of the sacrum (lower spine) and the pelvis. It belongs to a family of inflammatory conditions called *spondyloarthropathies*.

The human spine is a complex structure responsible for many tasks, including:

- Bearing the weight of the upper body
- Keeping the body upright and erect when standing
- Providing structure and support to the skeletal system
- Maintaining flexibility of movement of the upper body
- Housing and protecting the spinal cord

The spine is comprised of many components including 24 vertebrae and more than 100 joints. The vertebrae are divided into three sections, namely:

- *Cervical* vertebrae - These seven vertebrae are found in the neck and upper back.
- *Thoracic* vertebrae - These vertebrae are found in the chest region. Each of the thoracic vertebrae has a rib attached to it which arches around to the front of the body and encompasses the lungs, heart, and the uppermost part of the abdominal organs.
- *Lumbar* vertebrae - These five vertebrae lie behind the lower abdominal organs.

The *sacrum* is a triangular bone which sits below the lumbar vertebrae and attaches the spine to the pelvis. The joint that connects the sacrum and the pelvis is called the *sacroiliac joint*. Inflammation of the sacroiliac joint is the hallmark sign of ankylosing spondylitis, and is the place where lower back pain associated with AS typically originates. Involvement of the *axial* joints (joints related to the spine), primarily the sacroiliac joint, is the earliest manifestation of AS, although peripheral joints and extra-articular (outside the joints) sites can be involved as well. Older names that have been used in the past to describe AS include "poker back," "rheumatoid spondylitis," and "Marie-Strumpell's spondylitis."

It is important not to confuse *spondylitis* with another spinal condition called *spondylosis*. While spondylosis reflects a condition resulting from "wear and tear" of the spine and is seen more frequently in older people, spondylitis is an inflammatory condition that leads to new bone formation and fusion and is seen at a younger age.

Spondyloarthropathies

Ankylosing spondylitis is a member of a group of rheumatic diseases that affects the mobility of the spine, collectively known as *spondyloarthropathies* (SpAs). Spondyloarthropathies are a group of related inflammatory joint diseases associated almost exclusively with the presence of a genetic marker called HLA-B27 and are characterized specifically by sacroiliac joint involvement in addition to other symptoms. Spondyloarthropathies affect axial joints (the vertebral column, ribs, and the sternum) and can also involve peripheral joints (e.g., feet and shoulders). The clinical features of SpA are distinct from other rheumatologic conditions such as rheumatoid arthritis.

Spondyloarthropathies include the following subgroups of conditions:

- Ankylosing spondylitis - This is the most common subgroup and the subject of this Medifocus Guidebook.
- Reiter's syndrome (reactive arthritis) - This is characterized by arthritis (especially in the legs), conjunctivitis, and inflammation of the urethra.
- Enteropathic arthritis - This form of arthritis involves the lower extremities, typically the knees and ankles. It is associated with inflammatory bowel disease (IBD). Inflammatory bowel disease refers to two similar but distinct conditions called *Crohn's disease* and *ulcerative colitis* that produce inflammation of the tissue lining the gastrointestinal tract, resulting in abdominal pain, cramping, fatigue, and diarrhea.
- Psoriatic arthritis - This type of joint inflammation affects people with a skin condition known as *psoriasis* (thick, inflamed patches of skin covered by silver or gray scales). Inflammation may occur in joints of the hands and/or feet, large joints (e.g., knees), and the sacroiliac joint.
- Undifferentiated spondyloarthropathy (USpA) - This is a term used to describe individuals who have symptoms associated with AS but do not meet all of the criteria for diagnosis of AS or other specific types of SpA. Typically, some symptoms are present but not enough to make a definitive diagnosis. People who suffer from USpA face significant frustration when seeking a diagnosis since many health care providers do not recognize or identify the grouping of symptoms as an independent entity. They may be told that they are "anxious and depressed" or may be misdiagnosed with fibromyalgia. The prognosis of individuals with USpA is generally good, though some develop AS later. Some clinicians have noted that people with USpA who test positive for the presence of the HLA-B27 gene are more likely to develop AS.

What Happens in Ankylosing Spondylitis?

The primary mechanism and process that characterizes AS is *enthesitis*, inflammation at the junction where the joint capsule, tendons, and ligaments attach to the sacrum. Enthesitis is the cause of the hallmark symptoms of AS, namely back pain and back stiffness, especially in the

morning. Symptoms of AS affect each individual differently in symptom severity and disease progression, but back pain is almost universal. Chronic inflammation and irritation of the spinal joints cause changes to those vertebral joints and may result in extra bone formation due to the body's natural process of healing and repairing itself following inflammation. This process may lead to fusion of the vertebrae. The stiffening of the joints due to abnormal fusion is referred to as *ankylosis*. Thus if a person has severe AS for many years, the continuous inflammation and process of repair leads to bony fusion of spinal joints and sometimes of other joints as well.

The degree of fusion in AS ranges from partial fusion (limited to the pelvic bones) to fusion of the entire spine. In its later stages, AS may cause total loss of spinal mobility and function, significantly impacting the individual's quality of life. If the process of joint and bone ossification ascends the spine in advanced stages of disease, the spine becomes a bony column and is often referred to as a "bamboo spine". Progression of the disease to this point, however, is rare.

In addition to the sacroiliac joint, enthesitis can take place in multiple sites called "hot spots" and may lead to painful swelling and tenderness. Subchondral tissue (smooth tissue at the ends of bones) becomes granulomatous (characterized by small or granular nodular inflammatory lesions) and is then infiltrated with various types of immune cells such as plasma cells and lymphocytes. Joints that are affected show markings of *sclerosis* (hardening of tissue) and irregular erosion (wearing down). The tissue is gradually replaced with fibrous cartilage and becomes ossified (bony) leading to ankylosis. Outer muscle fibers of the spine are replaced by bone which eventually fuses the vertebrae. Since bone formed during fusion is inherently weak, there is an increased risk of spinal fracture.

Progression of Ankylosing Spondylitis

The progression of AS is highly individual and can range from very slow to progressive and highly symptomatic. While symptoms may remain mild for some, others with AS may experience progressive structural deterioration, pain, and functional disability. Within a few months of onset, pain in the lower back/buttocks may become unilateral (affect one side only) or may alternate from side to side. Over time (months or years) the pain and stiffness may spread up the spine and into the neck. Pain and tenderness also affect the ribs, shoulder blades, hips, thighs, and heels. Progression of AS is not related to age or gender.

As noted above, the pain in AS is initially caused by enthesitis at the sacroiliac joint but may be intensified by active "hot spots", additional joints with enthesitis. Patients may experience periods of painful, active inflammation called "flares", and periods during which the disease is inactive, known as "remissions". In patients with progressive AS, pain becomes more persistent during flares, and the duration of remissions decreases. The number of sites of enthesitis and their locations are two important factors that determine the extent of the impact AS has on quality of life. For example, if enthesitis appears in the Achilles tendon at the back of the heel or in the plantar fascia at the base of the heel, walking can be significantly impaired. Enthesitis may deteriorate into *enthesopathy* (calcification of joints, tendons, and ligaments) that may further impair movement and mobility.

Because AS is also a systemic rheumatic disease, it can lead to additional inflammation in other

parts of the body, in addition to the spine. People with AS may develop arthritis, pain or stiffness in other locations, including the hips, knees, ankles, heels, shoulders, and ribs. Complications that may arise as a result of the chronic inflammation can affect several organs including the eyes, heart, and kidneys. Ankylosing spondylitis is typically more severe in men than in women.

Many people do not seek help early in the disease process because the symptoms they feel are vague and progress very slowly. Although inflammatory back pain may occur five to ten years before being diagnosed with AS, progressive structural damage occurs in the interim. The diagnosis is usually established once the damage and structural abnormalities of the sacroiliac joint or spine become visible on X-ray, although recent guidelines enable a highly probable diagnosis of AS to be made before X-ray or MRI evidence appears.

Ankylosing spondylitis is also associated with the presence of *syndesmophytes*, thin, bony outgrowths that develop in the ligaments of the spinal intervertebral joints. Syndesmophytes play a role in vertebral fusion and are associated with the progression of AS. The results of a study published in 2012 on syndesmophytes and AS. A total of 132 patients with AS was included in the study and X-rays (radiographs) of all participants were compared at baseline (beginning of study), and at 2-year and 4-year follow-up periods. The data indicated that:

- At baseline, 81 (61%) of patients had syndesmophytes
- At 2-year follow-up, new syndesmophytes developed in 44 (33%) of patients
- At 4-year follow-up, new syndesmophytes developed in 63 (48%) of patients

The relative risk of developing new syndesmophytes was 5.0 (substantial). Factors that were associated with the development of new syndesmophytes included older age, lower functional status, male gender, erythrocyte sedimentation rate, and existing syndesmophytes. More information about this study can be seen by clicking on the following link:

<http://www.ncbi.nlm.nih.gov/pubmed/21989544>

If AS is not treated in a timely fashion, it may continue to deteriorate and can cause significant health problems, including:

- Postural changes
- Atrophy of the buttocks
- Forward positioning of the neck over the chest
- Lumbar lordosis (exaggeration of the forward curve of the lower back, sometimes called "swayback")
- Exaggerated thoracic spine kyphosis (outward curvature of the upper back giving a "hunchback" appearance)

Complications of Ankylosing Spondylitis

Patients with progressive AS may encounter *joint-related complications* or *extra-articular complications* (complications outside the joints).

Joint-Related Complications

Spine

Spinal fracture is the most serious complication for people with AS. Since the bone that forms from fusion is inherently weak, the spine becomes very rigid and fragile, and even mild trauma can result in fracture. The cervical spine is at greatest risk and fractures at this level may result in quadriplegia. In advanced cases of AS, fusion may lead to *kyphosis*, a forward-directed curvature of the spine which causes a stooped posture, or to *lordosis* ("swayback"). However, these conditions are not common today due to increasingly effective treatments for AS.

Hip, Leg, and Shoulder

Hip, leg, or shoulder involvement affects approximately one-third of patients with AS. Hip symptoms (inflammation and pain) typically develop slowly and may initially be felt in the groin. Sometimes patients may feel referred pain from the hip in the back of their knees or the front of their thighs, which can confuse the diagnostic workup. Hip involvement is more common in younger patients and is thought to indicate a risk for progression to more severe AS. Shoulder involvement is usually mild, in part because the shoulder is not a weight-bearing joint.

Other joint complications of the leg in AS include:

- Knee
- Ankle (more common as initial symptom of juvenile AS)
- Heel (Achilles tendon or plantar fascia)
- Toes ("sausage-shaped" toes due to chronic inflammation of the small joints of the toes)

Chest

The joints between the ribs, spine, and where the ribs attach to the chest may show increased scarring from long-term inflammation in patients with AS. Scarring and continued inflammation may limit chest expansion causing chest pain that mimics angina (heart spasms) or pleurisy (inflammation of the outer layer of the lung). Patients should seek medical attention quickly to determine the source of any chest pain.

Jaw

Approximately 10% of patients with AS experience inflammation in the jaw, which can limit the degree of oral opening, thereby affecting eating and speech.

Extra-Articular Complications

In addition to the changes that take place in the sacroiliac and other joints, there are additional non joint-related complications that are associated with AS including:

Ophthalmic Complications

The eye is the most common organ affected by AS. Approximately 40% of patients with AS develop a condition called *anterior uveitis* (inflammation of the uvea) or *iritis* (inflammation of the iris). The *uvea* is the middle layer of the eye that lies beneath the *sclera* (the white of the eye). It consists of the iris (the colored part of the eye), the ciliary body that changes the shape of the lens when focusing, and the choroid (vascular layer in the eye). These structures control many of the functions of the eye such as adjusting to different levels of light or different distances of objects.

Symptoms of anterior uveitis include:

- Blurred vision (usually in one eye)
- Sharp pain in the eye
- Bloodshot eye
- Increased lacrimation (tear production)
- Photophobia (fear and avoidance of light)

Patients who develop symptoms of anterior uveitis should seek medical attention promptly in order to avoid permanent damage to the eye.

Inflammatory Bowel Disease

While symptomatic inflammatory bowel disease (IBD) is thought to occur in up to 10% of patients with AS, the incidence of asymptomatic IBD may be as high as 60% in patients with AS.

Approximately 20% of patients with inflammatory bowel disease (Crohn's disease and ulcerative colitis) also experience spinal inflammation, which highlights the close association between IBD and AS. Symptoms of inflammatory bowel disease include abdominal pain, cramping, fatigue, and diarrhea.

Cardiac Complications

Cardiac complications are being recognized as occurring more frequently than previously thought. Complications include:

- Aortitis (inflammation of the aorta) - This is the most important cardiovascular complication. It is related to aortic root thickening, stiffness, and dilatation of the portion of the aorta that is attached to the heart, and may lead to valvular insufficiency.
- Valvular insufficiency - Flaps of the cardiac valves do not completely seal, resulting in regurgitation (backflow of blood) when the heart pumps.
- Cardiac insufficiency - Inability of the ventricle to eject a sufficient amount of blood (heart failure)

According to an article published in 1998 in the *Journal of the American College of Cardiology* (Vol.32(5):1397-1404), aortic root disease and valve disease are thought to occur in up to 82% of patients and are associated with AS-related morbidity. To read more about aortic complications of AS, please click on the following link: <http://www.ncbi.nlm.nih.gov/pubmed/18799070>

Other cardiac conditions that may develop include:

- Angina pectoris - temporary chest pain due to insufficient blood and oxygen reaching the heart
- Pericarditis - inflammation of the pericardial membranes surrounding the heart
- Arrhythmia - electrical conduction heart abnormalities

Osteoporosis

Osteoporosis (reduced bone mineral density) is a common complication in patients with AS and occurs in up to 62% of patients. The occurrence of osteoporosis increases with increasing patient age and disease duration. In AS patients, osteoporosis is usually limited to the spine while

peripheral bones remain unaffected. Affected patients are at greater risk for developing spinal fractures. To read more about osteoporosis and AS, please click on the following link:

<http://www.ncbi.nlm.nih.gov/pubmed/20680529>

Systemic Involvement

Because AS is a systemic disease, it can produce other symptoms in addition to those listed above. Systemic effects of AS may include:

- Fatigue
- Low-grade fever
- Weight loss
- Anemia

Most individuals with AS experience fatigue. It is a major complaint among patients that significantly impacts activities of daily living and quality of life in general. It may be caused by lack of sleep, by pain, or as a result of the natural inflammatory process that takes place in AS.

Lungs and Chest

Pulmonary complications are rare and, if they do occur, are usually related to:

- Poor chest wall movement - Joint stiffness limits chest wall movement which prevents full ventilation of the lungs (filling and emptying to capacity) during inhalation and exhalation.
- Costochondritis - Chronic inflammation of the cartilage around the sternum (breast bone) may lead to reduced chest expansion and difficulty breathing.
- Pulmonary fibrosis - Chronic inflammation of the lungs that is associated with progressive scarring of lung tissue. (Some health care providers recommend that patients with AS should have an X-ray every five years to check for presence of lung fibrosis.)
- Rib stiffness - This may result in painful deep breathing, sneezing, coughing, or yawning.

Chest pain associated with AS can mimic angina (as noted above) or *pleurisy*, pain upon breathing when the outer lining of the lung is inflamed. If either of these symptoms occurs, medical attention is needed quickly to rule out serious cardiac or pulmonary conditions.

Some people with AS who experience limited chest expansion find that it takes them longer to recover from colds or other upper respiratory infections. Smoking cessation is vitally important for all patients with AS.

Kidneys

In rare cases, chronic inflammation associated with AS may produce *renal amyloidosis* (deposits of amyloid proteins in the kidney) which may cause *albuminuria* (presence of albumin protein in the urine) with subsequent deterioration of kidney function. Amyloidosis may also occur with long-term use of non-steroidal anti-inflammatory drugs (NSAIDs).

Nerves

Neurologic complications are very rare and may be seen only after very long-term illness. Some patients with advanced AS may develop a condition called *cauda equina syndrome* that is caused by compression of a bundle of nerves called the *cauda equina* at the base of the spine. This is a

very rare complication, but when it occurs, it may include:

- Urinary retention and/or incontinence
- Sexual dysfunction
- Pain or weakness in the legs

Measuring Disease Activity in Ankylosing Spondylitis

A team of rheumatologists, physical therapists, and AS research specialists determined the basis on which a series of tests was created to measure various aspects of disease activity. Known as the *BATH Indices*, these tests include:

- BATH AS Metrology Index (BASMI)
- BATH AS Functional Index (BASFI)
- BATH AS Disease Activity Index (BASDAI)
- BATH AS Patient Global Score (BAS-G)

BATH AS Metrology Index (BASMI)

This test reflects clinically significant changes in *spinal movement* and consists of measuring the status of the spine (cervical, thoracic, and lumbar), hips, and pelvic soft tissue. Higher scores indicate more severe limitation of movement.

BATH AS Functional Index (BASFI)

This test determines the degree of *functional limitation* due to AS. It consists of 10 questions about coping with activities of daily living. Responses are made in conjunction with a *visual analog scale*. A visual analog scale is a questionnaire that is formatted in such a way that a patient can rate the intensity of certain sensations and feelings, such as pain, by indicating their level of agreement to a statement on a continuous line between two end-points (e.g., "very painful" to "no pain"). It provides patients with a broad range of possible responses and thus offers a more accurate representation of functional status than verbal description. Another advantage of the visual analog scale is that it reflects a greater sensitivity to any change of status with subsequent testing.

The *Dougados Functional Index* (DFI) is another score used to evaluate functional capacity of patients with AS. The BASFI may be more precise in its discriminative capacity and reflects a wider range of parameters than the DFI.

BATH AS Disease Activity Index (BASDAI)

This test is administered in conjunction with a visual analog scale and measures *disease activity* relating to:

- Fatigue
- Spinal pain
- Joint pain and swelling
- Areas of localized tenderness
- Morning stiffness

The BASDAI is also sensitive to changes that may occur on subsequent testing.

BATH AS Patient Global Score (BAS-G)

This test enables the health care provider to objectively measure how patients evaluate their own well-being over time (previous week and previous six months). It is not meant to be administered as a stand-alone test, but rather is evaluated in context with the scores from other BATH indices. Scores are measured from 1-10, with the higher numbers indicating a greater degree of AS involvement in everyday life. The BATH indices can be given to all ages, are easy to use, and can be completed quickly.

Incidence of Ankylosing Spondylitis

Symptoms of AS usually begin between the ages of 15-40, although the disease can also affect children or adolescents, as well as adults over 40 years of age. According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), approximately 80% of people with AS develop symptoms before the age of 30, and only 5% develop symptoms after the age of 45.

Ankylosing spondylitis is three times more common in Caucasians than in African-Americans. The Centers for Disease Control and Prevention (CDC) and the National Arthritis Data Workshop estimate that up to 2.4 million Americans suffer from AS. Internationally, AS is thought to occur in up to 1% of the general population, with the highest incidence occurring in northern European countries and the lowest occurrence in sub-Saharan Africa. The prevalence of AS is about two to three times higher in males than females, with males accounting for about 65% or more of cases.

There is increasing evidence that AS is commonly under-diagnosed in women since its presentation often differs considerably than in men. This has led some researchers to believe that AS may be more prevalent in women than formerly thought.

When AS appears in children as young as 11 years old, it is called *juvenile ankylosing spondylitis*. Ankylosing spondylitis in children or adolescents tends to involve the knees, ankles, feet, hips, and buttocks. Back pain, however, is rare.

Risk Factors for Ankylosing Spondylitis

Despite an extensive amount of research that has been conducted over the past few decades, the exact cause of AS remains unknown. Investigators are puzzled by the insidious onset that leads to diagnosis only after several years. The pathogenesis appears to be related to a complex interaction of immunological, genetic, and environmental factors which are not yet clearly understood. Scientists, however, have identified certain risk factors that may increase a person's chances of developing ankylosing spondylitis.

Risk factors for ankylosing spondylitis include:

- Genetic predisposition
- Family history

- Immune response mediators
- Inflammatory bowel disease

Genetic Predisposition

Evidence for a genetic predisposition to AS is supported by the findings that a specific Human Leukocyte Antigen (HLA), known as HLA-B27, occurs in approximately 90-95% of individuals with AS. (The HLA complex is a family of genes that helps the immune system function by distinguishing between its own proteins and those that are foreign.) In contrast, the HLA-B27 gene is only found in about 6% of the overall general population, suggesting that individuals with the HLA-B27 gene may be more genetically predisposed to developing AS than people who do not have it. The presence of the HLA-B27 gene is considered to account for 20-40% of the overall risk of developing AS.

Most people with the HLA-B27 gene do not develop AS, nor does the HLA-B27 gene need to be present in order to develop AS. It is estimated that less than 2% of individuals with the HLA-B27 gene in the general population develop AS. The HLA-B27 gene does not cause AS, but seems to make people more susceptible to the condition.

Additional genes that have been identified as being associated with AS include ERAP1, IL1A, and IL23 although their direct involvement is not yet understood.

Family History

Ankylosing spondylitis tends to run in families and is 10-20 times more common among individuals with a first-degree relative (parent or sibling) who has AS than in the general population. If one parent has the HLA-B27 gene, there is a 50% chance that each of the children of this parent will inherit the gene. Among children who inherit the gene, fewer than 10% will develop AS.

Immune Response Mediators

Ankylosing spondylitis may be related to the secretion of *cytokines* (immune response mediators) such as *TNF-alpha* that develop as a result of prolonged immune response to infection. Studies have suggested a role for TNF-alpha in the pathogenesis of AS based on the following observations:

- Elevated levels of TNF-alpha in the sacroiliac joints of patients with AS
- Elevated levels of TNF-alpha in certain joints of patients with psoriatic arthritis, which is one type of spondyloarthropathy
- Elevated levels of TNF-alpha in the mucosa of the gut (intestines) in biopsy samples of patients with Crohn's Disease, which is highly associated with AS

Several other pro-inflammatory cytokines, including *interleukins 23 and 17* are under investigation for their role in the etiology or origin of AS.

Inflammatory Bowel Disease

There is some evidence that bacterial infections may "trigger" the underlying chronic inflammation that leads to the development of AS. The association between AS and inflammatory

bowel diseases (Crohn's disease and ulcerative colitis) suggests that an exaggerated immune response to bacteria in the gastrointestinal tract may be involved in the underlying pathogenesis of AS. Ankylosing spondylitis may develop when host defenses in the intestine break down and bacteria from the intestines travel through the bloodstream into the region of the sacroiliac joint, where they trigger a chronic inflammatory response.

The **Intelligent Patient Overview** in the complete **Medifocus Guidebook on Ankylosing Spondylitis** also includes the following additional sections:

- **Diagnosis of Ankylosing Spondylitis**
- **Treatment Options for Ankylosing Spondylitis**
- **Quality of Life Issues and Ankylosing Spondylitis**
- **New Developments in Ankylosing Spondylitis**
- **Questions to Ask Your Health Care Provider About Ankylosing Spondylitis**

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3 - Guide to the Medical Literature

Introduction

This section of your *MediFocus Guidebook* is a comprehensive bibliography of important recent medical literature published about the condition from authoritative, trustworthy medical journals. This is the same information that is used by physicians and researchers to keep up with the latest advances in clinical medicine and biomedical research. A broad spectrum of articles is included in each *MediFocus Guidebook* to provide information about standard treatments, treatment options, new developments, and advances in research.

To facilitate your review and analysis of this information, the articles in this *MediFocus Guidebook* are grouped in the following categories:

- Review Articles - 37 Articles
- General Interest Articles - 36 Articles
- Drug Therapy Articles - 26 Articles
- Clinical Trials Articles - 42 Articles

The following information is provided for each of the articles referenced in this section of your *MediFocus Guidebook*:

- Title of the article
- Name of the authors
- Institution where the study was done
- Journal reference (Volume, page numbers, year of publication)
- Link to Abstract (brief summary of the actual article)

Linking to Abstracts: Most of the medical journal articles referenced in this section of your *MediFocus Guidebook* include an abstract (brief summary of the actual article) that can be accessed online via the National Library of Medicine's PubMed® database. You can easily access the individual abstracts online via PubMed® from the "electronic" format of your *MediFocus Guidebook* by clicking on the URI that is provided for each cited article. If you purchased a printed copy of the *MediFocus Guidebook*, you can still access the abstracts online by entering the individual URI for a particular abstract into your computer's web browser.

Recent Literature: What Your Doctor Reads

Database: PubMed <January 2012 - June 2017>

Review Articles

1.

Role of HLA-B27 in the pathogenesis of ankylosing spondylitis (Review).

Authors: Chen B; Li J; He C; Li D; Tong W; Zou Y; Xu W
Institution: Department of Joint Surgery and Sports Medicine, Changhai Hospital, The Second Military Medical University, Shanghai 200433, P.R. China. Military Medical University, Shanghai 200433, P.R. China. Military Medical University, Shanghai 200433, P.R. China. Military Medical University, Shanghai 200433, P.R. China. Military Medical University, Shanghai 200433, P.R. China. Military Medical University, Shanghai 200433, P.R. China. Military Medical University, Shanghai 200433, P.R. China.
Journal: Mol Med Rep. 2017 Apr;15(4):1943-1951. doi: 10.3892/mmr.2017.6248. Epub 2017 Feb 24.
Abstract Link: <http://www.medifocus.com/abstracts.php?gid=RH001&ID=28259985>

2.

An update on the use of tumor necrosis factor alpha inhibitors in the treatment of ankylosing spondylitis.

Authors: Osman MS; Maksymowych WP
Institution: a Division of Rheumatology, Department of Medicine , University of Alberta , Edmonton , AB , USA. Edmonton , AB , USA.
Journal: Expert Rev Clin Immunol. 2017 Feb;13(2):125-131. doi: 10.1080/1744666X.2016.1218761. Epub 2016 Aug 10.
Abstract Link: <http://www.medifocus.com/abstracts.php?gid=RH001&ID=27479149>

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- Review Articles - 37 Articles
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4 - Centers of Research

This section of your *MediFocus Guidebook* is a unique directory of doctors, researchers, medical centers, and research institutions with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition. The *Centers of Research* directory is a valuable resource for quickly identifying and locating leading medical authorities and medical institutions within the United States and other countries that are considered to be at the forefront in clinical research and treatment of this disorder.

Use the *Centers of Research* directory to contact, consult, or network with leading experts in the field and to locate a hospital or medical center that can help you.

The following information is provided in the *Centers of Research* directory:

- **Geographic Location**

- United States: the information is divided by individual states listed in alphabetical order. Not all states may be included.
- Other Countries: information is presented for select countries worldwide listed in alphabetical order. Not all countries may be included.

- **Names of Authors**

- Select names of individual authors (doctors, researchers, or other health-care professionals) with specialized research interest, and in many cases, clinical expertise in the management of this specific medical condition, who have recently published articles in leading medical journals about the condition.
- E-mail addresses for individual authors, if listed on their specific publications, is also provided.

- **Institutional Affiliations**

- Next to each individual author's name is their **institutional affiliation** (hospital, medical center, or research institution) where the study was conducted as listed in their publication(s).
- In many cases, information about the specific **department** within the medical institution where the individual author was located at the time the study was conducted is also provided.

Centers of Research

United States

CA - California

<u>Name of Author</u>	<u>Institutional Affiliation</u>
Caplan L	National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, Maryland. Hamilton, Ontario, Canada. Bethesda, Maryland. California, Irvine.
Deodhar A	Ankylosing Spondylitis Clinic, University of California, San Francisco, USA.
Gensler L	Ankylosing Spondylitis Clinic, University of California, San Francisco, USA.
Kavanaugh A	Division of Rheumatology, Department of Medicine, University of Massachusetts Medical School and UMass Memorial Medical Center, Worcester, Massachusetts, USA. Dallas, Texas, USA. of Pennsylvania, Philadelphia, Pennsylvania, USA. of Pennsylvania, Philadelphia, Pennsylvania, USA. Diego, California, USA.
Kay J	Division of Rheumatology, Department of Medicine, University of Massachusetts Medical School and UMass Memorial Medical Center, Worcester, Massachusetts, USA. Dallas, Texas, USA. of Pennsylvania, Philadelphia, Pennsylvania, USA. of Pennsylvania, Philadelphia, Pennsylvania, USA. Diego, California, USA.
Ward MM	National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, Maryland. Hamilton, Ontario, Canada. Bethesda, Maryland. California, Irvine.

CO - Colorado

<u>Name of Author</u>	<u>Institutional Affiliation</u>
Caplan L	Denver Veterans Affairs Medical Center, University of Colorado, Denver, Colorado, USA.
Inman RD	Denver Veterans Affairs Medical Center, University of Colorado, Denver, Colorado, USA.

The **Centers of Research** in the complete **Medifocus Guidebook on Ankylosing Spondylitis** includes the following sections:

- Centers of Research for relevant states in the United States
- Centers of Research listed for relevant countries outside the United States

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5 - Tips on Finding and Choosing a Doctor

Introduction

One of the most important decisions confronting patients who have been diagnosed with a serious medical condition is finding and choosing a qualified physician who will deliver a high level and quality of medical care in accordance with currently accepted guidelines and standards of care. Finding the "best" doctor to manage your condition, however, can be a frustrating and time-consuming experience unless you know what you are looking for and how to go about finding it.

The process of finding and choosing a physician to manage your specific illness or condition is, in some respects, analogous to the process of making a decision about whether or not to invest in a particular stock or mutual fund. After all, you wouldn't invest your hard earned money in a stock or mutual fund without first doing exhaustive research about the stock or fund's past performance, current financial status, and projected future earnings. More than likely you would spend a considerable amount of time and energy doing your own research and consulting with your stock broker before making an informed decision about investing. The same general principle applies to the process of finding and choosing a physician. Although the process requires a considerable investment in terms of both time and energy, the potential payoff can be well worth it--after all, what can be more important than your health and well-being?

This section of your Guidebook offers important tips for how to find physicians as well as suggestions for how to make informed choices about choosing a doctor who is right for you.

Tips for Finding Physicians

Finding a highly qualified, competent, and compassionate physician to manage your specific illness or condition takes a lot of hard work and energy but is an investment that is well-worth the effort. It is important to keep in mind that you are not looking for just any general physician but rather for a physician who has expertise in the treatment and management of your specific illness or condition. Here are some suggestions for where you can turn to identify and locate physicians who specialize in managing your disorder:

- **Your Doctor** - Your family physician (family medicine or internal medicine specialist) is a good starting point for finding a physician who specializes in your illness. Chances are that your doctor already knows several specialists in your geographic area who specialize in your illness and can recommend several names to you. Your doctor can also provide you with information about their qualifications, training, and hospital affiliations.

The **Tips on Finding and Choosing a Doctor** in the complete **Medifocus Guidebook on Ankylosing Spondylitis** includes additional information that will assist you in locating a highly qualified and competent physician to manage your specific illness.

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6 - Directory of Organizations

American Academy of Physical Medicine and Rehabilitation

330 N. Wabash Avenue; Suite 2500; Chicago, IL 60611
312.464.9700; 312.464.0227 (fax)

info@aapmr.org

www.aapmr.org

American College of Rheumatology

1800 Century Place; Suite 250; Atlanta, GA 30345
404.633.3777; 404.633.1870 (fax)

acr@rheumatology.org

www.rheumatology.org

Ankylosing Spondylitis International Federation

www.asif.rheumanet.org

Arthritis Foundation Information Line; American Juvenile Arthritis Organization

POB 7669; Atlanta, GA 30309
404.872.7100; 800-283-7800

help@arthritis.org

www.arthritis.org

Arthritis National Research Foundation

200 Oceangate; Suite 830; Long Beach, CA 90802
800.588.2873; 562.983.1410 (fax)

anrf@ix.netcom.com

www.curearthritis.org

National Ankylosing Spondylitis Society

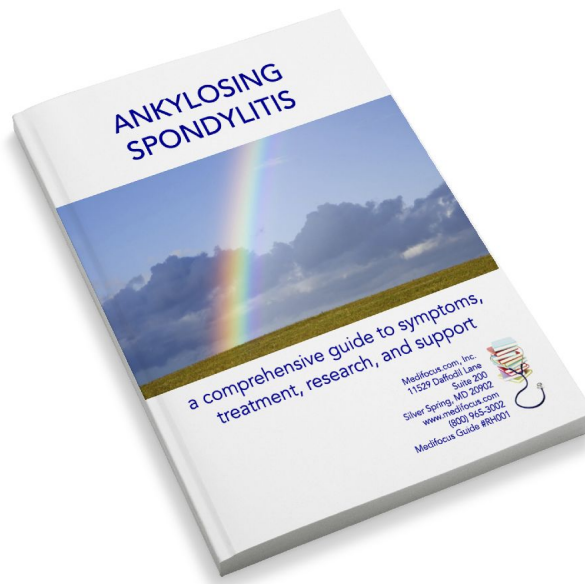
Unit 0.2, One Victoria Villas, Richmond, Surrey, TW9 2GW UK
020 8948 9117

nass@nass.co.uk

www.nass.co.uk

The **Directory of Organizations** in the complete **Medifocus Guidebook on Ankylosing Spondylitis** includes a list of selected disease organizations and support groups that are helping people diagnosed with Ankylosing Spondylitis.

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This document is only a SHORT PREVIEW of the **Medifocus Guidebook on Ankylosing Spondylitis**. It is intended primarily to give you a general overview of the **format and structure** of the Guidebook as well as select pages from each major Guidebook section listed in the Table of Contents.

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