CHAPTER Spondylarthropathies

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The spondylarthropathies are a group of overlapping chronic inflammatory rheumatic diseases that includes ankylosing spondylitis (the prototype of this group), reactive arthritis, psoriatic arthritis, arthritis of inflammatory bowel disease, and undifferentiated spondylarthritis (1–4). There can be some overlap in the clinical features of the spondylarthropathies, especially in their early stages (1), which may make it difficult to differentiate between them. However, this overlap does not usually influence treatment decisions.

EPIDEMIOLOGY

The prevalence of spondylarthopathies varies among different ethnic groups and ranges from 0.5% to 1% in Europe (2,3). Spondylarthopathies affect both sexes, although they are somewhat more common in men. They tend to cluster in families, and symptoms usually start in late teens and early twenties.

ETIOLOGY AND PATHOGENESIS

The etiology of the spondylarthopathies is unknown; but they show a strong association with the HLA-B27 allele. The strength of this association varies among the different spondylarthropathies and among various ethnicities (5). There is an increased incidence of spondylarthropathies in first-degree relatives of affected individuals (6). An immune-mediated mechanism supported by the activation of T cells and macrophages results in local increase in the concentration of the proinflammatory cytokines, especially tumor necrosis factor α (TNF α), interleukin-1, and interferon-gamma (7). Inflammation may result in erosions, followed by a healing phase and ossification of the ligaments with resultant bony fusion or ankylosis, as seen in ankylosing spondylitis (AS). The primary pathologic sites include the entheses (the sites of bony insertion of ligaments and tendons) in the axial skeleton and extremities. Some nonarticular structures, such as the eye, gut, skin, and aortic valve can also be involved (1,6,8,9). Ankylosing spondylitis begins with sacroiliitis in most patients before it involves the spine.

The role of infection has been demonstrated in reactive arthritis, usually triggered by genitourinary infection with *Chlamydia trachomatis*, or enteritis due to bacteria such as *Shigella*, *Salmonella*, *Yersinia*, or *Campylobacter*. However, inflamed joints do not show evidence of active infection when fluid is cultured for bacteria (1,10). There is no evidence to support the role of infection in other forms of spondylarthropathies.

CLINICAL MANIFESTATIONS

Ankylosing Spondylitis

AS usually presents with chronic inflammatory low back pain, which is defined by having at least 4 of the following 5 characteristics: 1) insidious onset, 2) onset before age 45 years, 3) duration of at least 3 months,

4) worsening of pain with inactivity and improving with physical exercise, and 5) stiffness on waking up in the morning (1,6,11,12). The disease usually involves the axial skeleton, including the sacroiliac joints. In very early stages the patient may complaint of alternating buttock pain due to inflammation of the sacroiliac joints. The disease can involve the hip and shoulder joints, and sometimes the more peripheral joints of the limbs can be affected, especially in the presence of associated reactive arthritis, psoriasis, or inflammatory bowel disease.

Back pain results from involvement of the discovertebral, facet, costovertebral, and costotransverse joints of the spine and the paravertebral ligaments (1,6,8). With disease progression, there is a gradual loss of mobility, flattening of the lumbar spine, and exaggerated thoracic spine kyphosis (6,8,11). Enthesitis can also result in plantar fasciitis, Achilles tendinitis, or patellar tendinitis (13).

One or more episodes of acute anterior uveitis occur in 25-40% of patients with AS (1,8,14). Involvement of the gastrointestinal tract, aorta, heart, or lung can also be seen as a part of this disease in some patients, and they may have an increased risk of coronary artery disease (1,8,15,16).

Physical findings in AS include tenderness over the sacroiliac joints and pain with sacroiliac stress tests, such as FABERE (hip Flexion, **AB**duction, External Rotation, and Extension). Enthesitis may cause tenderness over the spinal processes, the heels, iliac crest, anterior chest wall, and other bony prominences (1,8,13). There might be a decrease in chest expansion, which is normally at least 5 cm in healthy young individuals at the level of the xiphisternum. Measures of spinal mobility, such as modified Schober's test and lateral flexion, are important in the assessment of the AS (11,17). Occiput-to-wall or tragus-to-wall distances measure forward stooping deformity of the cervical spine (18). Cervical spine involvement can result in progressive limitation of the ability to turn or fully extend or laterally bend the neck.

Psoriatic Arthritis

Psoriatic arthritis is defined as an inflammatory arthritis associated with psoriasis. Inflammatory arthritis occurs in 10–30% of patients with psoriasis, and may present in different forms: monarthritis, asymmetric oligoarthritis (<5 joints), polyarthritis, arthritis of distal interphalangeal joints, arthritismutilans, and spondylitis, although there can be significant overlap among these subtypes (1,19,20). The polyarthritis form can clinically resemble rheumatoid arthritis, although it is relatively less painful (21,22). Psoriatic arthritis is often associated with tendinitis or enthesitis. Inflammation of the entire digit involving the joints, ligaments, and the tendon sheaths (dactylitis or "sausage digits") is one of the typical features of psoriatic arthritis. Axial disease can be similar to AS, although it can sometimes be relatively asymptomatic.

It is important to extensively search the whole skin for lesions of psoriasis when evaluating a patient with any form of inflammatory arthritis or spondylitis. This search should include the scalp, ears, umbilicus, pelvic area, perineum, and perianal area. There is no correlation between the severity of skin lesions and the severity of arthritis (23).

The onset of psoriatic arthritis is usually in the fourth or fifth decade. Patients usually have had psoriasis for some time before the arthritis

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starts, but in about 15% of patients, arthritis precedes psoriasis (1). Nail changes of psoriasis, such as pitting or onycholysis, are more common in patients with psoriatic arthritis than in psoriasis patients without arthritis (1,19,20). Occurrence of psoriasis and psoriatic arthritis or undifferentiated spondylarthropathy in sub-Saharan Africa has been associated with HIV infection (19,20,24,25).

Reactive Arthritis

Reactive arthritis typically occurs within 1 month of an inciting genitourinary or enteric infection. It usually manifests by acute, asymmetric oligoarthritis and is often associated with conjunctivitis, uveitis, enthesitis, dactylitis, genital psoriasiform lesions (circinate balanitis or circinate vulvitis), urethritis, or cervicits (10,16,26,27). The term Reiter syndrome has been used to describe the association of reactive arthritis with conjunctivitis and urethritis, although most patients with reactive arthritis do not have the complete triad.

Enteropathic Arthritis

Inflammatory bowel disease (ulcerative colitis and Crohn disease) can be associated with a form of inflammatory arthritis called enteropathic arthritis or spondylarthropathy of inflammatory bowel disease (28–30). Up to 37% of patients with ulcerative colitis or Crohn disease may show sacrolliitis, spondylitis, enthesitis, or peripheral arthritis. Definite AS is seen in ~10% of these patients (28). Peripheral arthritis is usually self-limited and nondestructive; it, contrary to axial disease, parallels the activity of bowel involvement. On endoscopy, subclinical enteric mucosal inflammation is found in 26–69% of patients with AS and related spondylarthropathies, and could be considered as one of the extraskeletal manifestations (29). The risk of developing clinical inflammatory bowel disease approaches 6% in such patients when the histology is acute and it is 15–25% in patients with histologically chronic inflammation (28–30).

Undifferentiated Spondlyarthropathies

The undifferentiated forms of spondylarthropathies include HLA– B27-associated enthesitis, dactylitis, and rheumatoid factor-negative oligoarthritis or polyarthritis (31). The arthritis usually involves the lower extremities, without an identifiable infectious trigger or the presence of psoriasis or inflammatory bowel disease (1,31). Some patients may present with episodes of isolated acute anterior uveitis (1,14,32), which may precede the onset of the spondylarthropathy.

RADIOGRAPHIC FEATURES

The spondylarthropathies are characterized by the radiographic evidence of sacroiliitis, which ranges from suspicious changes to sclerotic margins, erosions, and pseudowidening to complete ankylosis of the sacroiliac joints. Spinal changes on plain films include squaring of the vertebral bodies, formation of syndesmophytes, involvement of the facet joints, spondylodiscitis, ligament ossification, and a *bamboo spine*. Spinal osteoporosis is commonly seen and it correlates with disease severity and duration (33). Conventional radiographs may also reveal soft-tissue swelling or erosive changes in the peripheral joints. Some of the classic findings of psoriatic arthritis include periosteal reactions, ankylosis, and pencil-in-cup deformities in the hands and feets.

Radiographic sacroiliitis is required for the definite diagnosis of AS according to the Modified New York Classification Criteria (34).

An anteroposterior film of the pelvis is usually adequate for detecting sacroiliitis (35). However, in the presence of high clinical suspicion but normal x-ray, a magnetic resonance image (MRI) with the STIR (Short Tau Inversion Recovery) (or a computed tomograph) can be very helpful (35–38).

LABORATORY FEATURES

There are no specific laboratory tests for spondylarthropathies. Acute phase reactants, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) can be elevated, especially when peripheral joints are inflamed; but their sensitivity and specificity are low in patients with pure axial disease (39,40). There is no association with rheumatoid factor and antinuclear antibody tests. Synovial fluid analysis is nonspecific. Stool testing may be of value in screening for inflammatory bowel disease.

Testing for HLA–B27 can be helpful in certain clinical situations, but it is not a routine or test because the spondylarthropathies can occur in the absence of HLA–B27. Moreover, HLA–B27 can be present in perfectly healthy people (4,5,41,42).

When there is a clinical suspicion of reactive arthritis, throat cultures for streptococcal infection and tests for urogenital *Chlamydia* and enteric infection, such as *Salmonella*, *Yersinia* and *Campylobacter*, are indicated (10,26). Testing for HIV should always be considered in high-risk patients (43,44).

DIAGNOSIS

The diagnosis of spondylarthropathies is based on a combination of clinical and radiographic manifestations, and there are no validated diagnostic criteria. Instead, there are classification criteria, which are by design highly specific (to be used in clinical studies) and therefore have a relatively low sensitivity. The Modified New York Criteria (Table 1) (34) are the most commonly used classification criteria for AS.

The diagnosis of AS can be challenging due to the lack of a specific diagnostic test and the insidious onset with mild and nonspecific symptoms especially early in its course (11). Furthermore, radiologic changes are often not apparent in the early stages (36). Thus, the diagnosis, which averages 3 to 11 years from the onset of symptoms, is often missed or markedly delayed. The delay can be even longer in women, children, adolescents, and HLA–B27-negative patients (2,45,46).

Table 1. The modified New York criteria for ankylosing spondylitis*

Diagnosis

- Clinical criteria
- Low back pain and stiffness for >3 months that improves with exercise but not with rest
- Limitation of lumbar spine mobility in both the sagittal and frontal planes
- Limitation in chest expansion as compared with normal range for age and sex

Radiologic criteria

- Unilateral sacroiliitis of grade 3–4 OR
- Bilateral sacroiliitis of grade ≥2

Grading

- Definite AS if the radiological criterion is associated with at least 1 clinical criterion
- Probable AS if:
 - 3 clinical criteria are present OR
- The radiological criterion is present without any signs or symptoms satisfying the clinical criteria

* Adapted with permission from reference 24.

Rudwaleit et al (47) have proposed decision trees to help primary care physicians who suspect the presence of axial spondylarthropathy appropriately refer patients to rheumatologists in early phase of the disease. They have highlighted some of the clinically pertinent parameters (Figure 1), with each parameter having a diagnostic value, expressed as the likelihood ratio. The presence of 4 or more of these parameters in a patient with inflammatory back pain without radiographic evidence of sacroiliitis would strongly support the diagnosis of axial undifferentiated spondylarthritis (45).

CLINICAL COURSE

The course of AS varies among patients and can be characterized by spontaneous remissions and exacerbations (1,6). However, the typical spinal deformities may become noticeable within the first 10 years. The longer the diagnosis is delayed, the worse the functional outcome could be, especially in patients with juvenile-onset disease (46). Some patients have a limited disease and may never develop spinal ankylosis (1,48).

The course of psoriatic arthritis depends, in part, on the clinical presentation. Patients with symmetric polyarthritis tend to have a similar course to rheumatoid arthritis, with the development of deformities and more tendency for bony ankylosis of the proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints (19,20,49). Arthritis mutilans, a rare form of psoriatic arthritis, results in osteolysis of the hand bones with severe destruction and deformity. Axial disease in psoriatic arthritis is similar to that in AS in that it may lead to spinal fusion, although it tends to be milder (19,20).

Reactive arthritis symptoms usually last for up to 5 months, although some patients may continue to have mild symptoms for >1 year (10). Up to one-third of the patients may continue to have chronic or recurrent arthritis, sacroiliitis, or spondylitis (10,50).

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TREATMENT

The treatment of spondylarthropathies should be individualized based on the symptoms and signs, the disease activity and severity, functional status, deformities, general health status, comorbid conditions, and the patient's wishes (51).

The ASAS (Assessment in Ankylosing Spondylitis) International Society and the European League Against Rheumatism (EULAR) have recently published international recommendations for the management of AS that will be updated regularly to incorporate any future advances (51). They contain 10 key recommendations (not guidelines) based on scientific evidence and expert opinion. The optimal management requires a combination of nonpharmacologic and pharmacologic treatments, with appropriate monitoring that depends on symptoms, severity, and drug treatment (51).

Nonpharmacologic Treatment

Patient education is an essential part of the nonpharmacologic treatment in AS, and should include a life-long program of regular exercise. Usefulness of individual and group physical therapy, patient associations, and self-help groups is also emphasized.

Exercise tends to improve outcome. Unsupervised recreational exercise with specific back exercises improves pain, stiffness, function, and quality of life in patients with AS (52,53). Prolonged formal physical therapy is costly and is not covered by most health insurance



Figure 1. Decision tree to assist in the diagnosis of axial spondylarthritis. AS = ankylosing spondylitis; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; MRI = magnetic resonance imaging; Neg = negative; NSAIDs = nonsteroidal antiinflammatory drugs; Pos = positive; SpA = spondylarthritis. Reprinted with permission from reference 37.^{F0:1}

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plans, but a physical therapist can instruct patients about proper posture and self-administered exercise in addition to recreational sports and a regular exercise program. Written instructions and illustrations should be provided to patients. An individual therapeutic exercise program along with education significantly improves function after a few months; this improvement can be maintained by minimal maintenance therapy (54,55). Home-based exercise may decrease pain and improve spinal mobility, as well as the general sense of wellbeing (56).

Stretching exercises for different muscle groups relieve acute muscle spasm and improve mobility, chest expansion, endurance, and posture (54,57). Deep-breathing exercises should be encouraged, which can be prepared for by local heat or analgesics to relieve pain from costochondritis. Patients should be advised to avoid smoking. After adequate pain and stiffness control is achieved, muscle-strengthening exercises can be initiated. Patients should exercise when their tiredness is at minimum. They should prepare for exercise by taking a warm shower or applying local heat and engaging in a light warm-up, including gentle arm movement or walking.

Swimming and water exercises are very helpful. Warm water helps promote relaxation and reduces the discomfort of stretching. Furthermore, water exercises strengthen muscles because of the water's resistance and increase cardiovascular conditioning and endurance. Patients with heart disease should be assessed by their physician, which may require an exercise tolerance test prior to initiation of exercise. Patients with psoriasis should avoid chlorinated water (57).

Physical therapy is cost-effective and beneficial for patients with AS, although there is no clear evidence that favours a specific treatment protocol (54,55,58–60). Short-term intensive physical therapy and exercise improves mobility of the spine, hip, and shoulder (61). Group physical therapy with home exercises may be superior to individual physical therapy in terms of patient global assessment of improvement and spinal mobility (60), although results from another clinical study did not reproduce the same results (62). Intensive in-patient physio-therapy and hydrotherapy with home exercises may provide short-term advantages over home exercise alone in improving pain and stiffness (63). This form of therapy can be considered in patients with severe decline in functional capacity.

Pharmacologic Treatment

Nonsteroidal antiinflammatory drugs (NSAIDs) are the cornerstone of treatment, and they need to be taken regularly in full antiinflammatory doses to achieve the desired therapeutic effect (64–67). The traditional disease-modifying antirheumatic drugs (DMARDs), including methotrexate, leflunomide, and sulfasalazine, are not recommended for the treatment of axial disease. Sulfasalazine may be considered in patients with peripheral arthritis.

The use of systemic corticosteroids is not supported by evidence, but topical use is very effective in treating acute iritis. Intraarticular or local steroid injection provides rapid relief of active inflammation of the peripheral joints and enthesitis in select patients in the absence of contraindications (51,68,69).

The use of antibiotics is not supported by evidence from the literature except for cases of reactive arthritis preceded by a known bacterial infection, especially *C trachomatis*. Appropriate antibiotics may reduce the duration of reactive arthritis (70), but this therapy does not seem to alter the long-term history of the disease (71).

EQ:1

TNF-blockers (discussed extensively in Chapter XX)^{EQ:1} are remarkably effective in treating AS patients with persistently high disease activity despite conventional therapy (51,72,97). In patients with axial disease, there is no need for an obligatory use of DMARDs prior to or concomitant with anti-TNF therapy. These drugs are also dramatically effective in treating psoriasis, psoriatic arthritis, and inflammatory bowel disease. Etanercept, however, is not effective in treating inflammatory bowel disease.

Effective TNF inhibition results in rapid and dramatic improvement in the symptoms and signs of spondylarthropathies, including back symptoms, peripheral arthritis, enthesitis, dactylitis, and psoriasis in the majority of patients. Both pain and function improve remarkably, with significant decrease in spinal inflammation as evident with MRI (72–84). TNF inhibition may also slow radiographic disease progression (78,79). Their efficacy has been shown to be persistent in the long term (78,85–89). Another advantage of TNF inhibitors may be the significant reduction in the frequency of anterior uveitis flares (90).

For initiation of anti-TNF therapy in AS, patients should fulfill the Modified New York Criteria for definitive AS. The disease must be active for at least 1 month as determined by a Bath Ankylosing Spondylitis Disease Activity Index score of ≥ 4 . Initiation of such treatment should be decided by an expert on the subject. The patient must have failed to show adequate therapeutic response to at least 2 different NSAIDs given for at least 3 months at maximal recommended or tolerated antiinflammatory dose (unless there is intolerance, toxicity, or contraindications to the use of NSAIDs). Those with AS and peripheral arthritis must have failed to respond to adequate therapy with both NSAIDs and sulfasalazine, and those with enthesitis must have failed at least 2 local steroid injections before anti-TNF therapy is started (91). A few patients with reactive arthritis refractory to traditional therapies have responded to treatment with TNF blockers (92).

For psoriatic arthritis, TNF inhibitors can be used in combination with other therapies, such as methotrexate, the required dose of which may be reduced (1). One may switch from one anti-TNF agent to another in cases of inefficacy (primary versus secondary) or development of side effects to one agent. This should not be applied when adverse events are related to TNF inhibitors as a class (93–95).

Treatment of AS and proriatic arthritis patients with TNF inhibitors needs to be continued indefinitely to maintain therapeutic effects, because discontinuation would result in inflammation recurrence (96). Unlike infliximab, etanercept does not risk losing it efficacy if readministered after repeated discontinuations (97).

Osteoporosis is common in AS patients, and should be recognized and treated appropriately. It can occur relatively early in the disease. Spinal osteoporosis is caused partly by the ankylosis and decreased mobility and also secondary to the effect of proinflammatory cytokines (98,99). Adequate calcium and vitamin D intake should be encouraged. Prevention and treatment of osteoporosis may help decrease the risk of spinal deformities and fractures. Measurements of bone density at the spine may be unreliable when there is ligamentous ossification and formation of syndesmophytes. Thus, femoral neck measurements should be relied on for the diagnosis. Sometimes a peripheral dual-energy x-ray absorptiometry scan might be needed in patients with bilateral hip arthroplasties. Treatment for osteoporosis includes bisphosphonates or, sometimes, parathyroid hormone.

Patient Education

Patient education, behavioral therapy, counseling, and self-help programs improve patients' compliance with therapeutic regimens; decrease their pain; may have a positive impact on general health, motivation, compliance, and functional status; and may reduce the cost of conventional therapy (100–105). Patients who smoke should be urged to quit because smokers tend to have more severe illness in addition to increased incidence of respiratory complications (106).

Impact of the disease on the family should be discussed with the patient and possibly family members who are engaged in the care of

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Useful Web Sites for Patients

Arthritis Foundation: www.arthritis.org Spondylitis Association of America: www.spondylitis.org UpToDate Patient Information: http://patients.uptodate.com/ Arthritis Society: www.arthritis.ca.

the patient. Possibility of familial aggregation should be discussed, and it may help to increase the likelihood of early diagnosis in other family members.

Patients should be always encouraged to take a central role in managing their illness, and should be given information about diseasespecific associations, books, pamphlets, videos, and audiotapes. Those who believe that exercise is beneficial, are followed by a rheumatologist, and are more educated are most likely to adhere to the treatment regimen (107,108). Some patients use superficial heat or cold in the form of packs or a hot shower or bath to decrease stiffness. Patients should be encouraged to swim regularly if they can, and encouraged to perform deep breathing exercises at least twice daily to maintain a good chest expansion (102).

Posture and Gait

Specific exercises, such as spinal extension, need to be performed at least twice daily to maintain good posture and spinal mobility. Patients should be advised on proper posture during activities of daily living, including walking, sitting, and sleeping. This includes sleeping on a firm mattress without a pillow, with a thin pillow, or with a contoured pillow to maintain neck extension and prevent the development of spinal deformities. They should walk erect, keeping the spine as straight as possible while maintaining normal, reciprocal arm swing and rotational movements of the lower spine and pelvis. They should avoid activities that cause strain on back muscles, such as prolonged stooping or bending. Posture can be monitored using occiput-to-wall distance, which should be measured with the patient standing against the wall with heels, buttocks, and shoulders touching the wall, and the chin parallel to the floor. Body height should also be checked on a regular basis.

Patients should avoid positions that may lead to a stooped posture, such as slouching in chairs or leaning over a desk for prolonged periods; stretches should be performed regularly. Patients who work with computers, for example, can use a slightly tilted table to avoid a bending posture. To maintain hip extension, a 15-minute period of prone lying daily is advised. A rolled towel under the forehead may help turning the head to the side (57). In case of inability to lie flat in the prone position, the patient can use a pillow under the abdomen; or the patient can lie supine with the buttocks at the edge of the bed and hips extended.

Patient Concerns

High-impact sports or those that involve significant abrupt movement of the spine should be discouraged because of the increased risk of spinal injury. When swimming, patients may use snorkels and masks for breathing if they have restricted motion of the neck. Badminton, walking, and cross-country (but not downhill) skiing are good options. Some modifications, such as raising the bicycle handlebars, can be applied in cases of sports that require forward-flexed posture. Footwear can be adjusted to reduce the impact of some activities on the spine and reduce the discomfort of heel spurs. Patients should always have a period of warm-up to help relieve stiffness and decrease the likelihood of injury (57). Workplace needs should be evaluated and necessary modifications should be advised. Changing position frequently and taking breaks for stretching helps improve endurance.

Restrictions and Disability

Some functional difficulties frequently encountered include dressing, body transfers, lifting and carrying, and endurance (54). Problems in performing activities of daily living should be identified and solutions sought to compensate for loss of motion and improve functional capacity. Assistive devices, including ones for walking, can be used in certain cases—such as when there is lower-extremity joint problems. Some helpful devices include long-handled devices for dressing and reaching, adjustable swivel chairs with lumbar support, and elevated and inclined writing surfaces (57).

Postural changes that affect balance because of a displacement of the center of mass of the trunk pose safety concerns (109). It is important to take measures to prevent falls. Bathrooms should have nonslippery floors and should be equipped with safety measures, such as railings, grab bars, and safety mats (57).

Decreased range of motion of the cervical spine makes driving a real challenge; however, support of the neck and back by seat and headrest can be helpful, and wide-angled mirrors help increase peripheral vision (110). Crossing roads should be done with caution due to impaired neck mobility.

Role of Surgery

Surgery may be indicated when there is severe hip and knee damage. Total hip arthroplasty deserves consideration in patients with structural damage causing refractory pain or disability, irrespective of age; and there is no need to discontinue NSAID therapy for this surgery (51). It provides pain relief and improves function (51,111). The need for future revision depends on the age and sex of the patient (112), but is not specifically higher in patients with AS. Moreover, there is no specific increase in the incidence of heterotopic bone formation and ankylosis following hip replacement in AS patients (113–115).

Elective spinal surgeries for AS patients include osteotomy to correct severe kyphosis and uncompensated loss of horizontal vision. Corrective spinal osteotomy for severe kyphosis and fusion procedures for segmental instability may provide excellent functional improvement (51,116). Spinal fusion is indicated in cases of atlantoaxial subluxation and to relieve pain and correct deformity resulting from pseudoarthrosis (117).

A challenging aspect in the care for ankylosing spondylitis patients is using general anesthesia because of intubation difficulties resulting from cervical spine ankylosis and deformity and involvement of the temporomandibular joint, which decrease the ability to open the mouth. Spinal anesthesia can even be impossible due to spinal fusion and ligament ossification. Special attention should be paid during the postoperative period to prevent pulmonary complications, which tend to increase because of decreased vital capacity from restricted chest wall expansion (118). It is wise for such patients to carry an identification bracelet (like Medic-Alert) that provides special attention to such limitations.

FOLLOWUP AND MONITORING

Patients with spondylarthopathies should be followed on regular basis even if their illness seems to be inactive. The frequency of monitoring in AS should be based on the clinical presentation and therapy used.

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Rehabilitation Considerations for the Spondylarthropathies

- Encourage physical activities that promote extension (e.g., reading newpaper while laying prone on floor.
- Promote use of stretching exercise for the lower back, hips, and shoulders. Stretch should be held for 30 seconds.
- Modalities, such as ulstrasound, followed by exercise may enhance benefit of exercise.
- Aerobic exercise should be encorporated to promote general fitness.
- Frequent monitoring of vitals signs and use of interval training of 3 sets of 10 minutes of exercise versus 30 minutes can be used in patients with more severe cardiovascular involvement.
- Swimming strokes, such as breast stroke and freestyle, promote extension while building strength.
- Recommend use of orthotics and proper footwear to prevent onset or exacerbation of achilles tendinitis and plantar fasciitis.
- Encourage respiratory exercises to promote chest mobility.
- Enforce use of proper posture.

Monitoring includes following patient symptoms and signs (including axial and peripheral disease and extraskeletal manifestations), laboratory testing, and imaging studies. Specific skeletal elements to be monitored include duration of morning stiffness, severity of pain, mobility of the lumbar and cervical spine, chest expansion, enthesopathy, and changes in joint inflammation and range of motion.

Laboratory testing can be used as an adjunctive measure in monitoring response to therapy; however, CRP and ESR do not always correlate with disease activity (39,40). Other laboratory tests include complete blood count, renal function, and liver function tests to monitor for any adverse effects that might be caused by pharmacologic therapy.

Radiographic monitoring once every 2 years is usually sufficient but can be done more frequently in select cases. However, radiographs are not sensitive for changes over <1 year (119). Lateral cervical and lumbar spine films are usually sufficient, but radiographs of the thoracic spine may sometimes be needed, especially when a fracture is suspected.

Any new-onset neck or back pain in a patient with AS, even in the absence of trauma, should be carefully evaluated for spinal fracture or instability. There is high morbidity and mortality associated with transverse-displaced fractures of the neck, which can result in paraplegia or quadriplegia (120,121). Spinal pseudoarthrosis should be always kept in mind; it should be differentiated from indolent infections. Other rare neurologic complications that might be associated with AS include cauda equina syndrome, which is characterized by dull pain in the lower back and upper buttock region; analgesia in the buttocks, genitalia, or thighs (saddle area); and a disturbance of bowel and bladder function (122–124). It may result from chronic adhesive arachnoiditis, due to fibrous entrapment and scarring of the sacral and lower lumbar nerve roots. AS patients may rarely develop spontaneous atlantoaxial sublux-ation that may require surgery in some instances (125,126).

REFERENCES

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AQ:2

- Khan MA. Update on spondyloarthropathies. Ann Intern Med 2002; 136:896–907.
- Akkoc N, Khan MA. Epidemiology of ankylosing spondylitis and related spondyloarthropathies. In: Weisman MH, Reveille JD, van der Heijde D, editors. Ankylosing spondylitis and the spondyloarthropathies: a companion to rheumatology. London: Mosby:- Elsevier: 2006. p. 117–31.
- Sieper J, et al. Concepts and epidemiology of spondyloarthritis. Best Pract Res Clin Rheumatol. 2006;20:401–17.^{AQ:1}
- Elyan M, Khan MA. Diagnosing ankylosing spondylitis. J Rheumatol Suppl. In press.^{AQ-2}
- Khan MA. Prevalence of HLA-B27 in world populations. In: Lopez-Larrea C, editor. HLA-B27 in the development of spondyloarthropathies. Austin (TX): Landes; 1997. p. 95–112.

- van der Linden S, et al. Ankylosing spondylitis. In: Harris EJ, editor. Kelly's textbook of rheumatology. 7th ed. Philadelphia: Elsevier Saunders; 2005. p. 1125–41.^{AQ3}
- Smith JA, et al. Pathogenesis of ankylosing spondylitis: current concepts. Best Pract Res Clin Rheumatol 2006;20:571–91.^{AQ:1}
- Khan MA. Spondyloarthropathies. In: Hunder GG, editor. Atlas of rheumatology. Philadelphia: Current Medicine; 2002. p. 141–67.
- Francois RJ, Braun J, Khan MA. Entheses and enthesitis: a histopathologic review and relevance to spondyloarthritides. Curr Opin Rheumatol 2001;13:255–64.
- Khan MA, Sieper J. Reactive arthritis. In: Koopman WJ, Moreland LW, editors. Arthritis and allied conditions. 15th edition. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 1335–55.
- Khan MA. Ankylosing spondylitis: clinical features. In: Hochberg M, Silman A, Smolen J, Weinblatt M, Weisman M, editors. Rheumatology. 3rd ed. London: Mosby. 2003; p. 1161–81.
- Calin A, Porta J, Fries JF, Schurman DJ. Clinical history as a screening test for ankylosing spondylitis. JAMA 1977;237:2613–4.
- Francois RJ, Braun J, Khan MA. Entheses and enthesitis: a histopathologic review and relevance to spondyloarthritides. Curr Opin Rheumatol 2001;13:255–64.
- Banares A, Hernandez-Garcia C, Fernandez-Gutierrez B, Jover JA. Eye involvement in the spondyloarthropathies. Rheum Dis Clin North Am 1998;24:771–84, ix.
- Divecha H, Sattar N, Rumley A, Cherry L, Lowe GD, Sturrock R. Cardiovascular risk parameters in men with ankylosing spondylitis in comparison with non-inflammatory control subjects: relevance of systemic inflammation. Clin Sci (Lond) 2005;109:171–6.
- Lautermann D, Braun J. Ankylosing spondylitis: cardiac manifestations. Clin Exp Rheumatol 2002;20(6 Suppl 28):S11–5.
- Haywood KL, Garratt AM, Jordan K, Dziedzic K, Dawes PT. Spinal mobility in ankylosing spondylitis: reliability, validity and responsiveness. Rheumatology (Oxford). 2004;43:750–7.
- Heuft-Dorenbosch L, Vosse D, Landewe R, Spoorenberg A, Dougados M, Mielants H, et al. Measurement of spinal mobility in ankylosing spondylitis: comparison of occiput-to-wall and tragus-to-wall distance. J Rheumatol 2004;31:1779–84.
- Höhler T, Märker-Hermann E. Psoriatic arthritis: clinical aspects, genetics, and the role of T cells. Curr Opin Rheumatol 2001;13:273–9.
- Gladman DD. Current concepts in psoriatic arthritis. Curr Opin Rheumatol 2002;14:361–6.
- 21. Buskila D, Langevitz P, Gladman DD, Urowitz S, Smythe HA. Patients with rheumatoid arthritis are more tender than those with psoriatic arthritis. J Rheumatol 1992;19:1115–9.
- 22. Helliwell PS, Porter G, Taylor WJ. Polyarticular psoriatic arthritis is more like oligoarticular psoriatic arthritis, than rheumatoid arthritis. Ann Rheum Dis 2006 (Jul 13). [Epub ahead of print]
- 23. Cohen MR, Reda DJ, Clegg DO, Department of Veteran Affairs Cooperative Study Group on Seronegative Spondyloarthropathies. Baseline relationships between psoriasis and psoriatic arthritis: analysis of 221 patients with active psoriatic arthritis. J Rheumatol 1999;26:1752–6.
- 24. Njobvu P, McGill P. Psoriatic arthritis and human immunodeficiency virus infection in Zambia. J Rheumatol 2000;27:1699–702.
- Mijiyawa M, Oniankitan O, Khan MA. Spondyloarthropathies in sub-Saharan Africa. Curr Opin Rheumatol 2000;12:281–6.
- Sieper J, Rudwaleit M, Braun J, van der Heijde D. Diagnosing reactive arthritis: role of clinical setting in the value of serologic and microbiologic assays. Arthritis Rheum 2002;46:319–27.
- Leirisalo-Repo M. Early arthritis and infection. Curr Opin Rheumatol. 2005;17:433–9.
- de Vlam K, Mielants H, Cuvelier C, De Keyser F, Veys EM, De Vos M. Spondyloarthropathy is underestimated in inflammatory bowel disease: prevalence and HLA association. J Rheumatol 2000;27:2860–5.
- Queiro R, Maiz O, Intxausti J, de Dios JR, Belzunegui J, Gonzalez C, Figueroa M. Subclinical sacroiliitis in inflammatory bowel disease: a clinical and follow-up study. Clin Rheumatol 2000;19:445–9.
- Smale S, Natt RS, Orchard TR, Russell AS, Bjarnason I. Inflammatory bowel disease and spondyloarthropathy. Arthritis Rheum 2001;44:2728–36.
- Olivieri I, et al. Ankylosing spondylitis and undifferentiated spondyloarthropathies: a clinical review and description of a disease subset with older age at onset. Curr Opin Rheumatol. 2001;13:280–4.^{AQ:1}
- Pato E, Banares A, Jover JA, Fernandez-Gutierrez B, Godoy F, Morado C, et al. Undiagnosed spondyloarthropathy in patients presenting with anterior uveitis. J Rheumatol 2000;27:2198–202.
- Barozzi L, Olivieri I, De Matteis M, Padula A, Pavlica P. Seronegative spondylarthropathies: imaging of spondylitis, enthesitis and dactylitis. Eur J Radiol. 1998;27(suppl 1):S12–7.

AO:1

- van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis: a proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.
- Bennett DL, Ohashi K, El-Khoury GY. Spondyloarthropathies: ankylosing spondylitis and psoriatic arthritis. Radiol Clin North Am 2004;42: 121–34.
- Oostveen J, Prevo R, den Boer J, van de Laar M. Early detection of sacroiliitis on magnetic resonance imaging and subsequent development of sacroiliitis on plain radiography: a prospective, longitudinal study. J Rheumatol 1999;26:1953–8.
- 37. Baraliakos X, Hermann KG, Landewe R, Listing J, Golder W, Brandt J, et al. Assessment of acute spinal inflammation in patients with ankylosing spondylitis by magnetic resonance imaging: a comparison between contrast enhanced T1 and short tau inversion recovery (STIR) sequences. Ann Rheum Dis 2005;64:1141–4.
- Hermann KG, Landewe RB, Braun J, van der Heijde DM. Magnetic resonance imaging of inflammatory lesions in the spine in ankylosing spondylitis clinical trials: is paramagnetic contrast medium necessary? J Rheumatol 2005;32:2056–60.
- Dougados M, Gueguen A, Nakache JP, Velicitat P, Zeidler H, Veys E, et al. Clinical relevance of C-reactive protein in axial involvement of ankylosing spondylitis. J Rheumatol 1999;26:971–4.
- Spoorenberg A, van der Heijde D, de Klerk E, Dougados M, de Vlam K, Mielants H, et al. Relative value of erythrocyte sedimentation rate and Creactive protein in assessment of disease activity in ankylosing spondylitis. J Rheumatol 1999;26:980–4.
- Gran JT, Husby G. HLA-B27 and spondyloarthropathy: value for early diagnosis? J Med Genet 1995;32:497–501.
- Khan MA, Khan MK. Diagnostic value of HLA-B27 testing ankylosing spondylitis and Reiter's syndrome. Ann Intern Med 1982;96:70–6.
- Stein CM, Davis P. Arthritis associated with HIV infection in Zimbabwe. J Rheumatol 1996;23:506–11.
- Blanche P, Taelman H, Saraux A, Bogaerts J, Clerinx J, Batungwanayo J, et al. Acute arthritis and human immunodeficiency virus infection in Rwanda. J Rheumatol 1993;20:2123–7.
- Rudwaleit M, Khan MA, Sieper J. The challenge of diagnosis and classification in early ankylosing spondylitis: do we need new criteria? Arthritis Rheum 2005;52:1000–8.
- Stone M, Warren RW, Bruckel J, Cooper D, Cortinovis D, Inman RD. Juvenile-onset ankylosing spondylitis is associated with worse functional outcomes than adult-onset ankylosing spondylitis. Arthritis Rheum 2005;53:445–51.
- Rudwaleit M, van der Heijde D, Khan MA, Braun J, Sieper J. How to diagnose axial spondyloarthritis early. Ann Rheum Dis 2004;63:535–43.
- Brophy S, Mackay K, Al-Saidi A, Taylor G, Calin A. The natural history of ankylosing spondylitis as defined by radiological progression. J Rheumatol 2002;29:1236–43.
- Fitzgerald O, Dougados M. Psoriatic arthritis: one or more diseases? Best Pract Res Clin Rheumatol 2006;20:435–50.
- Kanakoudi-Tsakalidou F, Pardalos G, Pratsidou-Gertsi P, Kansouzidou-Kanakoudi A, Tsangaropoulou-Stinga H. Persistent or severe course of reactive arthritis following Salmonella enteritidis infection: a prospective study of 9 cases. Scand J Rheumatol 1998;27:431–4.
- Zochling J, van der Heijde D, Dougados M, Braun J. Current evidence for the management of ankylosing spondylitis a systematic literature review for the ASAS/EULAR management recommendations in ankylosing spondylitis. Ann Rheum Dis 2006;65:423–32.
- Uhrin Z, Kuzis S, Ward MM. Exercise and changes in health status in patients with ankylosing spondylitis. Arch Intern Med 2000;160:2969–75.
- Lim HJ, Lee MS, Lim HS. Exercise, pain, perceived family support, and quality of life in Korean patients with ankylosing spondylitis. Psychol Rep 2005;96:3–8.
- Kraag G, Stokes B, Groh J, Helewa A, Goldsmith C. The effects of comprehensive home physiotherapy and supervision on patients with ankylosing spondylitis—a randomized controlled trial. J Rheumatol 1990;17:228–33.
- 55. Kraag G, Stokes B, Groh J, Helewa A, Goldsmith CH. The effects of comprehensive home physiotherapy and supervision on patients with ankylosing spondylitis—an 8-month followup. J Rheumatol 1994;21:261–3.
- Lim HJ, Moon YI, Lee MS. Effects of home-based daily exercise therapy on joint mobility, daily activity, pain, and depression in patients with ankylosing spondylitis. Rheumatol Int 2005;25:225–9.
- Helewa A, Stokes B. Spondylarthropathies. In: Robbins L, Burckhardt CS, Hannan, MT, DeHoratius RJ, editors. Clinical care in the rheumatic diseases. 2nd ed. Atlanta: Association of Rheumatology Health Professionals; 2001. p. 105–112.
- Dagfinrud H, Kvien TK, Hagen KB. The Cochrane review of physiotherapy interventions for ankylosing spondylitis. J Rheumatol 2005;32:1899–906.

- van der Linden S, van Tubergen A, Hidding A. Physiotherapy in ankylosing spondylitis: what is the evidence? Clin Exp Rheumatol 2002;20(6 Suppl 28):S60–4.
- Hidding A, van der Linden S, Boers M, Gielen X, de Witte L, Kester A, et al. Is group physical therapy superior to individualized therapy in ankylosing spondylitis? A randomized controlled trial. Arthritis Care Res 1993;6:117–25.
- Heikkila S, Viitanen JV, Kautiainen H, Kauppi M. Sensitivity to change of mobility tests; effect of short term intensive physiotherapy and exercise on spinal, hip, and shoulder measurements in spondyloarthropathy. J Rheumatol 2000;27:1251–6.
- Analay Y, Ozcan E, Karan A, Diracoglu D, Aydin R. The effectiveness of intensive group exercise on patients with ankylosing spondylitis. Clin Rehabil 2003;17:631–6.
- 63. Helliwell PS, et al. A randomised trial of three different physiotherapy regimes in ankylosing spondylitis. Physiotherapy 1996;82:85–90.^{AQ:4}
- Akkoc N, van der Linden S, Khan MA. Ankylosing spondylitis and symptom-modifying vs disease-modifying therapy. Best Pract Res Clin Rheumatol 2006;20:539–57.
- Toussirot E, Wendling D. Recent progress in ankylosing spondylitis treatment. Expert Opin Pharmacother 2003;4:1–12.
- 66. Dougados M, Behier JM, Jolchine I, Calin A, van der Heijde D, Olivieri I, et al. Efficacy of celecoxib, a cyclooxygenase 2-specific inhibitor, in the treatment of ankylosing spondylitis: a six-week controlled study with comparison against placebo and against a conventional nonsteroidal antiinflammatory drug. Arthritis Rheum 2001;44:180–5.
- Wanders A, et al. Inhibition of radiographic progression in ankylosing spondylitis (AS) by continuous use of NSAIDs. Arthritis Rheum 2005;52:1756–65.^{AQ:1}
- Maugars Y, et al. Corticosteroid injection of the sacroiliac joint in patients with seronegative spondylarthropathy. Arthritis Rheum 1992;35:564–8.^{AQ:1}
- Luukkainen R, et al. Periarticular corticosteroid treatment of the sacroiliac joint in patients with seronegative spondylarthropathy. Clin Exp Rheumatol 1999;17:88–90.^{AQ:1}
- Lauhio A, et al. Double blind, placebo controlled study of three months treatment with lymecycline in reactive arthritis, with special reference to Chlamydia arthritis. Arthritis Rheum 1991;24:6–14.^{AQ:1}
- 71. Laasila K, et al. Antibiotic treatment and long term prognosis of reactive arthritis. Ann Rheum Dis 2003;62:655–8.^{AQ:1}
- 72. Braun J, et al. Treatment of active ankylosing spondylitis with infliximab: a randomized controlled multi-center trial. Lancet 2002;359:1187–93.^{AQ:1}
- 73. Brandt J, et al. Successful treatment of active ankylosing spondylitis with the anti-tumor necrosis factor α monoclonal antibody infliximab. Arthritis Rheum 2000;43:1346–52.^{AQ:1}
- 74. Van Den Bosch F, Kruithof E, Baeten D, Herssens A, de Keyser F, Mielants H, et al. Randomized double-blind comparison of chimeric monoclonal antibody to tumor necrosis factor α (infliximab) versus placebo in active spondyloarthropathy. Arthritis Rheum 2002;46:755–65.
- Davis JC Jr, Van Der Heijde D, Braun J, Dougados M, Cush J, Clegg DO, et al. Recombinant human tumor necrosis factor receptor (etanercept) for treating ankylosing spondylitis: a randomized, controlled trial. Arthritis Rheum 2003;48:3230–6.
- Brandt J, Khariouzov A, Listing J, Haibel H, Sorensen H, Grassnickel L, et al. Six-month results of a double-blind, placebo-controlled trial of etanercept treatment in patients with active ankylosing spondylitis. Arthritis Rheum 2003;48:1667–75.
- Calin A, Dijkmans BA, Emery P, Hakala M, Kalden J, Leirisalo-Repo M, et al. Outcomes of a multicentre randomised clinical trial of etanercept to treat ankylosing spondylitis. Ann Rheum Dis 2004;63:1594–1600.
- Baraliakos X, Brandt J, Listing J, Haibel H, Sorensen H, Rudwaleit M, et al. Outcome of patients with active ankylosing spondylitis after two years of therapy with etanercept: clinical and magnetic resonance imaging data. Arthritis Rheum 2005;53:856–63.
- Baraliakos X, Listing J, Rudwaleit M, Brandt J, Sieper J, Braun J. Radiographic progression in patients with ankylosing spondylitis after 2 years of treatment with the tumour necrosis factor alpha antibody infliximab. Ann Rheum Dis 2005;64:1462–6.
- Ory P, et al. Etanercept (ENBREL) inhibits radiographic progression in patients with psoriatic arthritis. Arthritis Rheum 2002;46(suppl 9): S196.^{AQ:5}
- Mease PJ, Goffe BS, Metz J, VanderStoep A, Finck B, Burge DJ. Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomized trial. Lancet 2000;356:385–90.
- Mease PJ, Gladman DD, Ritchlin CT, Ruderman EM, Steinfeld SD, Choy EH, et al. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. Arthritis Rheum 2005;52:3279–89.

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CLINICAL CARE IN THE RHEUMATIC DISEASES

Antoni C, et al. The infliximab multinational psoriatic arthritis controlled 83. trial (IMPACT). Arthritis Rheum 2002;46(suppl 9):S381.^{AQ:5}

8

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AQ:5

AQ:5

- 84. Antoni C, Krueger GG, de Vlam K, Birbara C, Beutler A, et al. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. Ann Rheum Dis 2005;64:1150-7.
- Braun J, Brandt J, Listing J, Zink A, Alten R, Burmester G, et al. Two 85. year maintenance of efficacy and safety of infliximab in the treatment of ankylosing spondylitis. Ann Rheum Dis 2005;64:229-34.
- Nikas SN, Alamanos Y, Voulgari PV, Pliakou XI, Papadopoulos CG, Dro-86. sos AA. Infliximab therapy in ankylosing spondylitis: an observational study. Ann Rheum Dis 2005;64:940-2.
- 87. Van den Bosch F, et al. A prospective long-term study of the efficacy and safety of infliximab in 107 patients with spondyloarthropathy. Arthritis Rheum 2004;50(Suppl 9):S611.^{AQ:5}
- 88 Baraliakos X, et al. Clinical response to long-term therapy with infliximab in patients with ankylosing spondylitis-results after 3 years. Arthritis Rheum 2004;50(Suppl 9):S615. AQ:5
- 89. Braun J, Baraliakos X, Brandt J, Listing J, Zink A, Alten R, et al. Persistent clinical response to the anti-TNF-alpha antibody infliximab in patients with ankylosing spondylitis over 3 years. Rheumatology (Oxford) 2005:44:670-6.
- 90. Braun J, Baraliakos X, Listing J, Sieper J. Decreased incidence of anterior uveitis in patients with ankylosing spondylitis treated with the antitumor necrosis factor agents infliximab and etanercept. Arthritis Rheum 2005:52:2447-51.
- Braun J, Pham T, Sieper J, Davis J, van der Linden S, Dougados M, et al. 91. International ASAS consensus statement for the use of anti-tumour necrosis factor agents in patients with ankylosing spondylitis. Ann Rheum Dis 2003:62:817-24.
- 92. Meador R, Hsia E, Kitumnuaypong T, Schumacher HR. TNF involvement and anti-TNF therapy of reactive and unclassified arthritis. Clin Exp Rheumatol 2002;20(6 Suppl 28):S130-4.
- Wick MC, Ernestam S, Lindblad S, Bratt J, Klareskog L, van Vollen-93. hoven RF. Adalimumab (Humira) restores clinical response in patients with secondary loss of efficacy from infliximab (Remicade) or etanercept (Enbrel): results from the STURE registry at Karolinska University Hospital. Scand J Rheumatol 2005;34:353-8.
- Delaunay C, Farrenq V, Marini-Portugal A, Cohen JD, Chevalier X, 94. Claudepierre P. Infliximab to etanercept switch in patients with spondyloarthropathies and psoriatic arthritis: preliminary data. J Rheumatol 2005:32:2183-5.
- Cohen G, Courvoisier N, Cohen JD, Zaltni S, Sany J, Combe B. The effi-95. ciency of switching from infliximab to etanercept and vice-versa in patients with rheumatoid arthritis. Clin Exp Rheumatol 2005;23:795-800.
- Baraliakos X, Listing J, Brandt J, Zink A, Alten R, Burmester G, et al. Clinical response to discontinuation of anti-TNF therapy in patients with ankylosing spondylitis after 3 years of continuous treatment with infliximab. Arthritis Res Ther 2005;7:R439-44.
- Brandt J, Listing J, Haibel H, Sorensen H, Schwebig A, Rudwaleit M, 97 et al. Long-term efficacy and safety of etanercept after readministration in patients with active ankylosing spondylitis. Rheumatology (Oxford) 2005;44:342-8.
- 98 Gratacos J, et al. Significant loss of bone mass in patients with early, active ankylosing spondylitis: a followup study. Arthritis Rheum 1999;42: 2319-24. AQ:
- 99. Lange U, Jung O, Teichmann J, Neeck G. Relationship between disease activity and serum levels of vitamin D metabolites and parathyroid hormone in ankylosing spondylitis. Osteoporos Int 2001;12:1031-5.
- 100. Barlow JH, Barefoot J. Group education for people with arthritis. Pt Educat Counsel 1996;27:257-67.
- 101. de Klerk E, van der Linden S, van der Heijde D, Urquhart J. Facilitated analysis of data on drug regimen compliance. Stat Med 1997;16:1653-64.
- 102. Khan MA. Ankylosing spondylitis: the facts. Oxford (UK): Oxford University Press; 2002.
- 103. Lorig KR, Mazonson PD, Holman HR. Evidence suggesting that health education for self-management in patients with chronic arthritis has sustained health benefits while reducing health care costs. Arthritis Rheum 1993:36:439-46.
- 104. Basler HD, Rehfisch HP. Cognitive-behavioral therapy in patients with ankylosing spondylitis in a German self-help organization. J Psychosom Res 1991;35:345-54.

- 105. Krauth C, Rieger J, Bonisch A, Ehlebracht-Konig I. [Costs and benefits of an education program for patients with ankylosing spondylitis as part of an inpatient rehabilitation programs-study design and first results.] Z Rheumatol 2003;62(Suppl 2):II14-6.
- 106. Doran MF, Brophy S, MacKay K, Taylor G, Calin A. Predictors of longterm outcome in ankylosing spondylitis. J Rheumatol 2003;30: 316-20.
- 107. Santos H, Brophy S, Calin A. Exercise in ankylosing spondylitis: how much is optimum? J Rheumatol 1998;25:2156-60.
- 108. Jensen GM, Lorish CD. Promoting patient cooperation with exercise programs: linking research, theory and practice. Arthritis Care Res 1994;7:181-9.
- 109. Bot SD, Caspers M, Van Royen BJ, Toussaint HM, Kingma I. Biomechanical analysis of posture in patients with spinal kyphosis due to ankylosing spondylitis: a pilot study. Rheumatology (Oxford) 1999;38:441-3.
- 110. Eriendsson J. Car driving with ankylosing spondylitis. The Ankylosing Spondylitis International Federation and The National Ankylosing Spondylitis Society of Great Britain. AQ:6
- Sweeney S, Gupta R, Taylor G, Calin A. Total hip arthroplasty in ankylo-111 sing spondylitis: outcome in 340 patients. J Rheumatol 2001;28:1862-6.
- 112. Furnes O, Lie SA, Espehaug B, Vollset SE, Engesaeter LB, Havelin LI. Hip disease and the prognosis of total hip replacements: a review of 53,698 primary total hip replacements reported to the Norwegian Arthroplasty Register 1987-99. J Bone Joint Surg Br 2001;83:579-86.
- 113. Brinker MR, Rosenberg AG, Kull L, Cox DD. Primary noncemented total hip arthroplasty in patients with ankylosing spondylitis: clinical and radiographic results at an average follow-up period of 6 years. J Arthroplasty 1996;11:802-12.
- 114. Diaz de Rada P, et al. Follow-up of the outcome of hip arthroplasty in patients with ankylosing spondylitis. Rev Ortop Traumatol 2004;48: 340-4.^{AQ:7}
- 115. Sochart DH, Porter ML. Long-term results of total hip replacement in young patients who had ankylosing spondylitis. eighteen to thirtyyear results with survivorship analysis. J Bone Joint Surg Am 1997;79: 1181_{-9}
- 116. Van Royen BJ, et al. Polysegmental lumbar posterior wedge osteotomies for correction of kyphosis in ankylosing spondylitis. Eur Spine J 1998;7:104-10.AQ:1
- 117. Chen LH, et al. Surgical treatment of spinal pseudoarthrosis in ankylosing spondylitis. Chang Gung Med J 2005;28:621-8. AQ:1 AQ:1
- 118. Carter R, Riantawan P, Banham SW, Sturrock RD. An investigation of factors limiting aerobic capacity in patients with ankylosing spondylitis. Respir Med 1999;93:700-8.
- 119. Spoorenberg A, de Vlam K, van der Heijde D, de Klerk E, Dougados M, Mielants H, et al. Radiological scoring methods in ankylosing spondylitis: reliability and sensitivity to change over one year. J Rheumatol 1999:26:997-1002.
- 120. Tico N, Ramon S, Garcia-Ortun F, Ramirez L, Castello T, Garcia-Fernandez L, et al. Traumatic spinal cord injury complicating ankylosing spondylitis. Spinal Cord 1998;36:349-52.
- 121. Hitchon PW, From AM, Brenton MD, Glaser JA, Torner JC. Fractures of the thoracolumbar spine complicating ankylosing spondylitis. J Neurosurg 2002;97(2 Suppl):218-22.
- 122. Bilgen IG, Yunten N, Ustun EE, Oksel F, Gumusdis G. Adhesive arachnoiditis causing cauda equina syndrome in ankylosing spondylitis: CT and MRI demonstration of dural calcification and a dorsal dural diverticulum. Neuroradiology 1999:41:508-11.
- 123. Ginsburg WW, Cohen MD, Miller GM, Bartleson JD. Posterior vertebral body erosion by arachnoid diverticula in cauda equina syndrome: an unusual manifestation of ankylosing spondylitis. J Rheumatol 1997; 24:1417-20.
- 124. Ahn NU, et al. Cauda equina syndrome in ankylosing spondylitis (the CES-AS syndrome): meta-analysis of outcomes after medical and surgical treatments. J Spinal Disord 2001;14:427-33. AQ:1
- Shim SC, Yoo DH, Lee JK, Koh HK, Lee SR, Oh SH, et al. Multiple cerebellar infarction due to vertebral artery obstruction and bulbar symptoms associated with vertical subluxation and atlanto-occipital subluxation in ankylosing spondylitis. J Rheumatol 1998;25:2464-8.
- 126. Thompson GH, Khan MA, Bilenker RM. Spontaneous atlantoaxial subluxation as a presenting manifestation of juvenile ankylosing spondylitis: a case report. Spine 1982;7:78-9.

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