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Spondyloarthritis

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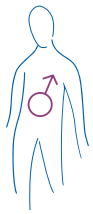

DEFINITION

Spondyloarthritis, formerly called *seronegative arthritis* or *sponydyloarthopathy,* is the name of a group of related inflammatory disorders that share certain clinical features unique among rheumatic diseases. The six types of spondyloarthritis in adults are ankylosing spondylitis, reactive arthritis, arthritis of inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis), psoriatic arthritis, and undifferentiated spondyloarthropathy. The juvenile form of spondyloarthropathy is similar to ankylosing spondylitis and usually persists into adulthood.

The cardinal clinical feature of spondyloarthritis is inflammation of the sacroiliac joints (i.e., sacroiliitis) and the spine (i.e., spondylitis). Inflammation of tendon insertion sites (i.e., enthesitis), inflammation of entire digits (i.e., dactylitis), and inflammation of one to four lower extremity joints (i.e., oligoarthritis) are typical extraspinal skeletal findings. A positive family history, eye inflammation (i.e., anterior uveitis or conjunctivitis), and the absence of rheumatoid factor and subcutaneous nodules are common.

Further classification of these disorders is based on the finding of psoriatic skin or nail changes, inflammatory bowel disease, or a history of preceding gastrointestinal or genitourinary infection. Alternatively, patients with spondyloarthritis can be classified based on the distribution pattern of joint involvement. Cases with dominant spinal disease are classified as *axial spondyloarthritis* (i.e., prototypically ankylosing spondylitis), and those without spinal disease are classified as predominately *peripheral spondyloarthritis.*

Spondyloarthritis is strongly associated with human leukocyte antigen B27 (HLA-27), a specific allele of the B locus of the HLA-encoding class I major histocompatibility complex genes. The frequency of HLA-B27 among whites is approximately 8%. However, up to 90% of white patients with ankylosing spondylitis and 80% of white patients with reactive arthritis or juvenile spondyloarthritis are HLA-B27 positive, and these percentages are even higher among patients with uveitis. The rate of HLA-B27 positivity among patients with inflammatory bowel disease or psoriasis with peripheral arthritis is not markedly increased unless they have spondylitis, in which case the frequency of HLA-B27 is 50%. The frequency of HLA-B27 varies widely among other ethnic groups and accounts for the broad variation of the prevalence of ankylosing spondylitis in different populations.

Ankylosing spondylitis is much more common among adolescent boys and young men, but this finding may reflect underdiagnosis in women, in whom disease manifestations may be milder than they are in men. Reactive arthritis is more common among men when it follows genitourinary *Chlamydia trachomatis* infection, but the sex distribution is even among patients after dysentery. Inflammatory arthritis including spondylitis affects approximately 5% to 8% of patients with psoriasis and 10% to 25% of patients with ulcerative colitis or Crohn's disease. Men and women are affected equally. The prevalence of spondyloarthritis, particularly psoriatic and reactive arthritis, is increased in populations with high human immunodeficiency virus (HIV) infection rates.

PATHOLOGY

Although the strong association of HLA-B27 with spondyloarthritis is well established, a specific role in the pathogenesis of these disorders has not been elucidated. Animal models in which rodents transgenic for HLA-B27 develop inflammatory abnormalities strikingly similar to those seen in HLA-B27–associated human diseases provide compelling indirect evidence for a pathogenic role. When raised in a germ-free environment, these animals remain disease free, suggesting a key additional environmental factor.

In addition to the strong genetic links for the risk of spondyloarthritis, important associations exist between specific bacterial agents and disease pathogenesis. Genitourinary infection with *C. trachomatis* or diarrheal illness with *Shigella, Salmonella, Campylobacter,* and *Yersinia* species can induce reactive arthritis. Several additional infectious agents are less commonly implicated. They appear to trigger an inflammatory response, possibly as a result of persistence of bacterial antigens, or cause an aberrant immunologic response to infection that results in misfolding of HLA-B27 molecules in antigen-presenting cells, generating a persistent inflammatory reaction.

No one theory of pathogenesis of spondyloarthritis explains the clinical spectrum of these disorders, and more research is clearly needed to solidify an understanding of their origin. The complex role of the immune system in the spondyloarthritis is highlighted by the observation that patients infected with HIV appear more likely to have severe disease, especially psoriatic arthritis. When HIV infection is treated with antiviral agents, the incidence of spondyloarthritis declines.

Although many of the cellular and molecular mechanisms of inflammatory joint disease have been elucidated, the pathophysiology of spondyloarthritis remains incompletely understood. Inflammation of the sacroiliac joints, spine, and entheses is a unique feature of these disorders. Pathophysiologic studies show