

Diagnosis and management of **axial spondyloarthritis** in primary care

KEY PRACTICE POINTS:

- Axial spondyloarthritis is relatively uncommon and is likely to be the cause of long-term back pain in only 5% of patients
- Axial spondyloarthritis is characterised by a slow onset of back pain in the absence of injury, onset before the age of 45 years, improvement with exercise rather than rest, back stiffness in the morning resolving with movement, pain or stiffness which wakes the patient and pain that responds well to non-steroidal anti-inflammatory medicines (NSAIDs)
- Diagnosis is aided by a family history, clinical examination, CRP, HLA-B27 testing and radiographic imaging. Imaging is usually reserved for patients with back pain of at least three months duration
- Early diagnosis and treatment is beneficial
- Many patients can be effectively managed in primary care with exercise, physiotherapy and NSAIDs
- Patients with ankylosing spondylitis who do not benefit from NSAIDs usually benefit from tumour necrosis factor (TNF) inhibitors initiated in secondary care

Ankylosing spondylitis is a relatively uncommon inflammatory cause of long-term back pain which can result in radiographic changes in the spine and sacroiliac joints. Ankylosing spondylitis is part of a spectrum of interrelated conditions collectively termed spondyloarthritis. Patients with axial spondyloarthritis have predominantly spinal symptoms and some will develop classical ankylosing spondylitis. Axial spondyloarthritis is an insidious disease and difficult to diagnose; patients have an average delay of eight years from the onset of symptoms to diagnosis. Recent evidence suggests early treatment with exercise, physiotherapy and pharmacological treatments may delay disease progression and therefore improve outcomes.

A new way of thinking about spondyloarthritis

Spondyloarthritis is a collective term for a group of diseases including ankylosing spondylitis, psoriatic arthritis, reactive arthritis and arthritis associated with inflammatory bowel

disease.¹ There is considerable overlap between the symptoms, signs and genetic risk factors for these diseases and patients may have more than one of these conditions (Table 1). Although these have historically been defined as separate conditions they are now thought to be a single disease with different phenotypes.²

Classifying spondyloarthritis

Spondyloarthritis is classified as axial or peripheral, depending on whether patients primarily experience symptoms in the spine, sacroiliac joints, hips and ribcage (the axial skeleton), as seen in patients with ankylosing spondylitis, or peripheral joints, as seen in those with psoriatic arthritis.⁵

Axial spondyloarthritis is a continuum

Axial spondyloarthritis is now viewed as a continuum of disease which can lead to ankylosing spondylitis (Figure 1). In patients with ankylosing spondylitis, inflammatory changes eventually affect the spinal and sacroiliac joints, leading to spinal fusion, reduced mobility and an increased risk of spinal fractures. Various diagnostic criteria have been used for ankylosing spondylitis, with all relying on evidence of radiographic damage as a criterion for diagnosis.⁶

It is now recognised that patients in earlier stages of disease do not have radiographic changes, but share similar symptoms and signs, family history and genetic risk factors, and can experience disability as severe as some patients with a confirmed diagnosis of ankylosing spondylitis.⁵

Table 1: Overlap between ankylosing spondylitis and other forms of spondyloarthritis.^{3,4}

Percentage of patients with ankylosing spondylitis who also have:			
Peripheral arthritis	Acute anterior uveitis	Psoriasis	Inflammatory bowel disease
50%	26%	9%	7%

Patients in the early stage of disease are classified as having “non-radiographic axial spondyloarthritis”. Follow-up studies report that among patients diagnosed at this early stage, 6% develop ankylosing spondylitis after five years, 17% after ten years and 26% after 15 years.⁷ Therefore, some patients may never develop ankylosing spondylitis, while others may live with inflammatory back pain for a considerable time before developing ankylosing spondylitis.

Early diagnosis and treatment may improve patient outcomes

Research suggests that early diagnosis of axial spondyloarthritis improves patient outcomes, resulting in less pain and functional limitation, and may avoid unnecessary testing, treatment or referral.⁹ Although long term studies are lacking, limited evidence associates early treatment with reduced skeletal damage on radiography.¹⁰

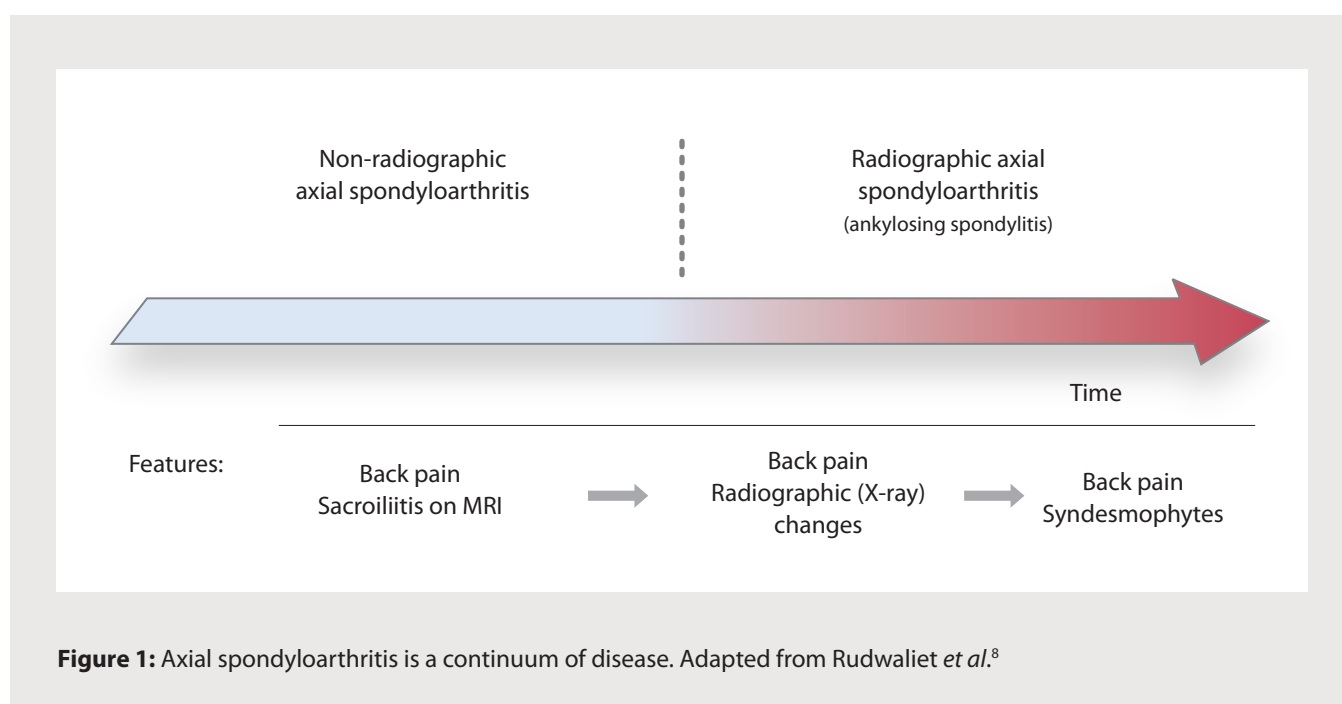


Figure 1: Axial spondyloarthritis is a continuum of disease. Adapted from Rudwalia *et al.*⁸

Evaluating patients with suspected axial spondyloarthritis

Low back pain lasting longer than three months is a common symptom in primary care; **spondyloarthritis is estimated to be the cause in only 5% of these patients.**³

In patients with complex histories, e.g. previous injuries, diagnosing spondyloarthritis can be challenging and the diagnosis may need to be revisited after other causes have been excluded. The clinical picture may be further complicated by co-morbidities such as depression which can compound pain and functional limitation.

Key features of spondyloarthritis

Symptoms of spondyloarthritis generally begin in early adulthood. Males and females are equally affected in the early stages, but males are two and half times more likely to progress to ankylosing spondylitis.^{1,2}

Key features which help identify patients with axial spondyloarthritis include back pain consistent with inflammation and a positive family or personal history of inflammatory diseases (see: "Criteria to assist the diagnosis of axial spondyloarthritis in primary care", below).¹¹

Criteria to assist the diagnosis of axial spondyloarthritis in primary care

In patients with back pain lasting more than three months beginning before age 45 years, the presence of two or more of the following criteria has a sensitivity of 100% and specificity of 60% for identifying patients with axial spondyloarthritis, compared to diagnosis by a rheumatologist:^{5,11}

- Inflammatory back pain*
- Peripheral manifestations, such as arthritis, dactylitis or enthesitis, especially of the Achilles tendon or plantar fascia
- Psoriasis, inflammatory bowel disease or a history of uveitis
- A family history of spondyloarthritis or related spectrum disorders†
- Back pain which improves after 24 – 48 hours of treatment with an NSAID
- Elevated C-reactive protein (CRP), where causes such as spinal infection or cancer have been excluded. Patients with axial spondyloarthritis or ankylosing spondylitis may have CRP levels ranging from > 6 mg/L (slightly elevated) to 20 – 30 mg/L.¹²

- Positive HLA-B27 test
- Sacroiliitis on X-ray or MRI

* At least four out of the five criteria from "Differentiate inflammatory back pain from pain due to other causes"

† A first-degree or second-degree relative with ankylosing spondylitis, psoriasis, uveitis, reactive arthritis or inflammatory bowel disease

Differentiate inflammatory back pain from other causes

Inflammatory back pain is a hallmark of axial spondyloarthritis, although it is not specific; patients with diseases such as rheumatoid arthritis may also have inflammatory back pain. Back pain in patients with axial spondyloarthritis typically has a gradual onset, without any specific injury, before the age of 45 years.

Features consistent with back pain due to inflammation include:¹³

- Improvement with exercise
- No improvement with rest
- Pain at night, including early morning
- Morning stiffness
- Pain which alternates between buttocks

Patients with four of these criteria are likely to have pain caused by inflammation rather than mechanical or other causes.¹³

Important differential diagnoses and their features include:^{14,15}

- **Muscle pain** from poor posture and core muscle weakness – may be exacerbated by injury
- **Fracture** – risk factors include older age, osteoporosis, osteopenia or the use of corticosteroids
- **Herniated disc** – characterised by leg pain with lower lumbar nerve root distribution
- **Spinal stenosis** – results in radiating leg pain, more common in older adults
- **Referred pain** – causes include abdominal aortic aneurysm, pelvic inflammatory diseases, endometriosis, prostatitis, renal or gastrointestinal disease
- **Vertebral infection** – assess whether patients have fever, have had a recent infection or have used intravenous drugs
- **Cauda equina syndrome** – features include urinary retention, motor deficits in the lower limbs, faecal incontinence and "saddle" anaesthesia – the most frequent finding is urinary retention, which has a sensitivity of 90%; the probability of cauda equina

syndrome without urinary retention is approximately 1 in 10,000 patients

- **Cancer** – consider in patients with history of cancer, unexplained weight loss, older age or ongoing back pain for more than one month
- **Other** – Scheuermann’s disease of the spine, most commonly occurring during adolescence and treated conservatively,¹⁶ and Diffuse Idiopathic Skeletal Hyperostosis (DISH); a severe form of degenerative thoracic and lumbar spondylosis which is more common in patients with diabetes.¹⁷

Assess whether patients have a family history of a spondyloarthritis

Spondyloarthritis is highly heritable. A family history of inflammatory bowel disease confers a three-fold increased risk of ankylosing spondylitis. A family history of psoriasis, recurrent uveitis or reactive arthritis are also risk factors.^{5,18}


Look for symptoms and signs in peripheral joints, the skin, eyes and gut

People with axial spondyloarthritis often have symptoms in peripheral joints and extra-articular features as inflammatory processes can cause damage in other organs. Most often this involves the eyes, skin, gastrointestinal and urogenital tracts.¹ Reactive arthritis can develop in response to a recent episode of gastroenteritis due to *Yersinia*, *Salmonella*, *Shigella*, and *Campylobacter*; symptoms typically begin two to ten days after onset of gastroenteritis. *Chlamydia* infections resulting in genitourinary symptoms are also a common trigger.¹⁹


Musculoskeletal system: examine patients for the presence of:³

- Achilles tendinitis and plantar fasciitis
- Chest wall pain, which can be caused by intercostal enthesitis
- Dactylitis (inflamed finger joints and swelling of the whole finger or toe, also referred to as “sausage digit”)


Eyes: acute anterior uveitis (iritis) occurs in approximately one-quarter of patients with ankylosing spondylitis.⁴ In patients with acute anterior uveitis, 20 – 25% can be expected to have spondyloarthritis.²⁰ Patients who present with acute anterior uveitis should be referred for ophthalmology assessment. HLA-B27 is highly prevalent in patients with recurrent anterior uveitis patients and is independently associated with recurrent anterior uveitis even in the absence of musculoskeletal symptoms.²⁰

 For further information on the diagnosis of acute anterior uveitis, see: www.bpac.org.nz/BPJ/2013/August/redeye.aspx

Skin and nails: check for psoriasis in the scalp line, behind the ears, extensor surfaces of elbows and knees, natal cleft and umbilicus. Examine nails for signs of psoriasis.

 For further information on diagnosing and treating psoriasis, see: www.bpac.org.nz/BPJ/2009/September/psoriasis.aspx

Gastrointestinal tract: ask patients about bowel habits and any changes consistent with inflammatory bowel disease or a recent gastrointestinal infection. Approximately 60% of patients with ankylosing spondylitis have mucosal inflammation detectable on colonoscopy, and up to 30% of patients with ankylosing spondylitis will report bowel symptoms if questioned.^{3,21}

 For further information on inflammatory bowel disease, see: www.bpac.org.nz/BPJ/2008/September/crohns.aspx

Genitourinary symptoms: patients may have ongoing urethritis following resolution of an infection, or a history of *Chlamydia* infection.¹⁹

Consider laboratory or imaging investigations

Testing CRP and HLA-B27 is appropriate for patients where there is a strong suspicion of axial spondyloarthritis. In cases with less certainty ordering CRP and HLA-B27 tests may not be helpful as the results are non-specific. An elevated CRP is associated with more aggressive disease and a worse prognosis.²

Radiographic imaging can detect changes consistent with ankylosing spondylitis, however, patients without radiographic changes may still have back pain due to early stage axial spondyloarthritis.

The HLA-B27 gene is the strongest genetic risk factor

Testing for HLA-B27 can assist diagnosis and a negative HLA-B27 may help rule out axial spondyloarthritis, but it is not a definitive test. HLA-B27 risk alleles are relatively common in the population; approximately 9% of New Zealand Europeans and 6–7% of Māori have HLA-B27 risk alleles.²² People with the HLA-B27 risk allele are approximately 60 times more likely to develop ankylosing spondylitis.²³ However, other genetic and environmental factors play a role in the development of disease as only 5% of people with risk alleles develop ankylosing spondylitis.³ Therefore HLA-B27 testing should not be used to screen asymptomatic people.

Radiographic imaging: to order or not to order?

Radiographic investigations can be reserved for patients with back pain for three months or more, or who meet criteria suggestive of axial spondyloarthritis.²⁴ If radiological investigations are indicated, initially request anterior-posterior lumbar X-rays which include the sacroiliac joints.¹⁵

The benefits of X-rays include:

- Changes in the spine or sacroiliac joints identified by radiography are required for a definitive diagnosis
- Radiography can demonstrate disease progression or identify prognostic factors, e.g. hip arthritis is associated with a poorer prognosis³

Factors which favour delaying or not requesting X-rays include:^{15,24}

- Early imaging, e.g. for back pain of six weeks or less, does not improve patient outcomes or rates of diagnosis
- Plain X-ray imaging cannot detect early disease
- Management may not be influenced by radiography as first-line treatments for all patients with axial spondyloarthritis include exercise and NSAIDs
- Radiographic changes are slowly progressive; imaging is recommended at intervals of at least two years even in patients with a definitive diagnosis

MRI is able to detect inflammatory changes in the axial spine and sacroiliac joints at an earlier stage of disease than plain X-ray. Consultation with a rheumatologist may be appropriate for patients where there is clinical suspicion of axial spondyloarthritis but no evidence of disease on X-ray.³

When should patients be referred to a rheumatologist?

For patients where there is a strong suspicion of axial spondyloarthritis, discussion with or referral to a rheumatologist is recommended as most will benefit from specialist assessment. After diagnosis, many of these patients can be managed in primary care with first-line treatments.

Patients with radiographic changes and a high burden of symptoms (see: "The BASFI and BASDAI scores") may be candidates for TNF inhibitor use (see: "Beyond NSAIDs") and should be reviewed by a rheumatologist.

Treatment of patients with axial spondyloarthritis

Treatment of patients with axial spondyloarthritis aims to improve quality of life and preserve spinal mobility by reducing inflammation.

Patients who are recently diagnosed require education and advice on living with spondyloarthritis, see: "Resources for patients with axial spondyloarthritis".

Assessing patients for inflammation and impairment

Ask patients about their ability to carry out tasks such as

dressing, their level of fatigue and any problems they have sleeping. Driving can be an issue for patients with advanced ankylosing spondylitis as fusion of the cervical spine makes neck rotation difficult. The patient may need driving advice, extra mirrors or a reversing camera.


A patient's symptoms are the most reliable marker of whether they have active disease. Symptoms can be assessed and monitored using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) scores:⁶

- The BASDAI score covers common features of pain and discomfort experienced by patients with axial spondyloarthritis. Special Authority criteria for TNF inhibitor medicines requires this score.
- The BASFI assesses patient impairment and monitors disease progression

CRP levels are not elevated in all patients with axial spondyloarthritis but are an additional marker for follow-up visits for patients with previously elevated levels.

Smoking cessation, exercise and physiotherapy are the cornerstones of treatment

Smoking is associated with an earlier age of onset of axial spondyloarthritis, high levels of disease activity, functional impairment and radiographic damage; smoking cessation should be strongly recommended.^{25, 26} Some, but not all, studies suggest smoking is associated with worse prognosis, and current smoking has been reported to reduce the effect of TNF inhibitor treatment.^{25,26}

 For further information on smoking cessation, see: www.bpac.org.nz/BPJ/2014/October/smoking-cessation.aspx

Encourage regular exercise

Regular exercise can improve pain, function and mood.²⁷ Patients should be referred to a physiotherapist to improve muscle relaxation, flexibility, strength, breathing and posture.²⁸ Other treatment options include walking, swimming or pool-based exercises or non-exercise options such as massage and the use of a spa pool.²⁸ Encourage patients to attend group-based classes as supervised group activity may be more beneficial and result in greater adherence than exercises conducted alone.²⁷

Exercises should be tailored to the patient's mobility and flexibility. High impact exercises should be avoided as these may exacerbate spinal pain and inflammation.²⁸ Patients with advanced ankylosing spondylitis are at increased risk of spinal fractures due to changes in spine biomechanics. For these patients the safety of exercise options becomes more important.

NSAIDs can be added to non-pharmacological approaches

NSAIDs produce modest improvements in axial spondyloarthritis. In clinical trials patients rated measures of pain, function and disease activity 9% to 22% lower after six weeks of NSAID use, compared to placebo treatment, with numbers-needed-to-treat (NNT) of 2 to 5.²⁹

Naproxen has a long half-life and has not been associated with increased cardiovascular risk, making it an appropriate first choice NSAID, however, other NSAIDs may be preferred by some rheumatologists.


Suitable NSAIDs and doses for patients with axial spondyloarthritis include:^{30,31}

- Naproxen, 500 – 1000 mg, daily
- Diclofenac, 75 – 150 mg, daily
- Ibuprofen, 1200 – 2400 mg, in daily divided doses, or modified release tablets 1600 mg, as a single daily dose, preferably in the evening
- Ketoprofen, 100 – 200 mg daily

For patients with intermittent disease activity, NSAIDs can be used as required, but continuous use is preferred for patients with ongoing symptoms and disease activity, e.g. consistently elevated CRP; preliminary evidence suggests continuous use may reduce disease progression.^{27, 29}

Recent studies suggest the incidence of upper gastrointestinal bleeding is very low in patients with spondyloarthritis, most likely because patients are young at diagnosis and seldom have co-morbidities.²⁹ For patients with an increased risk of gastrointestinal adverse effects a selective COX-2 inhibitor, such as celecoxib, 200–400 mg daily, or etoricoxib, 90 mg daily, could be used or a non-selective NSAID with a proton pump inhibitor.²⁹ Selective COX-2 inhibitors are unsubsidised.

Ask patients about any over-the-counter (OTC) pain relief and herbal supplements they are using, especially OTC NSAIDs.

 For further information on prescribing NSAIDs, see: www.bpac.org.nz/BPJ/2013/October/nsaids.aspx or www.nzf.org.nz/nzf_5476

The BASDAI and BASFI scores⁶

The BASDAI consists of six questions. Patients score on a scale of zero (none) to ten (very severe) their degree of symptoms (with the exception of question 5b). Questions 5a and 5b assess two features of inflammatory back pain: these responses are averaged before combining results for the remaining questions:

1. How would you describe the overall level of fatigue or tiredness (since the last visit)?
2. How would you describe the overall level of neck, back or hip pain?
3. How would you describe the overall level of pain or swelling in joints other than the neck, back or hips?
4. How would you describe the overall level of discomfort from any areas tender to touch or pressure?
- 5a. How would you describe the overall level of morning stiffness from waking?
- 5b. How long does morning stiffness last from waking? (Scored from 0 to 10, where 10 equals two hours)

The overall BASDAI score equals the sum of questions 1–4, plus the average of questions 5a and 5b, then dividing the total by 5, resulting in a score from zero to ten. Patients with scores ≥ 6 may be eligible for TNF inhibitor treatment.

The BASFI scores on a zero to ten scale the difficulty patients experience in daily activities and is routinely used in secondary care.⁶ BASFI can also be used to assess response to treatment. Zero is “easy” and ten is “impossible”:

1. Putting on socks or tights without help or aids
2. Bending forward from the waist to pick up a pen from the floor without an aid
3. Reaching up to a high shelf without help or aids
4. Getting up out of an armless chair without using hands or any other help
5. Getting up off the floor from supine without help
6. Standing unsupported for ten minutes without discomfort
7. Climbing 12 to 15 steps without using a handrail or walking aid, with one foot at each step
8. Looking over shoulder without turning the body
9. Doing physically demanding activities, e.g. exercises, gardening, sports
10. Doing a full day’s activities, whether at work or at home

The overall BASFI score is calculated as the average of the ten scores to give a value between 1 and 10.

Beyond NSAIDs

Referral or consultation with a rheumatologist may be required for patients who do not gain sufficient benefit from treatment with NSAIDs, exercise and physiotherapy. Additional treatments include:


Intra-articular corticosteroid injections which can assist with localised peripheral joint inflammation, however, oral corticosteroid treatment is not recommended.²⁷

Disease-modifying anti-rheumatic drugs (DMARDs) are not recommended for the treatment of axial symptoms in patients with axial spondyloarthritis or ankylosing spondylitis, due to a lack of efficacy. However, DMARDs such as sulfasalazine may be considered for patients with ongoing peripheral symptoms. Consider consulting with a rheumatologist to assess whether initiation is warranted. Evidence supports the use of sulfasalazine in the treatment of peripheral symptoms over methotrexate.²⁷

TNF inhibitors, adalimumab, etanercept and infliximab can be effective for patients with more advanced disease. These medicines are fully subsidised and must be initiated by a rheumatologist; renewal applications can be made by a general practitioner on recommendation from a rheumatologist. Patients need to fulfil various application criteria, including having:

- Ankylosing spondylitis for at least six months' duration with radiographic evidence of disease
- Back pain which is relieved by exercise but not rest
- A BASDAI score of ≥ 6
- Moderate to severe limitation of lumbar spine flexion or chest expansion
- Trialled two or more NSAIDs during a three month exercise regimen supervised by a physiotherapist

In trials of TNF inhibitors approximately half of patients achieved a clinical reduction in pain and improvement in function and wellbeing after six months, with an NNT ranging from 3 to 5. In addition, approximately one in five experienced a partial remission, with an NNT of 3 to 11.³²

 General practitioners caring for patients taking TNF inhibitors should be aware of the safety issues associated with these medicines (see: "Special precautions for patients taking TNF inhibitors" and Table 2).

Follow-up in primary care

Treatment success is based on improvements in the patient's pain, and mobility. Patients requiring follow-up are likely to fall under one of two categories:

1. Patients with early disease who are being managed in primary care

2. Monitoring of patients managed in secondary care

Patients managed in primary care

Self-reporting questionnaires, e.g. BASDAI, BASFI, can be used to track disease activity and patient wellbeing. There is no benefit from routine radiographic imaging during follow-up. Monitoring of CRP levels can be an additional measure of disease activity for patients with active symptoms and previously elevated CRP levels.

Monitoring patients managed in secondary care

Patients managed in secondary care are more likely to have advanced axial spondyloarthritis and meet criteria for diagnosis of ankylosing spondylitis. Ankylosing spondylitis is associated with an increased risk of complications, either due to the disease itself or associated treatments.

Patients with ankylosing spondylitis have an increased risk of osteoporosis and spinal fractures.²⁷ Assessment of osteoporosis should consist of bone densitometry (DEXA) scans of the spine and hips, and an earlier age of testing may be appropriate depending on disease severity.³³ Management of osteoporosis is the same as for other patients due to a lack of trials in patients with both conditions to guide treatment recommendations.²⁷ Consultation with a rheumatologist is recommended where there is clinical uncertainty.

Patients with ankylosing spondylitis have an increased risk of cardiovascular disease, due in part to higher rates of smoking, as well as decreased mobility and inflammation.³⁴ It is recommended that patients with ankylosing spondylitis undergo more frequent evaluation of cardiovascular risk, e.g. every three years or more frequently for patients with greater disease activity.³⁴ Clinicians may also consider adopting a lower threshold for initiation of cardiovascular risk management.³⁴

Patients with ankylosing spondylitis have an approximate two-fold increased risk of renal calculi, compared to the general population.³⁵

Consultation with a rheumatologist and obstetrician may be appropriate if patients with ankylosing spondylitis become pregnant. Patients with ankylosing spondylitis may have a higher risk of preterm birth, small for gestational age babies and emergency caesarean section delivery.³⁶

Special precautions for patients taking TNF inhibitors

Patients taking TNF inhibitors are at increased risk of infection, however, the overall risk of serious infection is low: a 2010 meta-analysis found that 257 patients would need to be treated for six months for one extra serious infection to occur.³⁷ Patients with spondyloarthritis are less prone to infection than those with rheumatoid arthritis, possibly because they are younger and generally healthier.³⁸ Table 2 provides precautions for clinicians treating patients with TNF inhibitors.

Do not administer live attenuated vaccines in patients

Table 2: Safety and monitoring of TNF inhibitor treatment.^{39, 40}

	Potential issue or complication	Clinicians	Patients
Prior to initiation *	Activation of latent tuberculosis (TB) infection	Test for TB prior to initiation	–
	Avoid use during pregnancy	Exclude pregnancy. TNF inhibitors should not be used by females trying to conceive and are not recommended until breastfeeding has finished; consultation with a rheumatologist and obstetrician is recommended if a patient becomes pregnant	Use adequate contraception and inform clinicians if planning a pregnancy or immediately if pregnancy occurs
During treatment	Increased risk of infection	Have a lower threshold for initiating antibiotics. Notify and consult with the initiating clinician if a severe infection occurs. Treatment may need to be withdrawn until the infection has resolved.	Have increased attention to food hygiene, and avoid foods containing unpasteurised milk, uncooked eggs or raw meat. Inform health professionals before major surgery about TNF inhibitor use. Withholding treatment for one to two doses may reduce infection risk.
	Possible increased risk of malignancy	Have a low threshold for investigating suspicious skin lesions for possible melanoma or non-melanoma skin cancers	Be “sun smart”

* TNF inhibitors are initiated by a rheumatologist and some tests may be conducted in secondary care


taking TNF inhibitors; other forms of vaccination may continue. If possible, vaccinate against influenza and pneumonia prior to starting treatment.^{39, 40}


Common adverse effects experienced by patients taking TNF inhibitors include injection site reactions in 20–30% of patients which usually subside within 24 hours, and chills and nausea following a dose.³⁹

Monitoring for adverse effects is conducted three months after initiating TNF inhibitor treatment, and every six months thereafter, including:⁴¹

- Full blood count
- Creatinine and electrolytes
- Liver function tests

Some patients develop anti-TNF inhibitor antibodies which reduce the efficacy of these medicines. Patients who fail to respond or have worsening symptoms during treatment may benefit from switching to a different TNF inhibitor.

 For further information on TNF inhibitors, see: www.bpac.org.nz/BPJ/2013/December/biologic.aspx

 For further information for patients using TNF inhibitors, see: www.rheumatology.org/I-Am-A/Patient-Caregiver/Treatments/Anti-TNF

Prognosis

The progression of axial spondyloarthritis is highly variable and complete spinal fusion is not inevitable. The majority of patients are likely to spend many years in early stages of disease with varying degrees of pain and impairment. During this time patients may benefit from treatment even if they do not meet the diagnostic criteria for ankylosing spondylitis. Untreated, patients with ankylosing spondylitis are less likely to be able to work and more likely to have disabling pain and depression.

Acknowledgement: Thank you to **Associate Professor Simon Stebbings**, Dunedin School of Medicine, University of Otago for expert review of this article.

Resources for patients with axial spondyloarthritis:

Information about ankylosing spondylitis and axial spondyloarthritis:

- www.arthritis.org.nz/campaign/
- www.rheumatology.org/l-Am-A/Patient-Caregiver/Diseases-Conditions/Spondyloarthritis
- www.arthritisresearchuk.org/arthritis-information/conditions/ankylosing-spondylitis.aspx

Advice and guidance on appropriate exercises:

- <http://nass.co.uk/exercise/>

NZF patient information leaflets on NSAIDs:

- Naproxen: www.mymedicines.nz/home/sheet/Naproxen
- Ibuprofen: www.mymedicines.nz/home/sheet/Ibuprofen
- Diclofenac: www.mymedicines.nz/home/sheet/Diclofenac

Advice for patients using TNF inhibitors:

- www.rheumatology.org/l-Am-A/Patient-Caregiver/Treatments/Anti-TNF

References:

1. Elewaut D, Matucci-Cerinic M. Treatment of ankylosing spondylitis and extra-articular manifestations in everyday rheumatology practice. *Rheumatology (Oxford)* 2009;48:1029–35. doi:10.1093/rheumatology/kep146
2. van Tubergen A. The changing clinical picture and epidemiology of spondyloarthritis. *Nat Rev Rheumatol* 2015;11:110–8. doi:10.1038/nrrheum.2014.181
3. Golder V, Schachna L. Ankylosing spondylitis: an update. *Aust Fam Physician* 2013;42:780–4.
4. Stolwijk C, van Tubergen A, Castillo-Ortiz JD, et al. Prevalence of extra-articular manifestations in patients with ankylosing spondylitis: a systematic review and meta-analysis. *Ann Rheum Dis* 2015;74:65–73. doi:10.1136/annrheumdis-2013-203582
5. Rudwaleit M, van der Heijde D, Landewé R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777–83. doi:10.1136/ard.2009.108233
6. Sieper J, Rudwaleit M, Baraliakos X, et al. The Assessment of SpondyloArthritis international Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis* 2009;68 Suppl 2:ii1–44. doi:10.1136/ard.2008.104018
7. Wang R, Gabriel SE, Ward MM. Progression of patients with non-radiographic axial spondyloarthritis to ankylosing spondylitis: a population-based cohort study. *Arthritis Rheumatol* 2016;68:1415–21. doi:10.1002/art.39542
8. Rudwaleit M, Khan MA, Sieper J. The challenge of diagnosis and classification in early ankylosing spondylitis: Do we need new criteria? *Arthritis Rheum* 2005;52:1000–8. doi:10.1002/art.20990
9. Seo MR, Baek HL, Yoon HH, et al. Delayed diagnosis is linked to worse outcomes and unfavourable treatment responses in patients with axial spondyloarthritis. *Clin Rheumatol* 2015;34:1397–405. doi:10.1007/s10067-014-2768-y
10. Robinson PC, Brown MA. The window of opportunity: a relevant concept for axial spondyloarthritis. *Arthritis Res Ther* 2014;16:109. doi:10.1186/ar4561
11. van Hooft L, Koes BW, Hazes JMW, et al. Evaluating the ASAS recommendations for early referral of axial spondyloarthritis in patients with chronic low back pain: is one parameter present sufficient for primary care practice? *Ann Rheum Dis* 2015;74:e68. doi:10.1136/annrheumdis-2015-208547
12. Wallman JK, Kapetanovic MC, Petersson IF, et al. Comparison of non-radiographic axial spondyloarthritis and ankylosing spondylitis patients - baseline characteristics, treatment adherence, and development of clinical variables during three years of anti-TNF therapy in clinical practice. *Arthritis Res Ther* 2015;17:378. doi:10.1186/s13075-015-0897-6
13. Sieper J, Heijde D van der, Landewé R, et al. New criteria for inflammatory back pain in patients with chronic back pain: a real patient exercise by experts from the Assessment of SpondyloArthritis international Society (ASAS). *Ann Rheum Dis* 2009;68:784–8. doi:10.1136/ard.2008.101501
14. Mok CC, Tam LS, Leung MH, et al. Referral strategy for early recognition of axial spondyloarthritis: consensus recommendations from the Hong Kong Society of Rheumatology. *Int J Rheumatol* 2013;16:500–8. doi:10.1111/1756-185X.12161
15. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med* 2007;147:478–91. doi:10.7326/0003-4819-147-7-200710020-00006
16. Bezalel T, Carmeli E, Been E, et al. Scheuermann's disease: current diagnosis and treatment approach. *J Back Musculoskelet Rehabil* 2014;27:383–90. doi:10.3233/BMR-140483
17. Al-Homood IA. Rheumatic conditions in patients with diabetes mellitus. *Clin Rheumatol* 2013;32:527–33. doi:10.1007/s10067-012-2144-8
18. Thjodleifsson B, Geirsson AJ, Björnsson S, et al. A common genetic background for inflammatory bowel disease and ankylosing spondylitis: a genealogic study in Iceland. *Arthritis Rheum* 2007;56:2633–9. doi:10.1002/art.22812
19. Stavropoulos PG, Soura E, Kanelleas A, et al. Reactive arthritis. *J Eur Acad Dermatol Venereol* 2015;29:415–24. doi:10.1111/jdv.12741
20. Khan MA, Haroon M, Rosenbaum JT. Acute anterior uveitis and spondyloarthritis: more than meets the eye. *Curr Rheumatol Rep* 2015;17:59. doi:10.1007/s11926-015-0536-x
21. Stebbings S, Jenks K, Treharne GJ, et al. Validation of the Dudley Inflammatory Bowel Symptom Questionnaire for the assessment of bowel symptoms in axial SpA: prevalence of clinically relevant bowel symptoms and association with disease activity. *Rheumatology (Oxford)* 2012;51:858–65. doi:10.1093/

rheumatology/ker359

22. Roberts RL, Wallace MC, Jones GT, et al. Prevalence of HLA-B27 in the New Zealand population: effect of age and ethnicity. *Arthritis Res Ther* 2013;15:R158. doi:10.1186/ar4341
23. Brown MA, Kenna T, Wordsworth BP. Genetics of ankylosing spondylitis—insights into pathogenesis. *Nat Rev Rheumatol* 2016;12:81–91. doi:10.1038/nrrheum.2015.133
24. Chou R, Qaseem A, Owens DK, et al. Diagnostic imaging for low back pain: advice for high-value health care from the American College of Physicians. *Ann Intern Med* 2011;154:181–9. doi:10.7326/0003-4819-154-3-201102010-00008
25. Ciurea A, Scherer A, Weber U, et al. Impaired response to treatment with tumour necrosis factor α inhibitors in smokers with axial spondyloarthritis. *Ann Rheum Dis* 2016;75:532–9. doi:10.1136/annrheumdis-2013-205133
26. Wendling D, Prati C. Spondyloarthritis and smoking: towards a new insight into the disease. *Expert Rev Clin Immunol* 2013;9:511–6. doi:10.1586/eci.13.35
27. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904. doi:10.1136/ard.2011.151027
28. Millner JR, Barron JS, Beinke KM, et al. Exercise for ankylosing spondylitis: An evidence-based consensus statement. *Semin Arthritis Rheum* 2016;45:411–27. doi:10.1016/j.semarthrit.2015.08.003
29. Kroon FPB, van der Burg LRA, Ramiro S, et al. Nonsteroidal antiinflammatory drugs for axial spondyloarthritis: a Cochrane review. *J Rheumatol* 2016;43:607–17. doi:10.3899/jrheum.150721
30. Coxib and traditional NSAID Trialists' (CNT) Collaboration, Bhala N, Emberson J, et al. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet* 2013;382:769–79. doi:10.1016/S0140-6736(13)60900-9
31. Song IH, Poddubnyy DA, Rudwaleit M, et al. Benefits and risks of ankylosing spondylitis treatment with nonsteroidal antiinflammatory drugs. *Arthritis Rheum* 2008;58:929–38. doi:10.1002/art.23275
32. Maxwell LJ, Zochling J, Boonen A, et al. TNF-alpha inhibitors for ankylosing spondylitis. *Cochrane Database Syst Rev* 2015;4:CD005468. doi:10.1002/14651858.CD005468.pub2
33. Chang J, Girgis L. Clinical use of anti-TNF-alpha biological agents - a guide for GPs. *Aust Fam Physician* 2007;36:1035–8.
34. Coates LC, Tillett W, Chandler D, et al. The 2012 BSR and BHPR guideline for the treatment of psoriatic arthritis with biologics. *Rheumatology (Oxford)* 2013;52:1754–7. doi:10.1093/rheumatology/ket187
35. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol* 2016;68:282–98. doi:10.1002/art.39298
36. Peters MJL, Symmons DPM, McCarey D, et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. *Ann Rheum Dis* 2010;69:325–31. doi:10.1136/ard.2009.113696
37. Jakobsen AK, Jacobsson LTH, Patschan O, et al. Is nephrolithiasis an unrecognized extra-articular manifestation in ankylosing spondylitis? A prospective population-based Swedish national cohort study with matched general population comparator subjects. *PLoS ONE* 2014;9:e113602. doi:10.1371/journal.pone.0113602
38. Jakobsson GL, Stephansson O, Askling J, et al. Pregnancy outcomes in patients with ankylosing spondylitis: a nationwide register study. *Ann Rheum Dis* 2015; [Epub ahead of print]. doi:10.1136/annrheumdis-2015-207992
39. Fouque-Aubert A, Jette-Paulin L, Combescure C, et al. Serious infections in patients with ankylosing spondylitis with and without TNF blockers: a systematic review and meta-analysis of randomised placebo-controlled trials. *Ann Rheum Dis* 2010;69:1756–61. doi:10.1136/ard.2008.098822
40. Burmester GR, Panaccione R, Gordon KB, et al. Adalimumab: long-term safety in 23 458 patients from global clinical trials in rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis and Crohn's disease. *Ann Rheum Dis* 2013;72:517–24. doi:10.1136/annrheumdis-2011-201244
41. Smith C, Anstey A, Barker J, et al. British Association of Dermatologists' guidelines for biologic interventions for psoriasis 2009. *Br J Dermatol* 2009;161:987–1019. doi:10.1111/j.1365-2133.2009.09505.x

MISSING THE QUIZ?

Interactive Quizzes & Case Studies

Interactive quizzes and case studies based on material found in the Best Practice Journal and Best Tests are now available online. To get started log on to mybpac on our website:

www.bpac.org.nz/quizzes



Peer Group Discussions

In this ongoing series, we look back at the key messages and practice points from selected articles in Best Practice Journals. Also included are suggested discussion questions for peer groups, or for personal review. Available from our website:

www.bpac.org.nz/peergroup