

the two marks is measured. This distance increases by  $\geq 5$  cm in the case of normal mobility and by  $< 4$  cm in the case of decreased mobility. Chest expansion is measured as the difference between maximal inspiration and maximal forced expiration in the fourth intercostal space in males or just below the breasts in females, with the patient's hands resting on or just behind the head. Normal chest expansion is  $\geq 5$  cm. Lateral bending measures the distance the patient's middle finger travels down the leg with maximal lateral bending. Normal is  $> 10$  cm.

Limitation or pain with motion of the hips or shoulders is usually present if these joints are involved. It should be emphasized that early in the course of mild cases, symptoms may be subtle and nonspecific, and the physical examination may be unrevealing.

The course of the disease is extremely variable, ranging from the individual with mild stiffness and normal radiographs to the patient with a totally fused spine and severe bilateral hip arthritis, accompanied by severe peripheral arthritis and extraarticular manifestations. Pain tends to be persistent early in the disease and intermittent later, with alternating exacerbations and quiescent periods. In a typical severe untreated case with progression of the spondylitis to syndesmophyte formation, the patient's posture undergoes characteristic changes, with obliterated lumbar lordosis, buttock atrophy, and accentuated thoracic kyphosis. There may be a forward stoop of the neck or flexion contractures at the hips, compensated by flexion at the knees. Disease progression can be estimated clinically from loss of height, limitation of chest expansion and spinal flexion, and occiput-to-wall distance. Occasional individuals are encountered with advanced deformities who report having never had significant symptoms.

The factors most predictive of radiographic progression (see below) are the presence of existing syndesmophytes, high inflammatory markers, and smoking. In some but not all studies, onset of AS in adolescence and early hip involvement correlate with a worse prognosis. In women, AS tends to progress less frequently to total spinal ankylosis, although there may be an increased prevalence of isolated cervical ankylosis and peripheral arthritis. In industrialized countries, peripheral arthritis (distal to hips and shoulders) occurs in less than one-half of patients with AS, usually as a late manifestation, whereas in developing countries, the prevalence is much higher, with onset typically early in the disease course. Pregnancy has no consistent effect on AS, with symptoms improving, remaining the same, or deteriorating in one-third of pregnant patients, respectively.

The most serious complication of the spinal disease is spinal fracture, which can occur with even minor trauma to the rigid, osteoporotic spine. The lower cervical spine is most commonly involved. These fractures are often displaced and cause spinal cord injury. A recent survey suggested a  $> 10\%$  lifetime risk of fracture. Occasionally, fracture through a diskovertebral junction and adjacent neural arch, termed *pseudoarthrosis*, most common in the thoracolumbar spine, can be an unrecognized source of persistent localized pain and/or neurologic dysfunction. Wedging of thoracic vertebrae is common and correlates with accentuated kyphosis.

The most common extraarticular manifestation is acute anterior uveitis, which occurs in up to 40% of patients and can antedate the spondylitis. Attacks are typically unilateral, causing pain, photophobia, and increased lacrimation. These tend to recur, often in the opposite eye. Cataracts and secondary glaucoma are not uncommon sequelae. Up to 60% of patients with AS have inflammation in the colon or ileum. This is usually asymptomatic, but frank IBD occurs in 5–10% of patients with AS (see "Enteropathic Arthritis," below). About 10% of patients meeting criteria for AS have psoriasis (see "Psoriatic Arthritis," below). Aortic insufficiency, sometimes leading to congestive heart failure, occurs in a small percentage of patients, occasionally early. Third-degree heart block may occur alone or together with aortic insufficiency. Subclinical pulmonary lesions and cardiac dysfunction may be relatively common. Cauda equina syndrome and upper pulmonary lobe fibrosis are rare late complications. Retroperitoneal fibrosis is a rare associated condition. Prostatitis has been reported to have an increased prevalence. Amyloidosis is rare (Chap. 137).

Several validated measures of disease activity and functional outcome are in widespread use in the study and management of AS,

particularly the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS), both measures of disease activity; the Bath Ankylosing Spondylitis Functional Index (BASFI), a measure of limitation in activities of daily living; and several measures of radiographic changes. The Harris hip score, although not specific for AS, can be helpful. Despite persistence of the disease, most patients remain gainfully employed. Some but not all studies of survival in AS have suggested that AS shortens life span, compared with the general population. Mortality attributable to AS is largely the result of spinal trauma, aortic insufficiency, respiratory failure, amyloid nephropathy, or complications of therapy such as upper gastrointestinal hemorrhage. The impact of anti-TNF therapy on outcome and mortality is not yet known, except for significantly improved work productivity.

#### LABORATORY FINDINGS

No laboratory test is diagnostic of AS. In most ethnic groups, HLA-B27 is present in 80–90% of patients. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are often, but not always, elevated. Mild anemia may be present. Patients with severe disease may show an elevated alkaline phosphatase level. Elevated serum IgA levels are common. Rheumatoid factor, anti-cyclic citrullinated peptide (CCP), and antinuclear antibodies (ANAs) are largely absent unless caused by a coexistent disease, although ANAs may appear with anti-TNF therapy. Circulating levels of CD8+ T cells tend to be low, and serum matrix metalloproteinase 3 levels correlate with disease activity. Synovial fluid from peripheral joints in AS is nonspecifically inflammatory. In cases with restriction of chest wall motion, decreased vital capacity and increased functional residual capacity are common, but airflow is normal and ventilatory function is usually well maintained.

#### RADIOGRAPHIC FINDINGS

Radiographically demonstrable sacroiliitis, usually symmetric, is eventually present in AS. The earliest changes by standard radiography are blurring of the cortical margins of the subchondral bone, followed by erosions and sclerosis. Progression of the erosions leads to "pseudowidening" of the joint space; as fibrous and then bony ankylosis supervenes, the joints may become obliterated.

In the lumbar spine, progression of the disease leads to straightening, caused by loss of lordosis, and reactive sclerosis, caused by osteitis of the anterior corners of the vertebral bodies with subsequent erosion, leading to "squaring" or even "barreling" of one or more vertebral bodies. Progressive ossification leads to eventual formation of marginal syndesmophytes, visible on plain films as bony bridges connecting successive vertebral bodies anteriorly and laterally.

Years may elapse before unequivocal sacroiliac abnormalities are evident on plain radiographs, and consequently, MRI is being increasingly used in diagnosing AS. Active sacroiliitis is best visualized by dynamic MRI with fat saturation, either T2-weighted turbo spin-echo sequence or short tau inversion recovery (STIR) with high resolution, or T1-weighted images with contrast enhancement. These techniques sensitively identify early intraarticular inflammation, cartilage changes, and underlying bone marrow edema in sacroiliitis (Fig. 384-1). They are also highly sensitive for evaluation of acute and chronic spinal changes (Fig. 384-2).

Reduced bone mineral density can be detected by dual-energy x-ray absorptiometry of the femoral neck and the lumbar spine. Use of a lateral projection of the L3 vertebral body can prevent falsely elevated readings related to spinal ossification.

#### DIAGNOSIS

It is important to establish the diagnosis of early AS before the development of irreversible deformity. This goal presents a challenge for several reasons: (1) Back pain is very common, but AS is much less common; (2) an early presumptive diagnosis often relies on clinical grounds requiring considerable expertise; and (3) young individuals with symptoms of AS often do not seek medical care. The widely used modified New York criteria (1984) are based on the presence of definite radiographic sacroiliitis and are too insensitive in early