SPONDYLOARTHRITIS

What is Spondyloarthritis?

Spondyloarthritis (SpA) is a descriptive term that essentially infers the presence of inflammation of the spine. A number of different terms have been used for that purpose including Spondyloarthropathy and Spondylitis. Following rigorous debate in the Rheumatology community,Spondyloarthritis has recently been agreed upon as the most appropriate.

Spondyloarthritis does not relate to one specific disease entity but instead covers a heterogeneous group of Rheumatic diseases that are characterised by common clinical features, most frequent of which is inflammatory back pain. These patients are categorised into one of two groups dependant upon which symptoms predominate.

That is, they can be classified as having Axial SpA when the spine is the primary target of the disease or Peripheral SpA when the joints away from the spine are affected.

> "Axial is the term used to describe the central aspect of the skeleton and includes the spine, pelvis, sternum, and skull."

Axial SpA is subclassified into a number of conditions, including:

1) AnkylosingSpondylitis (AS);
2) Psoriatic Arthritis: usually the patient also has psoriasis, an autoimmune skin condition;
3) Inflammatory Bowel Disease-related arthritis: associated with Crohn's disease or Ulcerative Colitis;
4) Reactive arthritis: when the condition is triggered by an infection, most commonly affecting the urinary of intestinal tracts.

There are a number of patients with SpA who do not demonstrate sufficient features to meet the criteria for the above classifications.

These patients have been described as having undifferentiated SpA when there is inflammatory back pain without structural changes in the sacroiliac joints or spine, the term non-radiographic Axial SpA has been used.

Although a proportion of these patients may evolve into one of the other categories, it should be noted that not all patients with SpA progress to develop AS.

A major impetus for identifying patients with inflammatory back pain and subsequently SpA is that there is often a significant delay in the diagnosis of AS and the other Spondyloarthritides described above.

The delay in diagnosis has been shown to be a predictor of functional outcome, radiographic progression and hence, damage associated with the disease, as well as the increased mortality associated with AnkylosingSpondylitis (especially when the diagnosis has been delayed for more than 12 years).

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Furthermore, recent developments in the treatment of SpA have demonstrated a positive impact upon numerous facets of the disease, highlighting the value of an early diagnosis.

How is Spondyloarthritis diagnosed?

The early diagnosis of Axial Spondyloarthritis (Axial SpA) has been the focus of the Rheumatological community, with the Assessment SpondyloArthritis international Society (ASAS) recently publishing classification criteria to assist in this regard.

The criterion presented below was published by Rudweleit and his associates in 2009 (Rudweleit et al. *Annals of Rheumatic disease* 2009; 68: 777-783):

The entry criteria requires back pain to be present for at least 3 months and the onset of the symptoms begin before the age of 45. These have been determined because back pain is very common in the community, most commonly related to a structural cause such as an injury to the intervertebral disc. However, back pain of this type resolves in the majority of those affected within the first 3 months. In addition, the young age of onset reflects the fact that SpA often affects patients in the 3rd decade of life, with the average age of onset commonly reported to be in the mid 20s.

Of the SpA features, inflammatory back pain (IBP) is most prominent. However, the definition of (IBP) has itself been often

ASAS classification criteria for axial SpA

(in patients with back pain ⩾ 3 months and age at onset < 45 years)

Sacroiliitis on imaging* plus ⩾ 1 SpA feature**	or	HLA-B27 plus ⩾ 2 other SpA features**

** SpA features:
- Inflammatory back pain
- Arthritis
- Enthesitis (heel)
- Uveitis
- Dactylitis
- Psoriasis
- Crohn's disease/ulcerative colitis
- Good response to NSAIDs
- Family history for SpA
- HLA-B27
- Elevated CRP

* Sacroiliitis on imaging:
- Active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
  or
- Definite radiographic sacroiliitis according to mod. New York criteria

Sensitivity 82.9%, specificity 84.4%; n = 649 patients with chronic back pain and age at onset < 45 years.
Imaging arm (sacroiliitis) alone has a sensitivity of 66.2% and a specificity of 97.3%.
** Note: Elevated CRP is considered a SpA feature in the context of chronic back pain

been debated with a number of criteria being put forward to identify this symptom most accurately. Most recently ASAS also put forward a criterion to define back pain as inflammatory in nature.

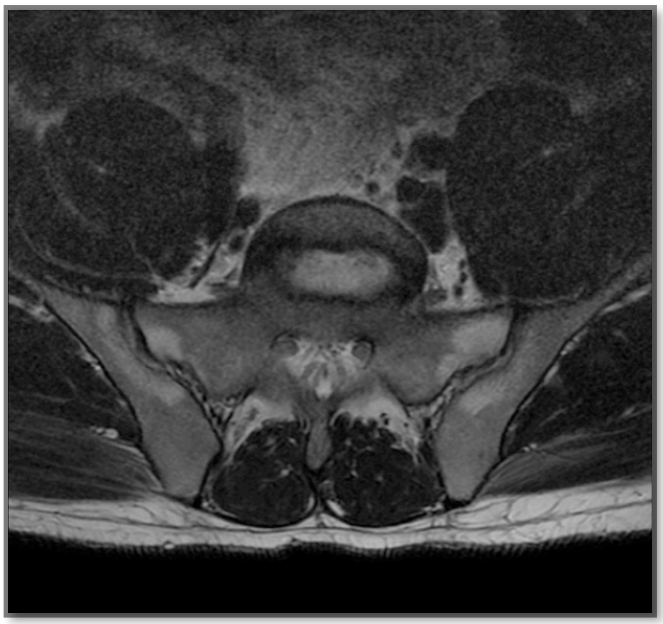
The clinical features of back pain that are suggestive of inflammation include:

1. Age at onset <40 years
2. Insidious onset
3. Improvement with exercise
4. No improvement with rest
5. Pain at night with improvement upon getting out of bed

They found that when 4 of these 5 features are present the pain can be confidently categorised as being inflammatory back pain. It should be noted however that the presence of a single feature is not sufficient to accurately discriminate back pain as either due to inflammation or a mechanical cause.

The ability to visualise inflammation involving the spine has been a major advance in the diagnosis of SpA.

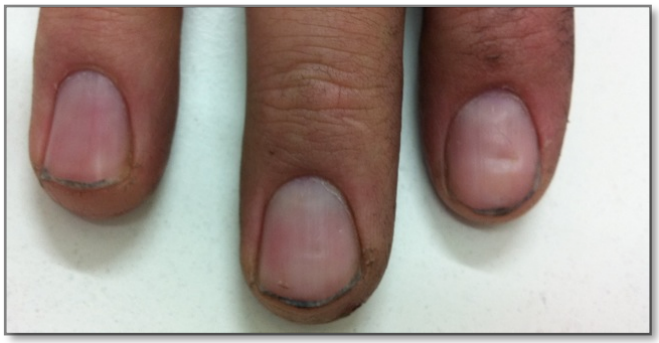
Magnetic Resonance Imaging (MRI) has revolutionised the approach to assessing patients with IBP, given the sensitivity this modality has demonstrated in the identification of inflammation present at involved joints, particularly at the sacroiliac joints (which are most commonly affected by the disease). However, MRI imaging does not identify inflammation in all patients with SpA(being negative in about 20% of those affected) and so a negative MRI scan does not rule out the disease.



MRI of the sacroiliac joints showing bone marrow oedema and irregularity of the joint margins, due to sacroiliitis. Image courtesy of Anatomate-Apps.

Therefore, ASAS has suggested HLA B27 can be helpful in the diagnosis of SpA. HLA B27 is a protein that is present on the surface of certain cells, where it has an important role in the action of the immune system. HLA B27 is strongly associated with Ankylosing Spondyitis and to a lesser extent the other Spondyloarthritides. This marker is present in 90-95% of those with AS, which is higher compared to those with Psoriatic spondyloarthritis, Enteropathic spondyloarthritis, or Reactive arthritis where HLA B27 is present in 50%, 60%, and 75% respectively. However, HLA B27 is present in 8-12% of the

'normal' Australian population and as such, on its own does not define SpA. Consequently, for the presence of HLA B27 to be considered relevant, two or more clinical features of SpA need to be present.



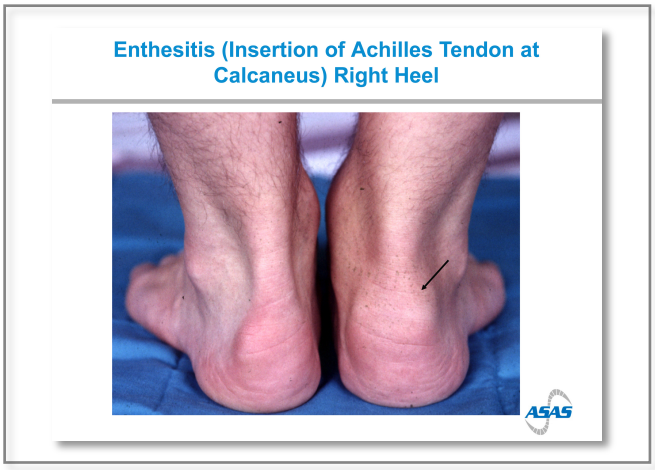
Psoriasis affecting the nails: pits and ridging

Assessing for the presence of inflammation throughout the body via blood tests, by measuring the level of C-Reactive Protein (CRP) and/or Erythrocyte Sedimentation Rate (ESR) can be useful in determining the severity of disease, even though these tests have limited utility in the diagnosis of the disease. They are elevated in only a proportion of patients with SpA, but when raised, suggest that the condition is more likely to develop damage and result in functional impairment as well as predict a shorter survival in those that develop AS.

As a result, certain treatment options that have recently become available are only subsidized by Medicare Australia in those in whom the inflammatory markers mentioned above are raised.

Finally and interestingly a rapid response to the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) is also considered as a diagnostic test for SpA. NSAIDs are an important component in the management of SpA as patients generally demonstrate a significant improvement in their symptoms, usually within the first two days of use. However, a lack of response to an NSAID certainly does not exclude the diagnosis of SpA.

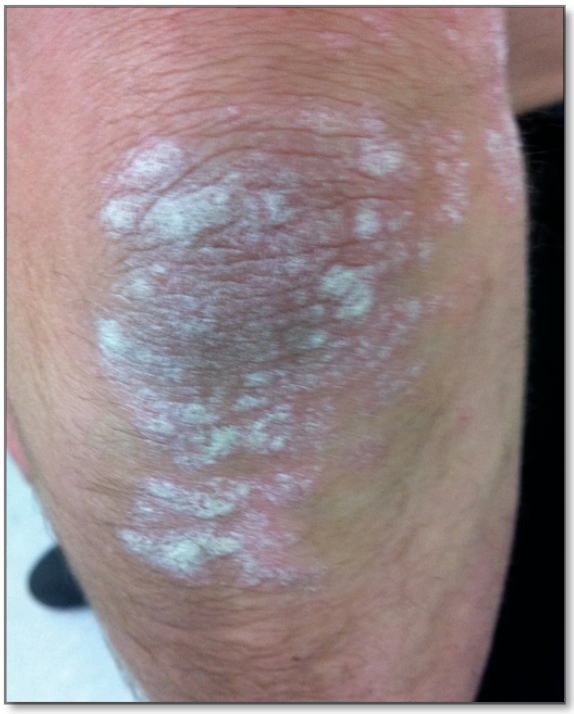
As described above, none of these diagnostic tests are individually able to rule the diagnosis either in or out, but rather it is the combination of positive results to these tests that allow the diagnosis of SpA to be made with confidence early in the course of the disease. This is of value since chronic back pain is a common problem in primary care, for which it has estimated that SpA is the cause in 5%.



Credit: ASAS Educational Slide Kit
(http://www.asas-group.org/education.php?id=04)

How is Spondyloarthritis treated?

The treatment of Spondyloarthritis (SpA) is the same as the treatment outlined for AnkylosingSpondylitis (AS). This essentially involves the combination of exercise therapy and NSAID therapy. There is increasing evidencethat the early implementation of therapy can affect the long-term outcomes of the disease with regards to the damage caused and the subsequent impairment in function that results.



Psoriasis affecting the elbow

The use of anti-TNF therapy to specifically block the driver of inflammation may lead to further additional improvements in these outcomes.

In Australia, these medications are not currently available for the management of undifferentiated SpA or non-radiographic SpA but are available for treating those with AS and Psoriatic Arthritis in whom the inflammatory markers (CRP and ESR) are raised. The specific anti-TNF blocking medications available in Australia include Infliximab (Remicade), Etanercept (Enbrel), Adalimumab (Humira), and Golimumab (Simponi).