Research Review Speaker Series™

Early detection of axial spondyloarthritis and psoriasis management

Making Education Easy — June 2014

Dr Douglas White

Dr White is a Rheumatologist at Waikato Hospital in Hamilton. He has trained in the UK, Australia, and New Zealand and has interests in inflammatory arthritis, connective tissue disease and biostatistics. His current research activity includes prognostication in early rheumatoid arthritis.

Associate Prof Amanda Oakley

Associate Professor Oakley is a specialist dermatologist in Hamilton and is an Honorary Associate Professor at Waikato Clinical School (Auckland University School of Medicine). She is the website manager and chief editor of the successful web site, DermNetNZ.org. She is a member of the International Society for the Study of Vulvovaginal Diseases and has recently been elected an International Honorary Member of the prestigious American Dermatological Association.

She is a trustee of the NZ Telepaediatric Trust, a member of the NZ Telehealth Forum, and on the National Melanoma Standards Working Group.

Abbreviations used in this review

AS = ankylosing spondylitis
BP = blood pressure
CBC = complete blood count
CRP = C-reactive protein
GP = general practitioner
HLA = human lymphocytic antigen
MRI = magnetic resonance imaging
NSAID = nonsteroidal anti-inflammatory drug
SC = subcutaneous

Welcome to this review of two presentations that were part of the GP CME 2014, held in Rotorua during June 12–15, 2014.

The first of these presentations by Dr Douglas White, a rheumatologist at Waikato hospital, provided the audience with detailed information on the importance of early detection of axial spondyloarthritis, including the impact the increased availability of MRI has had on the classification of spondyloarthritis, and its management. Assoc Prof Amanda Oakley, a dermatologist also from Waikato and Website Manager and Chief Editor of DermNetNZ, provided the audience with detailed guidance on managing psoriasis, with emphasis on assessing patients to ensure they receive the most appropriate individualised treatment. We have summarised these two quality presentations to provide those unable to attend with the valuable information provided.

EARLY DETECTION OF AXIAL SPONDYLOARTHRITIS

Dr Douglas White, Rheumatologist, Waikato Hospital

Definitions of and diagnosing spondyloarthritic diseases

Spondyloarthritis is an umbrella term for conditions including AS, reactive arthritis, psoriatic arthritis, enteropathic arthritis, enthesitis-related arthritis and undifferentiated spondyloarthritis. A recently published qualitative study reported that none of ten surveyed GPs from the Netherlands were able to accurately diagnose patients with suspected axial spondyloarthritis.[1] Comments made ranged from lack of knowledge, particularly the difference between mechanical and inflammatory disease, to referral to neurologist for any patient presenting with low back pain but no abnormalities on x-ray.

In contrast to rheumatoid arthritis, which is pathologically a synovitis, the pathology of spondyloarthritis is an enthesitis, or inflammation of tendons and ligaments joining to bone. The advent of MRI has allowed easy imaging of enthesitis, e.g. plantar fasciitis or spinal inflammation (Figures 1a–b). Enthesitis also underlies the psoriatic nail, due to inflammation of the tendons, which insert close to the nail bed.

The common theme of extra-articular manifestations is that they all occur at sites of mechanical stress and traction, and a lot of the active research at the moment is on the interaction between mechanical stress and inflammation. The 1984 criteria for AS, which were developed before MRI was widely available, included low back pain and stiffness for >3 months, limitation of spinal motion or chest expansion and an absolute requirement for radiographic changes. The latter was problematic, as inter-rater agreement of plain film findings is only moderate and changes occur over years, so x-rays may show accumulation of damage rather than active disease. In contrast, MRI clearly shows active disease. The newer ASAS criteria are for classifying 'spondyloarthritis', and they still require >3 months of back pain and age <45 years, but the remaining criteria are split into imaging (sacroiliitis and >1 spondyloarthritic feature) **or** clinical (HLA-B27 and >2 other spondyloarthritic features); spondyloarthritic features include inflammatory back pain, psoriasis, anterior uveitis, inflammatory bowel disease, HLA-B27 positivity, dactylitis, enthesitis (heel), good response to NSAIDs, family history of spondyloarthritis and elevated CRP level.

Figure 1a. MRI of enthesitis

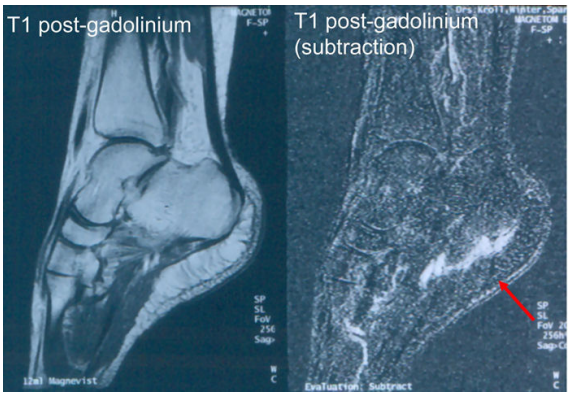
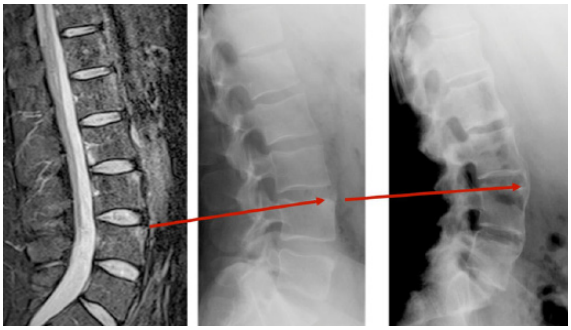


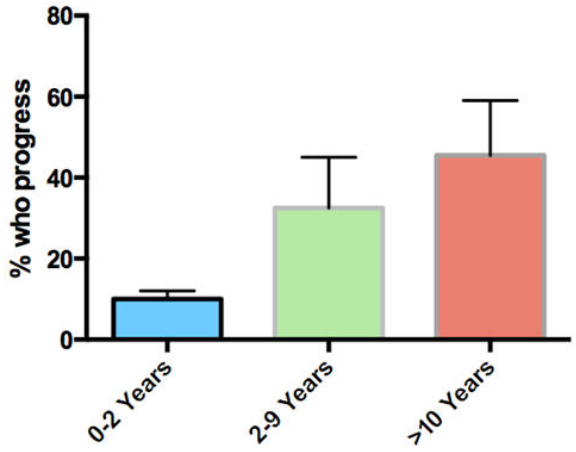
Figure 1b. MRI – inflammation to ankylosis



These criteria diagnose spondyloarthritis with sensitivity and specificity of 89.2% and 84.4%, respectively. Along with their use in the clinical setting, these criteria are also now used to stratify clinical trial participants.

This approach helps to break down spondyloarthritis into conditions that affect the spine and those that affect peripheral joints. The spinal conditions include those that cause changes that can be detected on radiography (e.g. AS), those that are not detected on radiography, but can be detected on MRI (nonradiographic), and those that are clinical. Studies have shown that most patients with nonradiographic spondyloarthritic conditions at baseline will develop radiographic changes over time [Figure 2].[2–8] Importantly, age, genetics, symptoms, disease activity measures and responses to treatment don't differ between patients with radiographic and nonradiographic spondyloarthritis, although mobility is lower and CRP level higher in those with radiographic spondyloarthritis. However, patients with nonradiographic spondyloarthritis are more difficult to identify. This is likely to be responsible for the long duration from the development of symptoms to diagnosis. Factors underlying this include delayed presentation (e.g. younger men), reliance on plain imaging from the older (1984) criteria, and the previously mentioned inability of GPs to accurately diagnose the conditions.

Figure 2. Progression from nonradiographic spondyloarthritis to AS

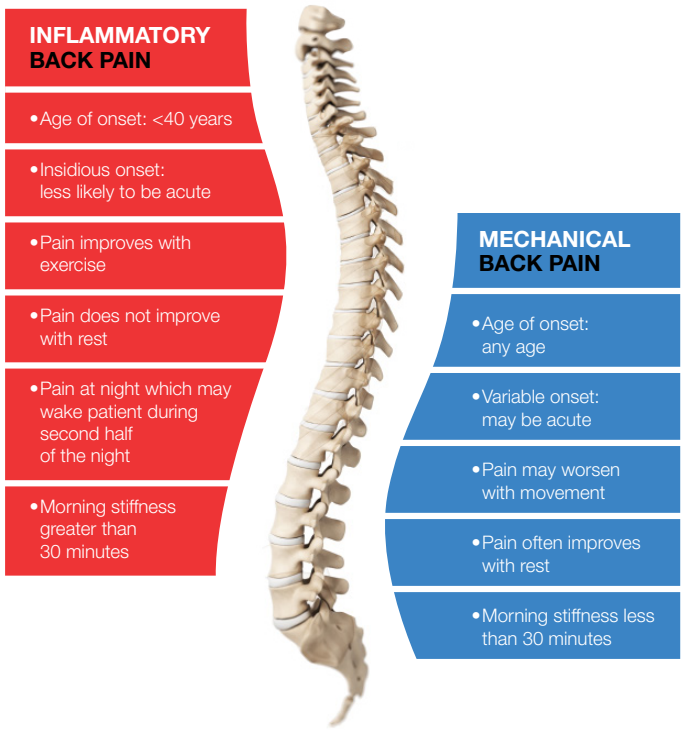


Individuals who develop spondyloarthritis include those who are HLA-B27 positive, and they are about twice as likely to be male. Symptoms develop at <16 years of age in ~15% of patients, and the disease is unlikely to develop in those aged >45 years. It is estimated that 7000–12,000 individuals in NZ have axial spondyloarthritis. There are also important implications associated with AS, with patients more likely to be unemployed and three times more likely to withdraw from work, and around three-quarter of those who are employed report poor performance as a result of their AS.

Early diagnosis is important

Detecting axial spondyloarthritis earlier is problematic, as physical examinations are often unhelpful, around 40% of patients have a CRP level in the normal range, and plain imaging is usually normal during the early stages of the disease. However, ~90% of patients with axial spondyloarthritis have inflammatory back pain, which constitutes about 5% of back pain presentations. Mechanical and inflammatory back pain have important differences (Figure 3), and distinguishing between the two types can help early diagnosis of spondyloarthritis. While there are various sets of criteria for inflammatory back pain, the most commonly used is the ASAS expert consensus criteria (see right column), which have sensitivity and specificity of 79.6% and 72.4%, respectively.

Figure 3. Differential characteristics of inflammatory and mechanical back pain



Adapted from NASS Module One. "Differentiating Inflammatory and Mechanical Back Pain," August 2012. (http://nass.co.uk/loose-leaf-pages/differentiating-inflammatory-and-mechanical-back-pain/) in consultation with Dr Doug White, Associate Professor Andrew Harrison, Dr Tracey Kain and Dr Rafi Raja. An initiative organised and funded by AbbVie, in collaboration with Arthritis New Zealand.

ASAS expert consensus criteria for inflammatory back pain

Any four of:

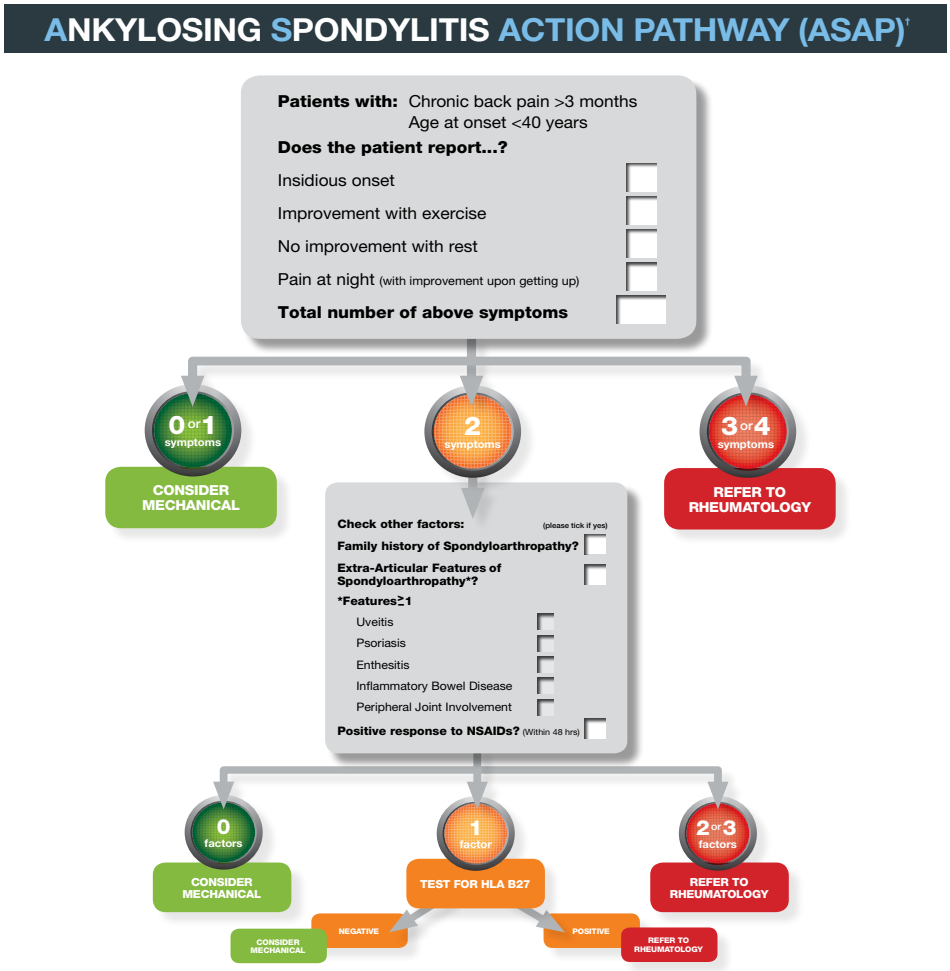
- Age <40 years
- Insidious onset
- Improvement with exercise
- No improvement with rest
- Pain at night

Who to refer

Criteria for which patients with chronic back pain should be referred has been evaluated by Sieper et al.[9] This group showed that among patients with chronic back pain of >3 months with the first symptom at age <45 years, ~20% of those with inflammatory back pain had spondyloarthritis, as did around one-third of HLA-B27-positive patients. Just less than half of patients referred using these two criteria along with sacroiliitis on imaging were found to have axial spondyloarthritis.[10] Dr White presented an action pathway for referrals for AS (Figure 4). It is clear that patients presenting with ≤1 criterion should be considered to have mechanical back pain and those with all criteria should be referred to a rheumatologist, but it is less clear for patients with 2–3 of the criteria – this group was not covered in the previous study. This action pathway addresses this, by investigating these patients further.

Following the television campaign undertaken in 2012, data published earlier this year show a 63% increase in spondyloarthritis referrals. A patient-resource website for spondyloarthritis is currently under development.

Figure 4. Action pathway for AS



†A referral guide for General Practitioners adapted from the following: Sieper J et al. Ann Rheum Dis 2013;72:1621-7; Sieper J et al. Ann Rheum Dis 2009;68:784-8; AS Awareness Council (ASAC) Ankylosing Spondylitis Action Pathway (http://www.isr.ie/images/stories/AS_Algorithm_form.pdf); by Dr Douglas White, Associate Professor Andrew Harrison, Dr Tracey Kain and Dr Rafi Raja. An initiative organised and funded by AbbVie in collaboration with Arthritis New Zealand.

Managing axial spondyloarthritis

Treating spondyloarthritis with infliximab for 24 weeks has been shown to significantly improve real-world productivity outcomes, including a significantly greater median change in productivity score (2.2 vs. 0.72 [p<0.05]),[11] and similar improvements have been shown for productivity outcomes with adalimumab therapy.[12] In addition to improving productivity, another reason for treating patients with AS is that the condition is associated with increased standardised mortality rates for both males and females of 1.61 and 1.29–1.93, respectively.[13] Most of the excess deaths are cardiovascular related, and factors independently associated with the increased mortality are increased CRP levels, infrequent NSAID use, diagnostic delay and work disability (respective odds ratios 2.68 [95% CI 1.774, 4.048], 4.35 [1.753, 10.771], 1.05 [1.006, 1.101] and 3.65 [1.400, 9.506]).

NSAIDs have a prominent role in the management of most of the clinical manifestations of axial spondyloarthritis, with 80–90% of patients benefiting; this is not the case for those with mechanical back pain. NSAIDs also have the added benefit in axial spondyloarthritis of reducing spinal fusion. Education, exercise, physical therapy, rehabilitation and self-help programmes are also important components of managing spondyloarthritis. Traditional agents and local injections are useful for peripheral joint problems, but are not as effective for axial disease. The three funded anti-TNF (tumour necrosis factor) agents available in NZ are useful for all disease manifestations.

Take-home points

- Spondyloarthritis is an important cause of back pain in younger adults
- Spondyloarthritis is associated with significant morbidity and productivity loss
- Diagnosis may be expedited by awareness of inflammatory back pain
- Several effective treatment options are available

REFERENCES

1. Van Onna M et al. General Practitioners' perceptions of their ability to identify and refer patients with suspected axial spondyloarthritis: a qualitative study. J Rheumatol 2014;14(5):879–901
2. Sampaio-Barro PD et al. Undifferentiated spondyloarthritis: a longterm followup. J Rheumatol 2010;37(6):1195–9
3. Poddubnyy D et al. Rates and predictors of radiographic sacroiliitis progression over 2 years in patients with axial spondyloarthritis. Ann Rheum Dis 2011;70(8):1369–74
4. Schattenkirchner M & Kruger K. Natural course and prognosis of HLA-B27-positive oligoarthritis. Clin Rheumatol 1987;6(Suppl 2):83–6
5. Sany J et al. Unclassified HLA-B27 inflammatory rheumatic diseases: followup of 23 patients. Arthritis Rheum 1980;23(2):258–9
6. Mau W et al. Clinical features and prognosis of patients with possible ankylosing spondylitis. Results of a 10-year followup. J Rheumatol 1988;15(7):1109–14
7. Oostveen J et al. Early detection of sacroiliitis on magnetic resonance imaging and subsequent development of sacroiliitis on plain radiography. A prospective, longitudinal study. J Rheumatol 1999;26(9):1953–8
8. Bennett AN et al. Severity of baseline magnetic resonance imaging-evident sacroiliitis and HLA-B27 status in early inflammatory back pain predict radiographically evident ankylosing spondylitis at eight years. Arthritis Rheum 2008;58(11):3413–8
9. Sieper J & Rudwaleit M. Early referral recommendations for ankylosing spondylitis (including pre-radiographic and radiographic forms) in primary care. Ann Rheum Dis 2005;64(5):659–63
10. Brandt HC et al. Performance of referral recommendations in patients with chronic back pain and suspected axial spondyloarthritis. Ann Rheum Dis 2007;66(11):1479–84
11. van der Heijde D et al. Infliximab improves productivity and reduces workday loss in patients with ankylosing spondylitis: results from a randomized, placebo-controlled trial. Arthritis Rheum 2006;55(4):569–74
12. Maksymowych WP et al. Impact of age, sex, physical function, health-related quality of life, and treatment with adalimumab on work status and work productivity of patients with ankylosing spondylitis. J Rheumatol 2010;37(2):385–992
13. Bakland G et al. Increased mortality in ankylosing spondylitis is related to disease activity. Ann Rheum Dis 2011;70(11):1921–5

MANAGING PSORIASIS

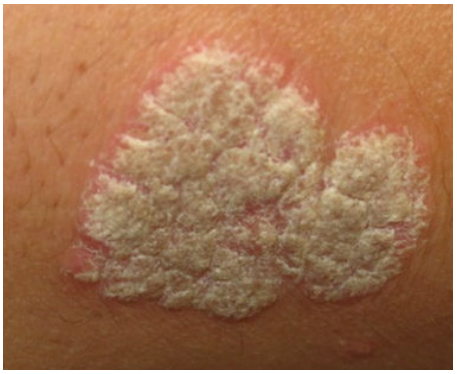
Assoc Prof Amanda Oakley, Dermatologist, Waikato

Psoriasis is a chronic skin disease that is clinically diagnosed by well-circumscribed, scaly plaques with a symmetrical distribution (Figure 5), which can also affect the nail (being part of the skin). There are various types, with genetic and environmental factors involved in their aetiology. It is an autoimmune disease, and is associated with other autoimmune diseases (e.g. psoriatic arthritis, spondyloarthritis, Crohn's disease, uveitis, etc). It is also a systemic condition, being associated with metabolic syndrome and its components. Its severity and extent are influenced by environmental factors including medications (e.g. lithium) and lifestyle factors (e.g. smoking, alcohol consumption).

Classifications of psoriasis

Determining the type of psoriasis is important when assessing patients. Factors that should be taken into account include onset age (<40 vs. >40 years), acute versus chronic, localised versus general and whether the patient has small or large plaques or pustular lesions. Acute psoriasis types include: i) guttate psoriasis (poststreptococcal); ii) exanthematic psoriasis; iii) erythrodermic psoriasis; iv) generalised pustular psoriasis; and v) unstable plaque psoriasis. Other types of psoriasis are classified as chronic psoriasis, and are more common. Psoriasis confined to the scalp, elbows/knees, flexures, palms/soles of the feet and nails is localised psoriasis, with other distributions classified as generalised psoriasis. The cutoff for small versus large plaques is 3cm.

Figure 5. Typical presentation of psoriasis



Assessment of psoriasis

Assessing psoriasis should involve a whole-body examination that includes the patient's head/neck, upper limbs, trunk, lower limbs and nails. The PASI (Psoriasis Area and Severity Index) score, PGA (Physician's/Patient's Global Assessment) and BSA (Body Surface Area) assessment are the three most commonly used methods for assessing psoriasis. The PASI is complicated, but is the most frequently used method in clinical trials. The DermNetNZ website includes a PASI spreadsheet tool and also a link to an easy-to-use online calculator with training. There are also a number of downloadable smartphone apps for calculating PASI scores. In contrast, the PGA is relatively simple, with the use of the descriptive terms 'clear', 'nearly clear', 'mild', 'moderate', 'severe' and 'very severe', but is therefore subjective. BSA is defined by percentages, using the area of the patient's hand to define 1% BSA. Mild, moderate and severe psoriasis are ascribed to BSA values of <5%, 5–10% and >10%, respectively. Online training is available for BSA assessment, and there is also a smartphone app.

Assessment of comorbidities is also important. Measurements of BMI (body mass index), arthropathy, BP, Hb_{A1c} (glycosylated haemoglobin) level, lipid levels, CBC and liver and kidney function tests are recommended. A good psoriatic arthropathy smartphone app is available, which will advise on whether a rheumatology referral is necessary. Such apps are based on PASE (Psoriatic Arthritis Screening and Evolution) or PEST (Psoriatic Epidemiology Study) questionnaire scores.

The impact of disease on the patient's daily life is also important to assess. A number of assessment tools are available, including the DLQI (Dermatology Life Quality Index), which can be downloaded from the Cardiff University website. DLQI scores usually correspond well with PASI scores. A low DLQI score indicates that a patient is less concerned with their symptoms, while a high DLQI score indicates the patient is very bothered by their symptoms (even though they might have a low PASI score).

Treatment of psoriasis and monitoring

Recommended treatment of psoriasis depends on disease severity and impact on daily life (see Table). Patient monitoring is required for many of these treatments, and most patients will be under shared care so it is important for GPs to understand their responsibilities for monitoring. Regular skin checks are needed for those receiving phototherapy; recipients of methotrexate, acitretin and ciclosporin require blood tests; and all those with severe psoriasis require cardiovascular assessments and BP, lipid and Hb_{A1c} level measurements.

Table. Recommended treatment of psoriasis

PASI/DLQI scores	Treatment options
≤10	Topical treatment • Emollient • Topical corticosteroid o 2 weeks on then 2 weeks off OR 2–3 days per week • Topical calcipotriol • Salicylic acid (to descale) • Coal tar Continue while symptoms are mild Switch to recommended treatment for moderate-to-severe psoriasis if symptoms worsen (see below)
PASI >10 **OR** PASI ≤10 and DLQI >10	Nonbiological systemic therapy ±phototherapy • Phototherapy • Generalised small plaque psoriasis does best • Requires patients to attend clinic 3 times per week for ~3 months • Methotrexate • Generalised large plaque psoriasis • Exclude if baby-making (females AND males) • Use with caution if systemic disease • Acitretin • Generalised erythrodermic, pustular psoriasis • Localised pustular psoriasis • Exclude if baby-making (females only) • Ciclosporin • Generalised acute psoriasis • BP, renal function concerns

Systemic treatments

Methotrexate is teratogenic and damages spermatozoa. It also suppresses bone marrow, and can cause acute hepatitis, chronic hepatic fibrosis and, rarely, pneumonitis. Hepatitis B/C serology tests should be undertaken prior to treatment, and liver and renal function tests and measurements of CBC and P3NP collagen should be performed both before and during treatment. A pretreatment chest x-ray is also recommended if the patient has lung disease. During long-term treatment, transient elastography scans should be performed.

Acitretin is also potentially teratogenic, and is associated with mucocutaneous effects, tiredness, myalgia, arthralgia and hyperlipidaemia. Small initial doses are usually tolerated, but adverse effects often begin to manifest as higher therapeutic doses are reached. CBCs, liver function and lipid levels should be ascertained prior to and during acitretin therapy, with ßHCG levels checked pretreatment. Statin therapy can be considered if hyperlipidaemia occurs on treatment.

Being an immunosuppressant, ciclosporin use can be associated with infections and skin cancer. Other adverse effects associated with this agent include hypertension, renal impairment, hirsutism, leg swelling, tremor, paraesthesias, nausea and headache. Pretreatment tests are extensive, and include CBCs, liver and renal function tests and tests for infections and markers of hypertension. Vaccinations for infectious diseases (e.g. influenza, pneumococcus, varicella zoster) may be needed. During treatment, frequent monitoring of CBC, creatinine and BP should continue, along with less frequent monitoring with the other blood tests. Ciclosporin dose reductions and eventually even cessation may be needed for renal impairment. It is very important that patients receiving ciclosporin therapy are advised to seek medical attention if they begin to feel unwell, particularly with febrile illness, and their threshold for antibiotic therapy should be lowered. As ciclosporin elevates a recipient's skin cancer risk, sun protection should be encouraged and regular skin checks performed.

Patients with a good response to systemic agents (PASI score improvement ≥75% and DLQI score ≤5) should continue with systemic or phototherapy. For those with a partial improvement (50–75% improvement in PASI score), systemic and/or phototherapy should be continued in those with a DLQI score ≤5, while those with a DLQI score >5 should have their treatment modified or changed. Treatment should also be modified/changed in those who have failed therapy (PASI improvement <50%). Biological agents should be considered for patients after ≥2 of four nonbiological treatment options have been trialled or contraindicated if their PASI and/or DLQI score remains >10.

Biologicals

The funded biological options are infliximab infusions every 8 weeks, SC adalimumab every 2 weeks and SC etanercept every week, while SC ustekinumab every 3 months is a nonfunded alternative. The issues associated with the use of biologicals are: i) cost, with Special Authority criteria required; ii) increased infection risk during the first year (not as high as for ciclosporin or systemic corticosteroids); iii) increased skin cancer risk (not as high as for ciclosporin); iv) possible bodyweight gain; and v) possible increased heart failure risk. Prior to biological treatment, patient screening should include CBC, liver and renal function tests, ANA (antinuclear antibody) status, hepatitis B/C serology, HIV status, tuberculosis tests and a chest x-ray. One of the advantages of biological therapy is the lower and relatively infrequent monitoring requirements, which include CBCs, liver function tests and bodyweight.

Assoc Prof Oakley concluded her talk by reminding the audience that the DermNetNZ website provides comprehensive guidelines on psoriasis. Question time included concerns regarding the time delay seen in the public health system between being referred to a specialist and actually being seen by one. Assoc Prof Oakley commented that there is hope that an advice service will be set up in all regions. There is currently a secure website where Waikato-based GPs can submit photographs of patients' lesions and documentation and receive advice on how to precede with managing the disease during this interim period, and Assoc Prof Oakley hoped that this service would be rolled out to other regions (depending on demand and funding).

abbvie

This article was commissioned and sponsored by AbbVie Ltd. Wellington, which has no control over editorial content. The views expressed by Dr Douglas White and Assoc Prof Oakley are their clinical opinions and not necessarily those of AbbVie Ltd. Products mentioned in this presentation are prescription medicines and detailed prescribing information is available at www.medsafe.govt.nz. HUMS-2014-13. TAPS PP5557