Seronegative Arthropathies

**Synonyms:** seronegative spondylarthropathy, spondyloarthritis

A heterogeneous group of inflammatory rheumatic diseases with predominant involvement of axial and peripheral joints and enthesitis (inflammation at the site of insertion of tendons and ligaments to bone). They also share other features such as anterior uveitis and bowel lesions similar to those found in Crohn's disease. Symptoms within the specific causes can overlap and may progress from one to another. There is a high incidence of HLA-B27 but negative rheumatoid factor tests.

Diseases belonging to the seronegative spondyloarthropathies' group include ankylosing spondylitis, Reiter's syndrome, enteropathic arthritis, psoriatic arthritis, Behçet's disease and juvenile idiopathic arthritis.

**The European Spondylarthropathy Study Group criteria for spondylarthropathy**[^1]

Inflammatory spinal pain, or synovitis (asymmetric, predominantly in the lower extremities) and one or more of the following:

- Family history: a first-degree or second-degree relative with ankylosing spondylitis, psoriasis, acute iritis, reactive arthritis or inflammatory bowel disease.
- Past or present psoriasis.
- Past or present ulcerative colitis or Crohn's disease.
- Past or present pain alternating between the two buttocks.
- Past or present spontaneous pain or tenderness on examination of the site of insertion of the Achilles tendon or plantar fascia (enthesitis).
- Episode of diarrhoea occurring within one month before onset of arthritis.
- Non-gonococcal urethritis or cervicitis occurring within one month before onset of arthritis.
- Bilateral grade 2-4 sacroiliitis or unilateral grade 3 or 4 sacroiliitis. Grade 0 is normal, 1 possible, 2 minimal, 3 moderate and 4 completely fused (ankylosed).

**Epidemiology**[^2]

- Ankylosing spondylitis is the most common, with prevalence in the Caucasian population of between 0.15% and 1.8%, being higher in populations with a higher background prevalence of HLA-B27 positivity.
- The prevalence of psoriatic arthritis ranges from 0.02% to 0.2%, and the incidence in the normal population is 7.2 per 100,000 per year. In patients with existing psoriasis, the prevalence of psoriatic arthritis rises to 6-42%.
- The prevalence of reactive arthritis is dependent on the background incidence of gastrointestinal or genitourinary infections. The incidence has been stated as up to 30-40 per 100,000. Seronegative spondyloarthritis symptoms are present in up to 50% of patients with inflammatory bowel disease.

**Risk factors**

- Family history: increased familial incidence
- HLA-B27 positive

**Presentation**

- The mean age at onset is 20 to 40 years. Spondyloarthropathies may sometimes be relatively mild and many patients do not seek medical advice.
- Inflammatory back pain: lumbar or dorsal pain at night or stiffness in the morning.
- Sacroilitis: buttock pain; pain alternating between the two buttocks is more specific.
- Peripheral arthritis: mainly affects the lower limbs and is often but not always asymmetrical.
Enthesitis.

Dactylitis: inflammation involving a whole finger or toe with tendovaginitis and arthritis (sausage digit).

Non-gonococcal urethritis or cervicitis, or acute diarrhoea one month or less before the onset of arthritis.

Psoriasis, balanitis or inflammatory bowel disease.

Anterior uveitis.

Family history of spondyloarthropathy.

**Differential diagnosis**

- Lumbosacral disc herniation with sciatica
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Whipple's disease
- Gout
- Osteoarthritis
- Infection: acute (eg, staphylococci, streptococci) or chronic (eg, tuberculosis, brucellosis)
- Malignancies: lymphomas, metastases

**Investigations**

These will depend on the clinical presentation and therefore the differential diagnosis.

- ESR and CRP: often raised in active disease.
- Serum urate, rheumatoid factor, antinuclear antibodies.
- Serology testing: in reactive arthritis to look for related bacterial infection.
- X-ray of the sacroiliac joints.
- MRI scan of the lumbar spine: if suspecting a lumbosacral disc lesion.
- X-ray in psoriatic arthritis may show periarticular osteolysis.

HLA testing is not normally done (high false-negative rate).

**Undifferentiated spondylarthropathy**

- Features are consistent with the spondyloarthropathies; however, the patients do not fulfil criteria for any specific spondyloarthropathy.
- May represent either an early phase or incomplete form of specific spondyloarthropathy, or may represent a distinct disease entity.
- Certain features (late average age of onset - 50 years, female to male ratio 3:1, low HLA-B27 positivity) suggest that undifferentiated spondyloarthropathy is distinct from other classic spondyloarthropathies.
- Prevalence appears to be as high as 0.6-1.9% of the population.

Management is usually based on physical therapy, non-steroidal anti-inflammatory drugs (NSAIDs) and possibly sulfasalazine, but there have been no well-designed clinical trials on the treatment of undifferentiated spondyloarthropathy.

**Management of seronegative arthropathies**

Management will depend on the type of seronegative arthropathy and individual patient presentation. See also the separate articles on Ankylosing Spondylitis, Reactive Arthritis (Reiter's syndrome), Enteropathic Arthropathies, Psoriatic Arthritis, Behçet's Disease and Juvenile Idiopathic Arthritis.

- Physical therapy: education, physiotherapy, hydrotherapy and occupational therapy.
- NSAIDs.
- Disease-modifying anti-rheumatic drugs (DMARDs) - eg, sulfasalazine and methotrexate. Indications depend on the specific classification of the spondyloarthropathy.
- Surgery: joint replacements.
Complications

- Extra-articular manifestations are very uncommon but may include:
  - Occasional aortitis, mitral valve insufficiency (rare), heart block
  - Restrictive lung disease
  - Amyloidosis

Prognosis

- The course of spondyloarthropathies is very variable and there may be spontaneous remissions or exacerbations, particularly in the early stages.
- Disease activity generally persists for many decades, rarely entering a long-term remission.

Further reading & references


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Current Version: Dr Colin Tidy
Peer Reviewer: Dr John Cox

Document ID: 2767 (v22)
Last Checked: 16/04/2014
Next Review: 15/04/2019

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