Together the spondyloarthropathies form a group of overlapping chronic inflammatory rheumatologic diseases that show a predilection for involvement of the axial skeleton, entheses (bony insertions of ligaments and tendons), and peripheral joints. They also may involve extraskeletal structures, especially the eyes, lungs, skin, and GI tract. These diseases are strongly associated with the HLA-B27 gene, but they lack association with rheumatoid factor (RF) and antinuclear antibodies.1

The spondyloarthropathies include ankylosing spondylitis, psoriatic arthritis, reactive arthritis, arthritis of inflammatory bowel disease (IBD), and undifferentiated spondyloarthropathy. They are more common than previously recognized. Recent data from Europe and Asia suggest that as a group, the spondyloarthropathies might be as common as rheumatoid arthritis (RA); in Europe, the prevalence is 0.5% to 1%.2-4

Because there are no diagnostic criteria for the wider spectrum of the spondyloarthropathies, the diagnosis is based primarily on clinical findings.1,2,4-8 European Spondylarthropathy Study Group (ESSG) classification criteria are used frequently to assist the clinical diagnosis (Table 1).9 Early diagnosis has become much more important in recent years as more effective therapeutic options have become available.

In this article, we describe the specific clinical entities in the spondyloarthropathies and their common laboratory and radiological features. Then we outline a variety of management strategies, including nonpharmacological modalities, pharmacological therapy, and ophthalmological or surgical referral.

CLINICAL MANIFESTATIONS

Ankylosing spondylitis. The prototype of the spondyloarthropathies, ankylosing spondylitis primarily involves the sacroiliac joints and spine (Figure) and, often, the hip and shoulder joints; patients typically present with chronic inflammatory back pain.2,8 Symptoms usually start insidiously when patients are in their late teens or early 20s; men are affected roughly twice as frequently as women.

Patients who have ankylosing spondylitis may awaken late at night or very early in the morning because of back pain and stiffness, which is eased with physical exercise or a hot shower. Enthesitis may cause pain and tenderness over the anterior chest wall, spinal processes, iliac crests, and sites of bony insertions of the Achilles and patellar tendons and plantar fascia. Peripheral arthritis, usually monoarticular or oligoarticular, is less common in primary ankylosing spondylitis than in “secondary” ankylosing spondylitis (in the context of psoriatic arthritis, reactive arthritis, or IBD).

Table 1 – The European Spondyloarthropathy Study Group classification criteria

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory spinal pain, including at least 4 of these 5 components: (1) duration of at least 3 months, (2) onset before age 45 years, (3) insidious onset, (4) improvement seen with exercise, and (5) association with morning spinal stiffness</td>
<td>History of spinal pain or current symptoms (low, middle, and upper back or neck region)</td>
</tr>
<tr>
<td>Synovitis</td>
<td>Past or present asymmetrical arthritis or arthritis seen mostly in the lower limbs</td>
</tr>
<tr>
<td>Spondyloarthropathy</td>
<td>Inflammatory spinal pain or synovitis and 1 or 2 of the following: (a) increased HLA-B27, (b) HLA-B27-antinuclear antibody positivity, or (c) HLA-B27-rheumatoid factor positivity</td>
</tr>
</tbody>
</table>

Page 1 of 8
more of the following:

- A family history of first- or second-degree relatives with AS, psoriasis, acute iritis, ReA, or IBD
- Past or present psoriasis (with a physician diagnosis)
- Past or present ulcerative colitis or Crohn disease (with a physician diagnosis confirmed by radiography or endoscopy)
- Past or present alternating buttocks pain
- Past or present spontaneous pain or tenderness at insertion site (Achilles tendon or plantar fascia)
- Episode of diarrhea within 1 month before onset of arthritis
- Nongonococcal urethritis or cervicitis within 1 month before onset of arthritis
- Bilateral grade 2 to grade 4 sacroilitis or unilateral grade 3 or grade 4 sacroilitis

AS, ankylosing spondylitis; ReA, reactive arthritis; IBD, inflammatory bowel disease.


---

Tenderness may be noted over the sacroiliac joints, spinal processes, and other bony prominences. In some patients, pain in the sacroiliac joint area may be elicited with sacroiliac stress testing by using maneuvers such as the FABERE test (hip Flexion, Abduction, External Rotation, and Extension). Costovertebral and costotransverse joint involvement may result in diminished chest expansion. Gradual impairment of spinal mobility may be noted on lateral and forward flexion, hyperextension, and axial rotation of the lumbar and cervical spine. Limitation of forward flexion of the lumbar spine may be measured with the modified Schober test; occiput-to-wall distance measures the forward stooping deformity of the neck.

Acute anterior uveitis, the most common extraskeletal manifestation of ankylosing spondylitis, occurs in up to 40% of patients with ankylosing spondylitis, especially those who possess the *HLA-B27* gene. If not recognized and managed early, uveitis may lead to visual impairment. Subclinical lung abnormalities are somewhat common in patients with ankylosing spondylitis; however, clinical pulmonary manifestations are uncommon. Other less common extraskeletal manifestations of ankylosing spondylitis may involve the gut, aorta, or heart. Cauda equina syndrome is a rare neurological complication of ankylosing spondylitis.

In the absence of diagnostic criteria for ankylosing spondylitis, the modified New York criteria are the most commonly used classification criteria (Table 2). These criteria are highly specific rather than sensitive and are used mainly for including patients in clinical studies.

**Psoriatic arthritis.** This inflammatory arthritis occurs in 10% to 30% of patients with psoriasis, which may not be readily apparent because psoriasis lesions may be limited to the scalp, ears, umbilicus, perineum, and perianal area. Therefore, a thorough skin examination should be performed in every patient with inflammatory arthritis.

The onset of arthritis usually follows or coincides with the onset of psoriasis, although it may antedate psoriasis in up to 15% of patients. Arthritis may present in various overlapping forms, including polyarthritis, asymmetrical oligoarthritis (involving fewer than 5 joints), arthritis that is primarily limited to the distal interphalangeal (DIP) joints, monarthrits, arthritis mutilans, sacroilitis, and spondylitis. The polyarthritis form resembles RA but has several features characteristic of psoriatic arthritis, including the involvement of the DIP joints; the presence of dactylitis, or “sausage digits,” and enthesitis; and nail involvement (discoloration, onycholysis, ridging and, especially, pitting). Psoriatic spondylitis is clinically similar to ankylosing spondylitis but is more often associated with peripheral arthritis and less often with uveitis.
Table 2 – The modified New York classification criteria for ankylosing spondylitis

<table>
<thead>
<tr>
<th>Clinical components:</th>
<th>low back pain and stiffness for more than 3 months that improves with exercise but not with rest; limitation of lumbar spine mobility in both the sagittal and frontal planes; and limitation in chest expansion, compared with normal range for patient’s age and sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiological component:</td>
<td>unilateral grade 3 or grade 4 sacroiliitis or bilateral grade 2 or higher sacroiliitis</td>
</tr>
<tr>
<td>Grading:</td>
<td>definite ankylosing spondylitis if the radiological component is associated with at least 1 clinical component; probable ankylosing spondylitis if 3 clinical components are present or the radiological component is present without signs or symptoms that satisfy the clinical component</td>
</tr>
</tbody>
</table>


Reactive arthritis. This condition classically occurs within 1 to 4 weeks after a triggering infection of the gut or the genitourinary tract, although many patients may not recall such a history. Patients with reactive arthritis usually present with acute, asymmetrical oligoarthritis of the lower extremities. They also may have constitutional symptoms, urethritis, cervicitis, conjunctivitis, uveitis, genital lesions (circinate balanitis or vulvitis), keratoderma blennorrhagica, dactylitis, enthesitis, nail discoloration and onycholysis without nail pitting, or sacroilitis/spondylitis. The uncommon classic triad of arthritis, conjunctivitis, and urethritis may be present in a subset of patients with reactive arthritis.

Reactive arthritis must be distinguished from other arthropathies that present in a similar fashion, especially psoriatic arthritis, septic arthritis, gout, pseudogout, juvenile arthritis, and sarcoid arthropathy. Poststrepococcal reactive arthritis has been described in patients who do not meet the classification criteria for rheumatic fever. HIV infection has been strongly associated with reactive arthritis, psoriatic arthritis, and undifferentiated spondyloarthropathy in sub-Saharan populations in Africa.

Arthritis of IBD. Arthritis occurs in about 30% of patients who have IBD; arthritis of IBD manifests with inflammatory back pain, enthesitis, or peripheral arthritis, fulfilling the ESSG criteria for spondyloarthritis; 10% of patients fulfill the criteria for ankylosing spondylitis. In addition, some patients have asymptomatic sacroiliitis. Peripheral arthritis usually is nonerosive and, unlike axial disease, correlates with the IBD activity.

Undifferentiated spondyloarthropathy. This encompasses related disorders such as isolated enthesitis or dactylitis and RF-negative oligoarthritis or polyarthritis; it usually involves the lower extremities and often is HLA-B27–associated. Patients who have undifferentiated spondyloarthropathy may have episodes of acute anterior uveitis with 1 of the above-mentioned features but not psoriasis or GI or genitourinary tract involvement.

LABORATORY FEATURES
The C-reactive protein (CRP) level and erythrocyte sedimentation rate (ESR) often are elevated with peripheral joint involvement in patients with spondyloarthropathies, but they may be normal in many patients, especially those who have isolated axial disease. Anemia of chronic disease might occur. Synovial fluid analysis shows inflammatory changes that are nonspecific; the results of bacterial studies typically are negative, although the studies should be performed to rule out septic arthritis. The results of a fecal occult blood test may be abnormal in patients with IBD. When reactive arthritis is suspected clinically, bacterial studies (eg, throat cultures and tests for urogenital and enteric infection) might provide helpful information, although they may not be necessary for making the diagnosis. Consider HIV testing in high-risk patients.

Testing for the HLA-B27 gene may help in some clinical situations (eg, when the clinician estimates that the pretest disease probability is about 50% and the radiographic evidence for sacroiliitis is equivocal or absent). Testing for HLA-B27 cannot be used for screening or as a routine test for making a diagnosis of ankylosing spondylitis and related spondyloarthropathies because these diseases may occur in the absence of this gene and it may be present in a sizable percentage of healthy persons.

RADIOLOGICAL FEATURES
Radiographic evidence of sacroiliitis is a characteristic feature of ankylosing spondylitis; it usually is...
bilateral and symmetrical in primary ankylosing spondylitis and typically first involves the lower synovial part of the joint (Table 3). However, sacroiliitis often is unilateral or asymmetrical in reactive arthritis and psoriatic arthritis.

### Table 3 - The New York criteria for grading radiological evidence of sacroiliitis in ankylosing spondylitis

<table>
<thead>
<tr>
<th>Grade</th>
<th>Label</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
<td>Clear margins, uniform width, no juxta-articular sclerosis</td>
</tr>
<tr>
<td>1</td>
<td>Suspicious</td>
<td>Abnormality suspected</td>
</tr>
<tr>
<td>2</td>
<td>Minimal sacroiliitis</td>
<td>Evidence of some sclerosis and minimal erosions, no marked joint-space narrowing</td>
</tr>
<tr>
<td>3</td>
<td>Moderate sacroiliitis</td>
<td>Definite sclerosis on both sides of joint, interosseous space erosions and widening</td>
</tr>
<tr>
<td>4</td>
<td>Ankylosis</td>
<td>Joint obliteration, possibly with residual sclerosis</td>
</tr>
</tbody>
</table>


Obtaining an anteroposterior x-ray film of the pelvis may be sufficient for detecting sacroiliitis, but the results may be normal or equivocal early in the disease course. MRI with short tau inversion recovery technique, without the need for gadolinium enhancement, may detect sacroiliitis or spondylitis long before these abnormalities become evident on plain x-ray films. This offers the clinician an opportunity for early diagnosis, especially with the availability of more effective treatment in recent years. If MRI is not available or cannot be used, CT scanning may be helpful. The recently described total body MRI scan may very nicely identify the characteristic bone edema that results from osteitis/enthesitis at axial as well as peripheral sites. The scan takes only 30 minutes to perform. Technetium bone scanning is not very helpful for early detection of sacroiliitis, but it may be used to detect pseudoarthrosis or fracture. Spinal involvement may gradually lead to the squaring of vertebral bodies, formation of syndesmophytes, erosions and, later, ankylosis of facet joints and ligament ossification that are characteristic of ankylosing spondylitis. These changes ultimately may result in a completely fused spine that resembles a bamboo stick, hence the name “bamboo spine” (see Figure). Atlantoaxial fusion or subluxation also may occur. Spinal osteopenia, which is common, correlates with disease severity and duration. Measurements of the spine by dual-energy x-ray absorptiometry (DEXA) scan to detect osteoporosis may be less reliable than measurements at the femoral neck because of the presence of spinal syndesmophytes and ligamentous ossification. Peripheral DEXA scanning may be used in patients who have had bilateral hip arthroplasty. Radiographic findings in patients with ankylosing spondylitis secondary to psoriatic arthritis or reactive arthritis may be asymmetrical, with skip lesions or nonmarginal, large, asymmetrical syndesmophytes or both. Radiographic features of psoriatic arthritis include erosions, periostitis, bony ankylosis, and destructive “pencil-in-cup” deformities (a bone’s distal head becomes pointed and the adjacent joint surface becomes cuplike because of erosions in the hands and feet). Periarticular osteopenia, often seen in RA, is a not a typical feature in the spondyloarthropathies. Radiographic evidence of sacroiliitis, especially unilateral or asymmetrical, may result from other causes, including infections (eg, brucellosis and tuberculosis), but the clinical presentation usually is sufficiently discernible from that of ankylosing spondylitis and related spondyloarthropathies. Osteitis condensans illi (sclerosis of the iliac side of the sacroiliac joints without cortical erosions or
joint-space changes) also must be distinguished from sacroilitis in women, especially those with a history of multiple pregnancies. Diffuse idiopathic skeletal hyperostosis (DISH), also known as ankylosing hyperostosis or Forestier disease, may be confused with ankylosing spondylitis but usually occurs in older patients. DISH is characterized by flowing ligamentous ossification, especially of the anterior longitudinal ligament, and the absence of typical sacroilitis, although capsular ossification may diminish the clarity of the sacroiliac joints on roentgenographic images.  

MANAGEMENT  
The management of spondyloarthropathies should be individualized according to the patient’s clinical presentation, comorbidities, and wishes. Guidelines have been published for ankylosing spondylitis management.  

Patient education. Provide patients with disease-specific written instructions and illustrations, handouts, books, pamphlets, videos, audiotapes, and information about useful Web sites. Self-help programs and patient education and counseling improve patients’ adherence to therapy regimens and benefit their general health and functional status.  

Exercise and physical therapy. A lifelong program of regular exercise should be encouraged; such a program should include spinal extension exercises; deep breathing; and range of motion exercises of the back, neck, shoulders, hips, and other joints. Swimming and aquatic exercises and other appropriate recreational exercises are especially useful. High-impact and contact sports activities and those that involve abrupt movement of the spine should be avoided, especially by patients who have axial disease with limited spinal mobility. Short-term intensive physical therapy followed by lifelong home exercises might be helpful for patients with spondyloarthropathies, including core strengthening of trunk muscles. However, the role of physical therapy has not been assessed since TNF-α inhibitors became available. 

Pharmacological treatment. NSAIDs given at the full anti-inflammatory dose are the first line of treatment for patients with the spondyloarthropathies; it is better to take them regularly. Because of variation of response, some patients may need to be switched to other NSAIDs in order to find the most effective one before giving up on NSAIDs for disease management. The traditional disease-modifying antirheumatic drugs—eg, methotrexate (MTX), leflunomide, and sulfasalazine—are not recommended for managing axial disease because they lack efficacy. However, they may be considered in patients with peripheral arthritis. Oral corticosteroids should be avoided, but intra-articular or local corticosteroid injection may provide rapid relief in monarticular or oligoarticular peripheral arthritis or enthesitis. Osteoporosis is common in patients with spondyloarthropathies and should be recognized and managed early; adequate intake of calcium and vitamin D should be ensured. Patients with Chlamydia-induced reactive arthritis and their sex partners may need to be treated with appropriate antibiotics simultaneously to more effectively eradicate the infection, although such treatment may not alter the natural disease course.  

All 3 TNF-α inhibitors—infliximab, etanercept, and adalimumab—are highly and equally effective in patients with active ankylosing spondylitis and in those with psoriatic arthritis and enteropathic arthritis that is unresponsive to conventional therapy. These biologic agents also are very effective in managing the cutaneous and nail lesions of psoriasis. Infliximab and adalimumab (monoclonal antibodies) are effective in managing IBD, but etanercept (receptor-fusion protein) lacks
such an effect. The monoclonals also are somewhat more effective in preventing recurrences of acute anterior uveitis.

The TNF-α inhibitors are effective as monotherapy without concomitant MTX, and they have maintained long-term effectiveness. 2,18,28 Clinical improvement is accompanied by a significant decrease in inflammation, as evidenced by a dramatic reduction of the CRP level and ESR; the improvement also may be demonstrated on MRI, but it is too early to say that these agents will slow down or prevent progressive bony ankylosis. 2,28 A few patients with reactive arthritis and with undifferentiated spondyloarthropathy that is refractory to traditional therapies who have been treated with TNF-α inhibitors also have shown good response. 29

Guidelines for the use of TNF-α inhibitors for the spondyloarthropathies have been developed (Table 4). 18,30 Treatment must be continued on a long-term basis to maintain disease control. When one TNF-α inhibitor has not succeeded or adverse effects develop that are not related to the TNF-α inhibitors as a class, switching to another agent may be indicated. The TNF-α inhibitors are expensive and may be associated with potentially serious adverse effects, including allergic and injection-site reactions, and an increased risk of infections, including reactivation of tuberculosis.

REFERRALS
In cases of acute anterior uveitis, ophthalmological evaluation is urgently needed. In cases of other extraskeletal complications, consider referral to a cardiologist, pulmonologist, or other specialist. In patients of all ages who have advanced hip or knee joint damage with intractable pain or disability or both, surgical referral should be considered for total joint replacement. The risk of heterotopic bone formation around the prosthesis may be reduced by use of NSAIDs for 7 to 10 days from the day of surgery. 31 Any new-onset neck or back pain in a patient with ankylosing spondylitis should be evaluated carefully for a spinal fracture or instability, even in the absence of trauma or after a seemingly trivial injury, because paraplegia or quadriplegia may result. If fracture is suspected, the neck should be immobilized as a precaution pending musculoskeletal imaging. The x-ray findings may be normal, but MRI, CT, or bone scan results may be more helpful in confirming or excluding spinal fracture.

Elective spinal surgeries that might be indicated include osteotomy to correct severe kyphosis and uncompensated loss of horizontal vision and fusion procedures for instability, including atlantoaxial subluxation, pseudoarthrosis, and fracture. General anesthesia is associated with intubation difficulties in cases of cervical spine ankylosis and deformity and involvement of the temporomandibular joint. The risk of pulmonary complications increases during the postoperative period, and special care is required.

**Therapeutic Agents in This Article**
Adalimumab (Humira)
Calcium*
Etanercept (Enbrel)
Infliximab (Remicade)
Leflunomide (Arava)
Methotrexate* (Trexall)
Sulfasalazine* (Azulfidine)
Vitamin D*
*Available in a generic formulation.

**References:**
Spondyloarthropathies: Update on Diagnosis and Therapy

Published on Patient Care Online (http://www.patientcareonline.com)


Source URL:

Links: