

# Spondyloarthropathies

## **Clinical Diagnosis**

[Kane D, Pathare S.](#) Early psoriatic arthritis. *Rheum Dis Clin North Am* 31:641, 2005.

[Rudwaleit M, Khan M, Sieper J.](#) The challenge of diagnosis and classification in early ankylosing spondylitis: do we need new criteria? *Arthritis Rheum* 52:1000, 2005.

[Healy P, Helliwell P.](#) Classification of the spondyloarthropathies. *Curr Opin Rheumatol* 17:395, 2005.

[Taylor W, Zmierzak H, Helliwell P.](#) Problems with the definition of axial and peripheral patterns in psoriatic arthritis. *J Rheumatol* 32 974, 2005.

[Kasapcopur O, Demirli N, Ozdogan H et al.](#) Evaluation of classification criteria for juvenile-onset spondyloarthropathies. *Rheumatol Int* 25:414, 2005.

[Selvaag A, Lien G, Sorskaar D et al.](#) Early disease course and predictors of disability in juvenile rheumatoid arthritis and juvenile spondyloarthropathy: a 3 year prospective study. *J Rheumatol* 32:1122, 2005.

[Gilgil F, Kacar C, Tuncer T et al.](#) The association of syndesmophytes with vertebral bone mineral density in patients with ankylosing spondylitis. *J Rheumatol* 32:292, 2005.  
*Presence of syndesmophytes distorts the BMD of a posteroanterior L2-L4 DEXA but not the BMD measured by lateral L3 DEXA.*

[Inanc N, Atagunduz P, Sen F et al.](#) The investigation of sacroiliitis with different imaging techniques in spondyloarthropathies. *Rheumatol Int* 25:591, 2005.

[Van der Heijde D, Landewe R.](#) Imaging in spondylitis. *Curr Opin Rheumatol* 17:413, 2005.

[Khan M.](#) Update on Spondyloarthropathies. *Ann Intern Med* 136:896, 2002.

[Cabral D, Malleson P, Petty R.](#) Spondyloarthropathies of childhood. *Pediatr Clin N Am* 42: 1051, 1995.

## **Disease Pathophysiology**

[Hofer M.](#) Spondylarthropathies in children-are they different from those in adults? *Best Pract Res Clin Rheumatol* 20:315, 2006.

[Reveille J, Arnett F.](#) Spondyloarthritis: update on pathogenesis and management. *Am J Med* 118:592, 2005.

Kim T, Uhm W, Inman R. Pathogenesis of ankylosing spondylitis and reactive arthritis. *Curr Opin Rheumatol* 17:400, 2005.

Divecha H, Sattar N, Rumley A et al. Cardiovascular risk parameters in men with ankylosing spondylitis in comparison with non-inflammatory control subjects: relevance of systemic inflammation. *Clin Sci (Lond)* 109:171, 2005.

Aydin T, Karacan I, Demir S et al. Bone loss in males with ankylosing spondylitis: its relation to sex hormone levels. *Clin Endocrinol (Oxf)* 63:467, 2005.

Chou C, Lin K, Wei J et al. Study of undifferentiated spondyloarthropathy among first-degree relatives of ankylosing spondylitis probands. *Rheumatology (Oxford)* 44:662-5, 2005.

Ritchlin CT. Pathogenesis of psoriatic arthritis. *Curr Opin Rheumatol* 17:406, 2005.

Ho P, Bruce I, Silman A et al. Evidence for common genetic control in pathways of inflammation for Crohn's disease and psoriatic arthritis. *Arthritis Rheum* 52:3596, 2005.

Kruthhof E, Baeten D, De Rycke L et al. Synovial histopathology of psoriatic arthritis, both oligo- and polyarticular, resembles spondyloarthropathy more than it does rheumatoid arthritis. *Arthritis Res Ther* 7:R569, 2005.

Johnson S, Schentag C, Gladman D. Autoantibodies in biological agent naïve patients with psoriatic arthritis. *Ann of Rheum Dis* 64:770, 2005.

*Anti-CCP antibodies in psoriasis, with and without arthritis (Acta Derm Venereol 85:253, 2005 and Rheumatology (Oxford) 44:1056, 2005).*

Wollheim F. Enteropathic arthritis: How do the joints talk with the gut? *Curr Opin Rheumatol* 13:305, 2001.

Orchard T, Thiyagaraja S, Welsh K et al. Clinical Phenotype is related to HLA genotype in the peripheral arthropathies of inflammatory bowel disease. *Gastroenterology* 118:274, 2000.

Brown M, Kennedy G, MacGregor A et al. Susceptibility to ankylosing spondylitis in twins - the role of genes, HLA, and the environment. *Arthritis Rheum* 49:1823, 1997.

*Concordance rates in twins with AS demonstrating that liability to this disease is largely genetic (97%), multiple genes are required and environmental contribution is probably ubiquitous.*

Sieper J, Braun J. Pathogenesis of spondyloarthropathies – persistent bacterial antigen, autoimmunity, or both? *Arthritis Rheum* 38:1547, 1995.

*A review of the major hypotheses regarding the pathogenesis of spondyloarthropathies.*

## **Clinical Treatment**

[Davis J, van der Heijde D, Dougados M et al.](#) Baseline factors that influence ASAS 20 response in patients with ankylosing spondylitis treated with etanercept. *J Rheumatol* 32:1751, 2005.

[Sieper J, Rudwaleit M.](#) How early should ankylosing spondylitis be treated with tumor necrosis factor blockers? *Ann Rheum Dis* 64 Suppl 4:iv61, 2005

[Furst D, Beedveld F, Kalden J et al.](#) Updated consensus statement on biological agents, specifically tumour necrosis factor blocking agents and interleukin-1 receptor antagonist, for the treatment of rheumatic diseases, 2005. *Ann Rheum Dis* 64 Suppl 4:iv2, 2005.

[Delaunay C, Farrenq V, Marini-Portugal A, et al.](#) Infliximab to etanercept switch in patients with spondyloarthropathies and psoriatic arthritis: preliminary data. *J Rheumatol* 32:2183, 2005.

[Wick M, Ernestam S, Lindblad S et al.](#) Adalimumab restores clinical response in patients with secondary loss of efficacy from infliximab or etanercept: results from the STURE registry at Karolinska University Hospital. *Scand J Rheumatol* 34:353, 2005.

[Collantes-Estevez E, Munoz-Villanueva M, Zarco P et al.](#) Effectiveness of reducing infliximab dose interval in non-responder patients with refractory spondyloarthropathies. An open extension of a multicentre study. *Rheumatology (Oxford)* 44:1555, 2005.

[Sieper J, Baraliakos X, Listing J et al.](#) Persistent reduction of spinal inflammation as assessed by magnetic resonance imaging in patients with ankylosing spondylitis after 2 yrs of treatment with the anti-tumor necrosis factor agent infliximab. *Rheumatology (Oxford)* 44:1525, 2005.

*Two year outcome data for etanercept in A&R 53:856-63, 2005.*

*52 week outcome data in open-label trial of Adalimumab in AS (Arthritis Rheum 54:678, 2006).*

[Baraliakos X, Listing J, Brandt J 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* 7:R439, 2005. [Erratum in *Arthritis Res Ther* 7:113, 2005]

*Clinical response deteriorates after TNF d/c'ed. Same in psoriatic arthritis (Clin Exp Rheumatol 23:145, 2005).*

[Flagg S, Meador R, Hsia E et al.](#) Decreased pain and synovial inflammation after etanercept therapy in patients with reactive and undifferentiated arthritis: an open label trial. *Arthritis Rheum* 53:613, 2005.

[Tse S, Burgos-Vargas R, Laxer R.](#) Anti-tumor necrosis factor alpha blockade in the treatment of juvenile spondylarthropathy. *Arthritis Rheum* 52:2103, 2005.

Van den Bosch R, De Keyser F, Mielants H, Veys E. Tumor necrosis factor-alpha blockade in ankylosing spondylitis: a potent but expensive anti-inflammatory treatment or true disease modification? *Arthritis Res Ther* 7:121, 2005.

Wanders A, Heijde D, Landewe R, Behier J et al. Nonsteroidal anti-inflammatory drugs reduce radiographic progression in patients with ankylosing spondylitis: a randomized clinical trial. *Arthritis Rheum* 52:1756, 2005.

Also: *COX-2 agent and older NSAID improve axial symptoms whether or not there is peripheral arthritis but works better in patients without peripheral arthritis (Ann Rheum Dis 64:1563, 2005)*

Colmegna I, Espinoza L. Recent advances in reactive arthritis. *Curr Rheumatol Rep* 7:201, 2005.

Boulos P, Dougados M, Macleod S et al. Pharmacological treatment of ankylosing spondylitis: a systematic review. *Drugs* 65:2111, 2005.

Braun J, Baraliakos X, Godolias G et al. Therapy of ankylosing spondylitis—a review. Part I: Conventional medical treatment and surgical therapy. *Scand J Rheumatol* 34:97, 2005.

Gladman D. Traditional and newer therapeutic options for psoriatic arthritis: an evidence-based review. *Drugs* 65:1223, 2005.

Cairns A, Wright S, Taggart A et al. An open study of pulse pamidronate treatment in severe ankylosing spondylitis, and its effect on biochemical markers of bone turnover. *Ann Rheum Dis* 64:338, 2005.

*Pamidronate works great on osteoporosis bone turnover markers in AS and has a small beneficial effect on disease activity.*

Haibel H, Rudwaleit M, Listing J, Sieper J. Open label trial of anakinra in active ankylosing spondylitis over 24 weeks. *Ann Rheum Dis* 64:296, 2005.

*Small subset of patients improved in spinal symptoms with no change in CRP/MRI.*

Van Denderen J, van der Paardt M, Nurmohamed M et al. Double blind, randomized, placebo controlled study of leflunomide in the treatment of active ankylosing spondylitis. *Ann Rheum Dis* 64:1761, 2005. *Doesn't work in AS.*

Fraser A, van Kuijk A, Westhovens R et al. A randomized, double blind, placebo controlled, multicentre trial of combination therapy with methotrexate plus ciclosporin in patients with active psoriatic arthritis. *Ann Rheum Dis* 64:859, 2005.

*CSA versus placebo after incomplete response to MTX showed improved inflammation but not HAC or pain. More adverse events in CSA/MTX group. Low completion rate-61%.*

Yli-Kerttula T, Luukkainen R, Yli-Kerttula U et al. Effect of a three month course of ciprofloxacin on the late prognosis of reactive arthritis. *Ann Rheum Dis* 62:880, 2003.

*4-7 yr f/u of pts treated with cipro vs. placebo – treated pts had better long-term outcomes.*

[Gorman J, Sack K, Davis J](#). Treatment of ankylosing spondylitis by inhibition of tumor necrosis factor alpha. *N Engl J Med* 346:1349, 2002.

*RCTs of infliximab and etanercept demonstrated efficacy. Since then the incidence of anterior uveitis in pts on TNF treatment has decreased (A&R 52:2447, 2005).*

[Braun J, Brandt J, Listing J et al](#). Treatment of active ankylosing spondylitis with infliximab: a randomised controlled multicentre trial. *Lancet* 359:1187, 2002.

[Mease P, Goffe B, Metz J et al](#). Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial. *Lancet* 356:385, 2000.

*RCT demonstrating the efficacy of etanercept in the treatment of psoriatic arthritis. Other TNF blocking agents have shown efficacy in RCTs as well. (Adalimumab- A&R 52:3279, 2005)*

[Clegg D, Reda D et al](#). Comparison of sulfasalazine and placebo in the treatment of [Ankylosing Spondylitis](#), [psoriatic arthritis](#), and [reactive arthritis](#) - a Department Of Veterans Affairs Cooperative Study. *Arthritis Rheum* 39:2004, 1996. [\(3 ARTICLES\)](#)

*Sulfasalazine is beneficial and so is MTX (The Cochrane Library, Oxford, Issue 1, 2003).*

[Gall V](#). Exercise in the spondyloarthropathies. *Arthritis Care Res* 7:215, 1994

*Review showing the importance of PT in the management of spondyloarthropathies.*

**Adverse Events/ Side Effects** (*mostly case reports*)

[Perez-Garcia C, Maymo J, Lisbona Perez M et al](#). Drug-induced systemic lupus erythematosus in ankylosing spondylitis associated with infliximab. *Rheumatology (Oxford)* 45:114, 2006. (*2 case reports in this issue*)

*Also evidence to suggest that development of dsDNA antibodies only happens with infliximab and not etanercept but needs further study (A&R 52:2103, 2005)..*

[Ferraro-Peyret C, Coury F, Tebib J et al](#). Infliximab therapy in rheumatoid arthritis and ankylosing spondylitis-induced specific antinuclear and antiphospholipid autoantibodies without autoimmune clinical manifestations: a two year prospective study. *Arthritis Res Ther* 6:R535, 2004.

[Germano V, Picchianti Diamanti A, Baccano G et al](#). Autoimmune hepatitis associated with infliximab in a patient with psoriatic arthritis. *Ann Rheum Dis* 64:1519, 2005.

[Starmans-Kool M, Peeters H, Houben H](#). Pustular skin lesions in patients treated with infliximab: report of two cases. *Rheumatol Int* 25:550, 2005.

*There are also reports of pustular lesions associated with both other TNFs.*

[Oh J, Arkfeld D, Horwitz D](#). Development of Crohn's disease in a patient taking etanercept. *J Rheumatol* 32:752, 2005.

[Favalli E, Varena M, Sinigaglia L](#). Drug-induced agranulocytosis during treatment with infliximab in enteropathic spondyloarthropathy. *Clin Exp Rheumatol* 23:247, 2005.

[Freeman H, Flak B](#). Demyelination-like syndrome in Crohn's disease after infliximab therapy. *Can J Gastroenterol* 19:313, 2005. *Similar case reports with other TNFs.*

### **Historical/Landmark Articles**

Mielants H, Veys E et al. The evolution of spondyloarthropathies in relation to gut histology. J Rheumatol 22:2266, 1995. [PART 1.](#) [PART 2.](#) [PART 3.](#)

*Large series documenting intestinal pathology as a likely etiologic factor in spondyloarthropathies.*

[Gladman D.](#) Natural history of psoriatic arthritis. Baillieres Clin Rheum 8:379, 1994.

*Describes psoriatic arthritis and distinguishes it from the other spondyloarthropathies.*

[Dougados M, van der Linden S, Juhlin R et al.](#) The European Spondyloarthropathy Study Group preliminary criteria for the classification of spondyloarthropathy. Arthritis Rheum 34:1218, 1991.

*Diagnostic criteria for "undifferentiated spondyloarthropathy," which, in subsequent studies, is the most common form of spondyloarthropathy.*

[Hammer R, Maika S, Richardson J, Tang J, Taurog J:](#) Spontaneous inflammatory disease in transgenic rats expressing HLA-B27 and human beta2m: an animal model of HLA-B27-associated human disorders. Cell 63:1099, 1990.

*First animal model (HLA-B27 transgenic rat of human spondyloarthropathies) demonstrating that HLA-B27 molecule itself directly participates in disease pathogenesis.*

[Moll J, Haslock I, MacRae I, Wright V.](#) Associations between ankylosing spondylitis, Psoriatic arthritis, Reiter's disease, the intestinal arthropathies, and Behcet's syndrome. Medicine (Baltimore) 53:343, 1974.

*Solidified the concept of "spondylarthropathies" as related diseases distinct from rheumatoid arthritis. Conducted prior to the discovery of HLA-B27.*

[Keat A.](#) Reiter's syndrome and reactive arthritis in perspective. N Engl J Med 309:1606, 1983.

*Argues that "Reiter's syndrome" is part of the spectrum of reactive arthritis.*

[Carette S, Graham D, Little H et al.](#) The natural disease course of ankylosing spondylitis. Arthritis Rheum 26:186, 1983.

*A 25-year follow-up of men diagnosed with AS while serving in the armed forces.*

[Brewerton D, Hart F, Caffrey M et al.](#) Ankylosing spondylitis and HLA 27. Lancet 1:904, 1973.

[Schlosstein L, Terasaki P, Bluestone R et al.](#) High association of an HLA antigen, W27, with ankylosing spondylitis. N Engl J Med 288:704, 1973.

*The two papers show the striking association of ankylosing spondylitis with HLA-B27.*

[Noer H.](#) An "experimental" epidemic of Reiter's syndrome. JAMA 198:693, 1966.

*Epidemic of reactive arthritis from Shigella on a U.S. naval vessel.*

[Paronen I.](#) Reiter's disease: a study of 344 cases observed in Finland. Acta Med Scand 130, suppl 212, 1948.

*Reactive arthritis cases from an outbreak of Shigella-induced dysentery during World War II.*

### **Cutting Edge Research/ Discoveries**

[Duftner C, Dejaco C, Klauser A et al.](#) High positive predictive value of specific antibodies cross-reacting with a 28-kDa antigen for diagnosis of ankylosing spondylitis. *Rheumatology (Oxford)* 45:38, 2006.

[Kuuliala A, Soderlin M, Kautiainen H et al.](#) Circulating soluble interleukin-2 receptor level predicts remission in very early reactive arthritis. *Scand J Rheumatol* 34:372, 2005.  
*Higher levels of sIL-2R predicted remission by 6 months.*

[Kim T, Stone M, Payne U et al.](#) Cartilage biomarkers in ankylosing spondylitis: relationship to clinical variables and treatment response. *Arthritis Rheum* 52:885, 2005.

[Baeten D, Kruithof E, De Rycke L et al.](#) Infiltration of synovial membrane with macrophage subsets and polymorphonuclear cells reflects global disease activity in spondyloarthropathy. *Arthritis Res Ther* 7:R359, 2005.

[McInnes I.](#) Cytokine targeting in psoriasis and psoriatic arthritis: beyond TNFalpha. *Ernst Schering Research Foundation Workshop* 63:467, 2005.

[Ritchlin C, Haas-Smith S, Li P et al.](#) Mechanisms of TNF – and RANKL mediated osteoclastogenesis and bone resorption in psoriatic arthritis. *J Clin Invest* 111:821, 2003.

*Study illustrating the role of osteoclasts, their precursors, dysregulated OPG and TNF mechanisms in the pathogenesis of erosions in psoriatic arthritis.*