To replace deficient tears, several ophthalmic preparations are readily available (hydroxypropyl methylcellulose; polyvinyl alcohol; 0.5% methylcellulose; Hypo Tears). If corneal ulcerations are present, eye patching and boric acid ointments are recommended. Certain drugs that may decrease lacrimal and salivary secretions, such as diuretics, antihypertensive drugs, anticholinergics, and antidepressants, should be avoided.

For xerostomia, the best replacement is water. Propionic acid gels may be used to treat vaginal dryness. To stimulate secretions, orally administered pilocarpine (5 mg thrice daily) or cevimeline (30 mg thrice daily) appears to improve sicca manifestations, and both are well tolerated. Hydroxychloroquine (200 mg) is helpful for arthralgias and mild arthritis.

Patients with renal tubular acidosis should receive sodium bicarbonate by mouth (0.5–2 mmol/kg in four divided doses). Glucocorticoids (1 mg/kg per day) and/or immunosuppressive agents (e.g., cyclophosphamide) are indicated only for the treatment of systemic vasculitis. Anti–tumor necrosis factor agents are ineffective. Monoclonal antibody to CD20 appears to be effective in patients with systemic disease, particularly in those with vasculitis, arthritis, and fatigability. Combination of anti-CD-20 with a classic CHOP regimen (cyclosporine, adriamycin [hydroxydaunorubicin], vincristine [oncovin], and prednisone) leads to increased survival rates among patients with high-grade lymphomas.

384 The Spondyloarthritides

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The spondyloarthritides are a group of overlapping disorders that share certain clinical features and genetic associations. These disorders include ankylosing spondylitis (AS), reactive arthritis, psoriatic arthritis and spondylitis, enteropathic arthritis and spondylitis, juvenile-onset spondyloarthritis (SpA), and undifferentiated SpA. The similarities in clinical manifestations and genetic predisposition suggest that these disorders share pathogenic mechanisms.

ANKYLOSING SPONDYLITIS

AS is an inflammatory disorder of unknown cause that primarily affects the axial skeleton; peripheral joints and extraarticular structures are also frequently involved. The disease usually begins in the second or third decade; male-to-female prevalence is between 2:1 and 3:1. The term *axial spondyloarthritis* is coming into common use, supported by criteria formulated in 2009 (Table 384-1). This classification includes both definite AS and early stages that do not yet meet classical criteria for AS, but it probably also includes other conditions with a different natural history.

EPIDEMIOLOGY

AS shows a striking correlation with the histocompatibility antigen HLA-B27 and occurs worldwide roughly in proportion to the prevalence of B27 (Chap. 373e). In North American whites, the prevalence of B27 is 7%, whereas it is 90% in patients with AS, independent of disease severity.

In population surveys, AS is present in 1–6% of adults inheriting B27, whereas the prevalence is 10–30% among B27+ adult first-degree relatives of AS probands. Concordance rate in identical twins is about 65%. Susceptibility to AS is determined largely by genetic factors, with B27 comprising less than one-half of the genetic component. Genome-wide single-nucleotide polymorphism (SNP) analysis has identified over 30 additional susceptibility alleles.

TABLE 384-1 ASAS CRITERIA FOR CLASSIFICATION OF AXIAL SPONDYLOARTHRITIS (TO BE APPLIED FOR PATIENTS WITH BACK PAIN ≥3 MONTHS AND AGE OF ONSET <45 YEARS)[a]

Sacroiliitis on Imaging Plus ≥1 SpA Feature	or	HLA-B27 Plus ≥2 Other SpA Features
Sacroiliitis on imaging • Active (acute) inflammation on MRI highly suggestive of SpA-associated sacroiliitis[b] and/or • Definite radiographic sacroiliitis according to modified New York criteria[c]		SpA features • Inflammatory back pain[d] • Arthritis[e] • Enthesitis (heel)[f] • Anterior uveitis[g] • Dactylitis[e] • Psoriasis[e] • Crohn's disease or ulcerative colitis[e] • Good response to NSAIDs[h] • Family history of SpA[i] • HLA-B27 • Elevated CRP[j]

[a]Sensitivity 83%, specificity 84%. The imaging arm (sacroiliitis) alone has a sensitivity of 66% and a specificity of 97%. [b]Bone marrow edema and/or osteitis on short tau inversion recovery (STIR) or gadolinium-enhanced T1 image. [c]Bilateral grade ≥2 or unilateral grade 3 or 4. [d]See text for criteria. [e]Past or present, diagnosed by a physician. [f]Past or present pain or tenderness on examination at calcaneus insertion of Achilles tendon or plantar fascia. [g]Past or present, confirmed by an ophthalmologist. [h]Substantial relief of back pain at 24–48 h after a full dose of NSAID. [i]First- or second-degree relatives with ankylosing spondylitis (AS), psoriasis, uveitis, reactive arthritis (ReA), or inflammatory bowel disease (IBD). [j]After exclusion of other causes of elevated CRP.

Abbreviations: ASAS, Assessment of Spondyloarthritis International Society; CRP, C-reactive protein; MRI, magnetic resonance imaging; NSAIDs, nonsteroidal anti-inflammatory drugs; SpA, spondyloarthritis.

Source: From M Rudwaleit et al: Ann Rheum Dis 68:777, 2009. Copyright 2009, with permission from BMJ Publishing Group Ltd.

PATHOLOGY

Sacroiliitis is often the earliest manifestation of AS. Knowledge of its pathology comes from both biopsy and autopsy studies that cover a range of disease durations. Synovitis and myxoid marrow represent the earliest changes, followed by pannus and subchondral granulation tissue. Marrow edema, enthesitis, and chondroid differentiation are also found. Macrophages, T cells, plasma cells, and osteoclasts are prevalent. Eventually the eroded joint margins are gradually replaced by fibrocartilage regeneration and then by ossification. The joint may become totally obliterated.

In the spine, the specimens studied have either been surgically resected in advanced disease or taken from autopsies. There is inflammatory granulation tissue in the paravertebral connective tissue at the junction of annulus fibrosus and vertebral bone, and in some cases along the entire outer annulus. The outer annular fibers are eroded and eventually replaced by bone, forming the beginning of a syndesmophyte, which then grows by continued endochondral ossification, ultimately bridging the adjacent vertebral bodies. Ascending progression of this process leads to the "bamboo spine." Other lesions in the spine include diffuse osteoporosis (loss of trabecular bone despite accretion of periosteal bone), erosion of vertebral bodies at the disk margin, "squaring" or "barreling" of vertebrae, and inflammation and destruction of the disk-bone border. Inflammatory arthritis of the apophyseal (facet) joints is common, with synovitis, inflammation at the bony attachment of the joint capsule, and subchondral bone marrow granulation tissue. Erosion of joint cartilage by pannus is often followed by bony ankylosis. This may precede formation of syndesmophytes bridging the adjacent disks. Bone mineral density is diminished in the spine and proximal femur early in the course of the disease.

Peripheral synovitis in AS shows marked vascularity, which is also evident as tortuous macrovascularity seen during arthroscopy. Lining layer hyperplasia, lymphoid infiltration, and pannus formation are also found. Central cartilaginous erosions caused by proliferation of subchondral granulation tissue are common. It should be