Psoriatic arthritis

Psoriatic arthritis is an inflammatory disease of the joints that affects 30% of people with psoriasis (Lloyd et al, 2012). It is an asymmetric arthropathy characterized by pain, stiffness and swelling of joints, tendons and ligaments. Around 50% of patients have subclinical radiographic evidence of bone erosions and 20–40% develop joint deformities and irreversible loss of function (Kane et al, 2003; Gladman et al, 2005). Patients with psoriasis and psoriatic arthritis are at increased risk of depression, obesity and metabolic syndrome, have a reduced quality of life and increased mortality compared to the general population (Lloyd et al, 2012). Despite these serious complications and comorbidities, there remains a misconception that psoriatic arthritis is a benign condition such that it can be under-diagnosed and undertreated.

Immunosuppressive drugs, including tumour necrosis factor-α (TNFα) inhibitors, are effective treatments but can have serious side effects. Advances in understanding of the immunopathogenesis of psoriasis and psoriatic arthritis have led to the identification of new therapeutic targets such as the IL-23/IL-17 axis. Drugs blocking IL-17 are highly effective in the treatment of psoriasis and clinical trials are underway in patients with psoriatic arthritis.

Dr LE Durham is Clinical Training Fellow. Centre for Molecular and Cellular Biology of Inflammation, Division of Immunology, Infection and Inflammatory Disease, King's College London, London

Professor LS Taams is Professor in Immunobiology and head of the Centre for Molecular and Cellular Biology of Inflammation, Division of Immunology, Infection and Inflammatory Disease, King's College London, London

Dr BW Kirkham is Consultant Rheumatologist in the Department of Rheumatology, Guy's & St Thomas' NHS Foundation Trust, London SE1 9RT

Correspondence to: Dr BW Kirkham (bruce.kirkham@gstt.nhs.uk)

Patients with psoriatic arthritis are frequently encountered outside of rheumatology and dermatology clinics. They may present to the accident and emergency department with joint inflammation, cardiovascular events or complications of immunosuppressive therapy. Understanding the clinical features, assessment and management of psoriatic arthritis is therefore important to trainees in many specialities.

Clinical features

Psoriatic arthritis affects men and women equally with onset typically between the ages of 30–50 years. Skin disease usually predates the onset of joint disease by an average of 10 years. Psoriatic arthritis is a heterogenous disorder traditionally classified into five subtypes (*Table 1*) (Moll and Wright, 1973). In reality patients rarely fit neatly into one subtype and the pattern of joint involvement varies over time. A patient presenting with asymmetric oligoarthritis affecting one knee may over time develop polyarthropathy affecting the metacarpophalangeal, proximal and distal interphalangeal joints (*Figure 1*). If untreated this can lead to bone erosions and deformities which in severe cases is called arthritis mutilans.

Features specific to psoriatic arthritis are diffuse swelling of a finger or toe (called dactylitis but best remembered as 'sausage finger/toe') and inflammation at the site of tendon insertion (enthesitis). Enthesitis often affects the Achilles tendon insertion where it is easy to diagnose but enthesitis at other sites can be difficult to recognize.

The wide variety of presentations and overlap with other rheumatological diseases can make it difficult to diagnose psoriatic arthritis. The most important clue is a personal or family history of psoriasis. A full skin examination including inspection of the scalp and behind the ears may identify previously undiagnosed psoriasis. In 2006 the Classification for Psoriatic Arthritis group proposed the CASPAR classification criteria (Taylor et al, 2006) (*Table 2*). These are standard inclusion criteria in clinical trials involving patients with psoriatic arthritis, and can help inform clinical diagnosis.

Assessing disease severity

The clinical variation in psoriatic arthritis presents a problem with assessment of disease severity. Severity scores are often borrowed from related conditions. For example, the disease activity score in 28 joints (DAS28) was developed for rheumatoid arthritis

Table 1. Moll and Wright classification of psoriatic arthritis

Asymmetric oligoarthritis	Involves five or fewer joints usually medium–large joints, for example the wrist and knee
Symmetrical polyarthritis	Symmetrical polyarthritis with predilection for the metacarpophalangeal and proximal interphalangeal joints. Resembles rheumatoid arthritis
Distal interphalangeal arthritis	Affects the distal interphalangeal joints and is often associated with the classic nail changes of pitting and onycholysis (*Figure 2*). Without skin changes, can be difficult to differentiate from osteoarthritis
Spondyloarthropathy	Affects the spine (spondylitis) or sacroiliac joints (sacroiliitis) causing lower back pain. Presentation is similar to ankylosing spondylitis but it can usually be differentiated from the latter by the later age of onset and presence of psoriasis
Arthritis mutilans	The most severe form of psoriatic arthritis in which extensive bone destruction and remodelling results in extreme deformities and loss of function

From Moll and Wright (1973)

Figure 1. Clinical features of psoriatic arthritis. **a.** Erythematous rash consistent with psoriasis, onycholysis of the right index fingernail, **(b)** asymmetrical arthritis with fusiform swelling of proximal and distal interphalangeal joints, onycholysis of the left middle finger and pitting of the right little finger nail, **(c)** shortening and onycholysis of the big toe and dactylitis of the fourth toe, **(d)** symmetrical deforming polyarthropathy with ulnar deviation (left middle finger injury is unrelated).

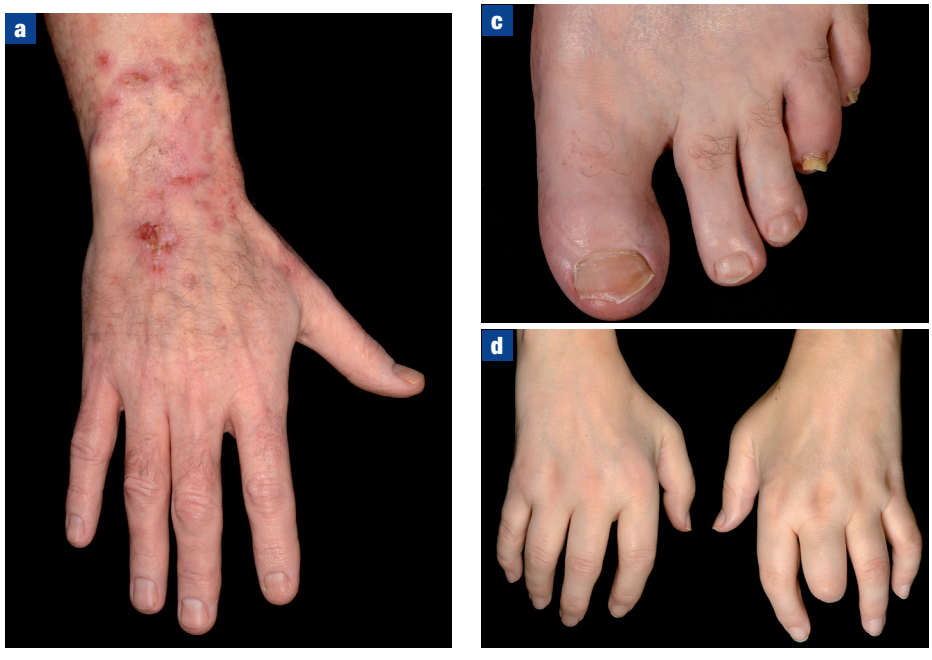


Figure 2. Tools to aid the clinical assessment of severity of arthritis. **a.** Disease activity score at 28 joints (DAS28). Score calculated from number of tender and number of swollen joints from the pre-specified 28 joints depicted, C-reactive protein, erythrocyte sedimentation rate and patient rating of their global health using a visual analogue scale. **b.** Joints counted in the 68 tender, 66 swollen joint count. (*hip joints assessed for tenderness not swelling).

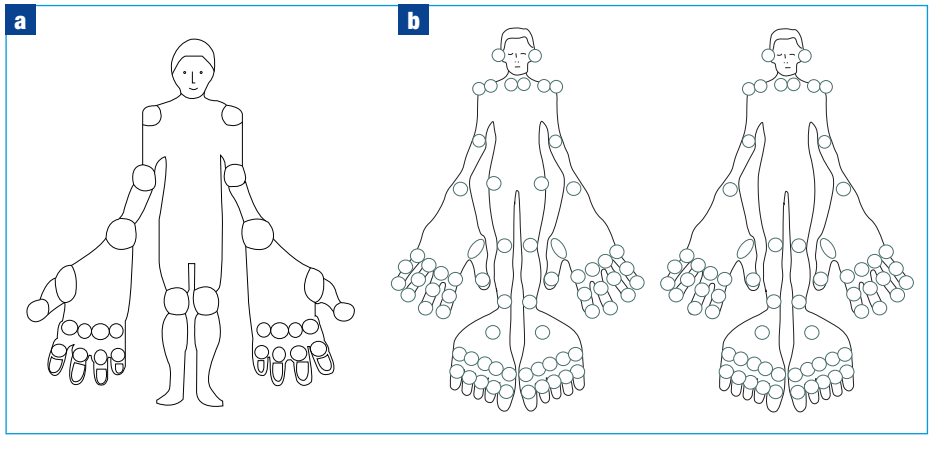


Table 2. CASPAR (CIASsification criteria for Psoriatic ARthritis) criteria

Patient must have an inflammatory articular disease and at least three points from the following:	
Current or personal or family history of psoriasis	2 points (current) 1 point (history)
Psoriatic nail dystrophy	1 point
Negative rheumatoid factor	1 point
Dactylitis	1 point
Radiographic evidence of juxta-articular new bone formation	1 point

From Taylor et al (2006)

(*Figure 2*). The DAS28 does not include distal interphalangeal joints, foot or lower back and thus underestimates severity in patients with arthritis of these joints. DAS28 also underestimates severity in patients with asymmetric oligoarthritis who, by definition, have five or fewer affected joints. Some of these problems can be mitigated by use of the 68 tender, 66 swollen joint count (*Figure 2*) (Coates et al, 2013a).

Unlike rheumatoid arthritis, inflammatory markers (C-reactive protein and erythrocyte sedimentation rate) can be normal in many patients with active psoriatic arthritis. However, a raised C-reactive protein level is one of the few biomarkers of increased risk of bone erosions.

Plain X-ray is the first-line imaging assessment for psoriatic arthritis. X-rays of peripheral joints may show joint space narrowing, erosions (sometimes at entheseal insertions) and rarely juxta-articular new bone formation (*Figure 3*). Radiographs of the spine may show asymmetric sacro-iliitis and in late disease, syndesmophyte formation. Ultrasound assesses joint inflammation, effusions and tendon and ligament involvement. Magnetic resonance imaging can assess sacroiliac and spinal inflammation. Both are increasingly used in clinical practice to detect inflammation and guide therapy before irreversible joint damage occurs.

Pathophysiology

Psoriasis and psoriatic arthritis are immune-mediated inflammatory diseases involving the innate and adaptive immune systems. The adaptive immune system protects the body from harm through two main arms:

1. Cell-mediated immunity with activation of cytotoxic (CD8+) T cells provides protection against intracellular pathogens, such as viruses, and malignant cells
2. Humoral immunity with activation of B cells and antibody production provides protection against extracellular pathogens including many bacteria and parasites.

The balance of activity between the arms is regulated by CD4+ 'T helper cells (Th)':

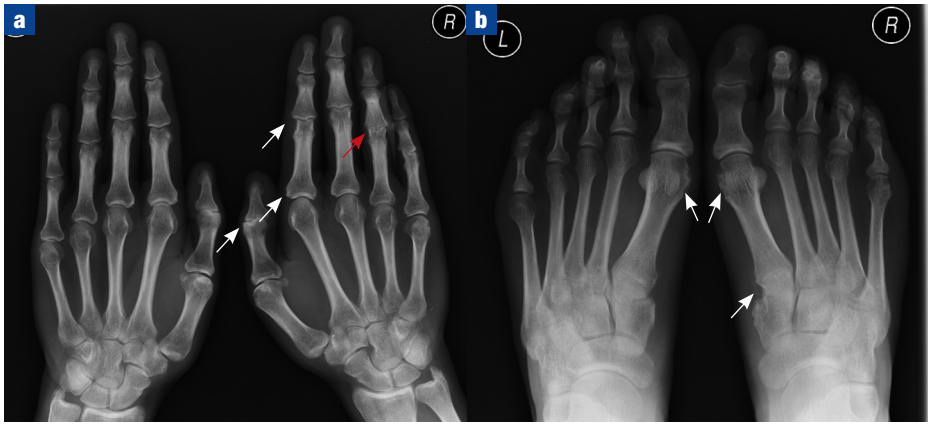
Th1 cells bias activity towards cell-mediated immunity and Th2 cells towards humoral immunity (Mosmann and Coffman, 1989). Inappropriate activation of either arm leads to diseases such as allergy (Th2 mediated) or autoimmune conditions (Th1 or Th2 mediated).

Psoriatic arthritis was originally thought to be a Th1/CD8+ T cell-mediated disease. This is supported by genetic studies showing an association between HLA class I alleles and psoriasis and psoriatic arthritis (Winchester et al, 2012) and reports of de novo psoriasis and psoriatic arthritis occurring in patients with HIV and low CD4+ counts (Morar et al, 2010).

Characterization of the IL-23/IL-17 axis and its role in many autoimmune diseases has drawn attention towards the role of this pathway in psoriasis and psoriatic arthritis. Genetic studies in humans have shown an association between a polymorphism of the IL-23 receptor gene and psoriasis and psoriatic arthritis (Capon et al, 2007). Local concentrations of IL-23, IL-17 and their receptors are increased in affected skin and joints of patients with psoriatic arthritis (Suzuki et al, 2014). IL-23 is secreted by antigen-presenting cells and binds IL-23 receptors on lymphoid and myeloid cells to stimulate IL-17 production. IL-17 stimulates immune cells, epithelial cells, keratinocytes and synovial fibroblasts to produce a wide variety of pro-inflammatory cytokines and chemokines such as TNFα, IL-6 and IL-8 that result in recruitment and activation of neutrophils. The IL-17 pathway cytokines also promote differentiation and activation of keratinocytes and osteoclasts hypothesized to lead to epidermal hyperplasia and bony erosions in psoriasis and psoriatic arthritis respectively (Suzuki et al, 2014) (*Figure 4*).

Th17 cells represent an additional CD4+ T cell lineage that exists alongside Th1 and Th2 cells. Th17 cells are stimulated by the presence of IL-23 and produce IL-17. They are present in the joints of patients with rheumatoid arthritis and psoriatic arthritis and are widely considered to play a role in pathogenesis (Leipe et al, 2010). More recently CD8+, IL-17 producing cells (Tc17 cells), have been identified in the skin and joints of patients with psoriasis and psoriatic arthritis (but not rheumatoid arthritis) at levels that correlate with disease severity (Res et al, 2010; Menon et al, 2014). This may indicate a specific or additional role for Tc17 cells in the pathogenesis of psoriasis and psoriatic arthritis. A central role for Tc17 cells satisfies both hypotheses: that psoriasis and psoriatic arthritis are CD8+ cytotoxic T cell-mediated diseases and that the IL-23/IL-17 axis has a fundamental role in pathogenesis. Whatever its origin, the IL-17/IL-23 axis presents exciting new therapeutic targets.

Figure 3. Plain radiograph of **(a)** hands and **(b)** feet showing typical radiographic features of psoriatic arthritis. Asymmetrical erosions (white arrows) and joint space narrowing secondary to loss of cartilage (red arrow).



Management

The British Society for Rheumatology recommends non-steroidal anti-inflammatory drugs and intra-articular corticosteroid injections as first-line treatment for psoriatic arthritis. However, many patients respond poorly and require further therapy. Disease-modifying anti-rheumatic drugs are recommended second line with biological agents reserved for patients who have trialled but either not responded to or not tolerated two disease-modifying anti-rheumatic drugs (Coates et al, 2013b).

Disease-modifying anti-rheumatic drugs

Methotrexate is the most widely prescribed disease-modifying anti-rheumatic drug for psoriatic arthritis and is generally considered to be effective. However, in keeping with

Figure 4. The role of IL-17 in the pathogenesis of psoriasis and psoriatic arthritis. Antigen-presenting cells (APC) produce IL-23. IL-23 stimulates immune cells, including Th17 and Tc17 cells, to produce IL-17. IL-17 triggers differentiation and activation of osteoclasts resulting in bone resorption and erosions. IL-17 binds receptors on keratinocytes and synoviocytes and stimulates production of pro-inflammatory cytokines including IL-6 and IL-8. This recruits and activates neutrophils resulting in inflammation. IL-22 binds receptors of keratinocytes resulting in aberrant differentiation and epidermal thickening.

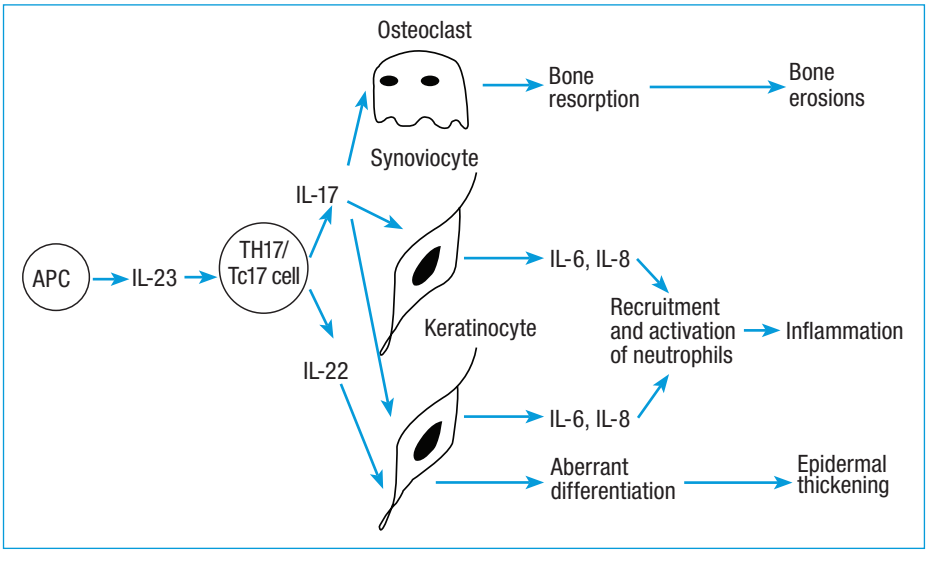


Table 3. Efficacy of each class of biologic therapy for psoriatic arthritis

Class	Therapy	Reference	Treatment groups	*n*	Primary end point	% patients achieving primary end point	*P* value compared to placebo
Tumour necrosis factor (TNF) α inhibitors	Adalimumab: human monoclonal antibody. Binds TNFα	Mease et al (2005)	Placebo	162	ACR20 at week 12	14%	
			Adalimumab 40 mg every 2 weeks	151		58%	*P*<0.001
	Certolizumab: pegylated Fab (antigen binding domain) of humanised mouse monoclonal antibody. Binds TNFα	Mease et al (2014a)	Placebo	136	ACR20 at week 12	24.3%	
			Certolizumab 200 mg every 2 weeks	138		58.0%	*P*<0.001
			Certolizumab 400 mg every 4 weeks	135		51.9%	*P*<0.001
	Etanercept: fusion protein: two human TNFα receptors fused to the Fc portion of IgG1. Binds TNFα	Mease et al (2004)	Placebo	104	ACR20 at week 12	15%	
			Etanercept 25 mg twice weekly	101		59%	*P*<0.0001
	Golimumab: human monoclonal antibody. Binds TNFα	Kavanaugh et al (2009)	Placebo	113	ACR20 at week 14	9%	
			Golimumab 50 mg every 4 weeks	146		51%	*P*<0.001
			Golimumab 100 mg every 4 weeks	146		45%	*P*<0.001
	Infliximab: chimeric (mouse/human) monoclonal antibody. Binds TNFα	Antoni et al (2005)	Placebo	100	ACR20 at week 14	11%	
			Infliximab 5 mg/kg on week 0, 2, 6, 14 and 22	100		58%	*P*<0.001
IL-23-receptor inhibitors	Ustekinumab: human monoclonal antibody. Binds p-40 subunit common to IL-12 and IL-23	PSUMMIT 1 (McInnes et al, 2013)	Placebo	206	ACR20 at week 24	22.8%	
			Ustekinumab 45 mg on week 0, 4 then 12-weekly	205		42.4%	*P*<0.0001
			Ustekinumab 90 mg on week 0, 4 then 12-weekly	204		49.5%	*P*<0.0001
		PSUMMIT 2 (Ritchlin et al, 2014)	Placebo	104	ACR20 at week 24	20.2%	
			Ustekinumab 45 mg on week 0, 4 then 12-weekly	103		43.7%	*P*<0.001
			Ustekinumab 90 mg on week 0, 4 then 12-weekly	105		43.8%	*P*<0.001
IL-17A inhibitors	Brodalumub: human monoclonal antibody. Binds IL-17A receptor	Mease et al (2014b)	Placebo	55	ACR20 at week 12	18%	
			Brodalumab 140 mg on weeks 1, 2 then every 2 weeks	57		37%	*P*=0.03
			Brodalumab 280 mg on weeks 1, 2 then every 2 weeks	56		39%	*P*=0.02
	Secukinumab: human monoclonal antibody. Binds IL-17A	McInnes et al (2015)	Placebo	? (397 total)	ACR20 at week 24	15.3%	
			Secukinumab 75 mg week 1, 2, 3, 4 then every 4 weeks	?		29.3%	*P*<0.05
			Secukinumab 150 mg week 1, 2, 3, 4 then every 4 weeks	?		51%	*P*<0.0001
			Secukinumab 300 mg week 1, 2, 3, 4 then every 4 weeks	?		54%	*P*<0.0001

most older therapies for psoriatic arthritis, the evidence base is limited. One trial comparing methotrexate with placebo found no significant difference (Kingsley et al, 2012). However, inclusion of patients with milder disease than most trials, a relatively low methotrexate dose (15 mg/week) and high loss to follow up (19.9%) limits generalization of these results to the wider psoriatic arthritis population.

Common side effects of methotrexate therapy include mouth ulcers and gastrointestinal upset which are usually prevented by folic acid. Regular blood monitoring is mandated by the rarer side effects of hepatitis, hepatic fibrosis and bone marrow suppression. Other disease-modifying anti-rheumatic drugs prescribed for psoriatic arthritis include leflunomide and sulphasalazine.

Biological agents

TNFα inhibitors

The National Institute for Health and Care Excellence has approved four TNFα inhibitors for psoriatic arthritis: etanercept, infliximab, adalimumab and golimumab. Certolizumab is awaiting appraisal but is increasingly used. Each has been shown to be efficacious in large phase III clinical trials (*Table 3*). However, there have been no head to head trials directly comparing the efficacy.

To meet National Institute for Health and Care Excellence criteria to receive a TNFα inhibitor, patients must have at least three tender and three swollen joints and have failed treatment with two disease-modifying anti-rheumatic drugs. Patients should be re-assessed at 12 weeks and only continue if they have shown improvement. If patients have not responded, an alternative TNFα inhibitor may be considered.

TNFα inhibitor therapies have a favourable risk–benefit comparison but do have significant side effects. An analysis of 837 patients with psoriatic arthritis who received adalimumab in a clinical trial identified serious infections, including opportunistic infections, as the commonest severe adverse event (2.8 events per 100 patient years). Malignancy was reported at low rates (0.2 events per 100 patient years) (Burmester et al, 2013). TNFα inhibitor therapy should be withheld and sometimes discontinued if patients develop a serious infection. Patients can also have re-activation of latent tuberculosis, so must be screened for tuberculosis before starting a TNFα inhibitor. Those positive for latent tuberculosis should begin chemoprophylaxis before starting TNFα inhibitor treatment.

IL-23 inhibitors

Ustekinumab is a human monoclonal antibody that blocks a protein subunit shared by IL-12 and IL-23. In psoriasis, its efficacy compared to placebo is comparable to TNFα inhibitors (*Table 3*) but head-to-head trials have not been reported.

Ustekinumab has a favourable safety profile. The commonest reported side effects are nasopharyngitis, upper respiratory tract infections and headaches. Commonest serious adverse events are serious infections and cardiac disorders (1.4 and 1.3 events per 100 patient years in patients taking the highest dose (90 mg) respectively) (Lebwohl et al, 2012). No cases of reactivation of tuberculosis were reported. However, patients were screened for tuberculosis before commencing ustekinumab.

National Institute for Health and Care Excellence has approved the use of ustekinumab either alone or in combination with methotrexate for patients with psoriatic arthritis who have either not responded to or are not able to take TNFα inhibitors. It is approved for the treatment of psoriatic arthritis in Scotland.

IL-17A inhibitors

IL-17A inhibitors have had unprecedented success in the treatment of psoriasis with studies quoting 81% of patients achieving 75% improvement of skin lesions (Langley et al, 2014). Trials in psoriatic arthritis have demonstrated efficacy comparable to TNFα inhibitors (*Table 3*). Long-term safety data are not yet available but the commonest reported side effects of IL-17A inhibitors are nasopharyngitis, headache, upper respiratory tract infections and diarrhoea (Langley et al, 2014)*.

Secukinumab, a monoclonal antibody that blocks IL-17A, has been approved by National Institute for Health and Care Excellence for treatment of certain patients with psoriasis and is currently being appraised for psoriatic arthritis (expected decision date February 2017).

*As of 22 May 2015 Amgen terminated its participation in the co-development and commercialization of the IL-17RA receptor blocker brodalumab with AstraZeneca. The decision was based on events of suicidal ideation and behaviour in the brodalumab programme and clinical trials have been halted (Amgen, 2015). At the time of submission suicidal ideation has not been reported in clinical trials of monoclonal antibodies directly targeting the IL-17A cytokine rather than the IL-17RA receptor.

KEY POINTS

- Psoriatic arthritis affects 30% of patients with psoriasis and is often under-diagnosed and undertreated.
- Psoriatic arthritis is a heterogeneous disease and thus can be difficult to diagnose. Key discriminating features are a personal or family history of psoriasis, asymmetrical arthritis, nail changes, dactylitis and enthesitis.
- Psoriatic arthritis is not a benign condition: up to 40% of patients will develop permanent joint deformities and irreversible loss of function.
- The IL-17/IL-23 cytokine pathway is important in the pathogenesis of psoriatic arthritis.
- Drugs blocking IL-17 are very effective in the treatment of psoriasis and early trial results suggest efficacy is comparable to tumour necrosis factor-α inhibitors in psoriatic arthritis.

Conclusions and future work

Psoriatic arthritis is a heterogeneous disease that is under-diagnosed and often undertreated. Although a large proportion of patients will have minimal joint damage, it is not possible to predict the 40% of patients who will develop severe erosive disease. Recent advances in the understanding of the immunopathology of psoriasis and psoriatic arthritis has led to the identification of new therapeutic targets and drug development. However, there remain significant gaps in our knowledge limiting the care we can deliver to patients: which patients with psoriasis will develop psoriatic arthritis? Which patients with psoriatic arthritis will have rapidly progressive bony erosions? How best can we assess disease severity? What similarities and differences are there in the pathogenesis of psoriasis and psoriatic arthritis and do they account for the apparent difference in efficacy of drugs targeting the IL-23/IL-17 pathway at treating psoriasis and psoriatic arthritis? **BJHM**

Conflict of interest: Dr LE Durham: none; Dr LS Taams has received speaker fees and research support from Novo Nordisk A/S, GSK and UCB; Dr BW Kirkham has received research support from UCB, Roche, and acted as a consultant/speaker for Abbott, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB.

Amgen (2015) Amgen to Terminate Participation in Co-development and Commercialization of Brodalumab. www.amgen.com/media/media_pr_detail.jsp?year=2015&releaseID=2052862 (accessed 10 March 2016)
Antoni C, Krueger GG, De Vlam K et al (2005) Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. *Ann Rheum Dis* **64**: 1150–7
Burmester GR, Panaccione R, Gordon KB, McIlraith MJ, Lacerda AP (2013) 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* **72**: 517–24
Capon F, Di Meglio P, Szaub J et al (2007) Sequence variants in the genes for the interleukin-23 receptor (IL23R) and its ligand (IL12B) confer protection against psoriasis. *Hum Genet* **122**: 201–6 (doi: 10.1136/annrheumdis-2011-201244)
Coates LC, Fitzgerald O, Gladman DD, McHugh N, Mease P, Strand V, Helliwell PS (2013a) Reduced joint counts misclassify patients with oligoarticular psoriatic arthritis and miss significant numbers of patients with active disease. *Arthritis Rheum* **65**: 1504–9 (doi: 10.1002/art.37939)
Coates LC, Tillett W, Chandler D et al (2013b) The 2012 BSR and BHPR guideline for the treatment of psoriatic arthritis with biologics. *Rheumatology (Oxford)* **52**: 1754–7 (doi: 10.1093/rheumatology/ket187)
Gladman DD, Antoni C, Mease P, Clegg DO, Nash P (2005) Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* **64** (Suppl 2): ii14–7
Kane D, Stafford L, Bresnihan B, Fitzgerald O (2003) A prospective, clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience. *Rheumatology (Oxford)* **42**: 1460–8
Kavanaugh A, McInnes I, Mease P et al (2009) Golimumab, a new human tumor necrosis factor alpha antibody, administered every four weeks as a subcutaneous injection in psoriatic arthritis: Twenty-four-week efficacy and safety results of a randomized, placebo-controlled study. *Arthritis Rheum* **60**: 976–86 (doi: 10.1002/art.24403)
Kingsley GH, Kowalczyk A, Taylor H et al (2012) A randomized placebo-controlled trial of methotrexate in psoriatic arthritis. *Rheumatology (Oxford)* **51**: 1368–77 (doi: 10.1093/rheumatology/kes001)
Langley RG, Elewski BE, Lebwohl M et al (2014) Secukinumab in plaque psoriasis--results of two phase 3 trials. *N Engl J Med* **371**: 326–38 (doi: 10.1056/NEJMoa1314258)
Lebwohl M, Leonardi C, Griffiths CE et al (2012) Long-term safety experience of ustekinumab in patients with moderate-to-severe psoriasis (Part I of II): results from analyses of general safety parameters from pooled Phase 2 and 3 clinical trials. *J Am Acad Dermatol* **66**: 731–41 (doi: 10.1016/j.jaad.2011.06.011)
Leipe J, Grunke M, Dechant C, Reindl C, Kerzendorf U, Schulze-Koops H, Skapenko A (2010) Role of Th17 cells in human autoimmune arthritis. *Arthritis Rheum* **62**: 2876–85 (doi: 10.1002/art.27622)
Lloyd P, Ryan C, Menter A (2012) Psoriatic arthritis: an update. *Arthritis* **2012**: 176298 (doi: 10.1155/2012/176298)
McInnes IB, Kavanaugh A, Gottlieb AB et al (2013) Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1 year results of the phase 3, multicentre, double-blind, placebo-controlled PSUMMIT 1 trial. *Lancet* **382**: 780–9 (doi: 10.1016/S0140-6736(13)60594-2)
McInnes IB, Mease PJ, Kirkham B et al (2015) Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet* **386**(9999): 1137–46 (doi: 10.1016/S0140-6736(15)61134-5)
Mease PJ, Kivitz AJ, Burch FX et al (2004) Etanercept treatment of psoriatic arthritis: safety, efficacy, and effect on disease progression. *Arthritis Rheum* **50**: 2264–72
Mease PJ, Gladman DD, Ritchlin CT et al (2005) Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* **52**: 3279–89
Mease PJ, Fleischmann R, Deodhar AA et al (2014a) Effect of certolizumab pegol on signs and symptoms in patients with psoriatic arthritis: 24-week results of a Phase 3 double-blind randomised placebo-controlled study (RAPID-PsA). *Ann Rheum Dis* **73**: 48–55 (doi: 10.1136/annrheumdis-2013-203696)
Mease PJ, Genovese MC, Greenwald MW et al (2014b) Brodalumab, an anti-IL17RA monoclonal antibody, in psoriatic arthritis. *N Engl J Med* **370**: 2295–306 (doi: 10.1056/NEJMoa1315231)
Menon B, Gullick NJ, Walter GJ et al (2014) Interleukin-17+CD8+ T cells are enriched in the joints of patients with psoriatic arthritis and correlate with disease activity and joint damage progression. *Arthritis Rheumatol* **66**: 1272–81 (doi: 10.1002/art.38376)
Moll JM, Wright V (1973) Psoriatic arthritis. *Semin Arthritis Rheum* **3**: 55–78
Morar N, Willis-Owen SA, Maurer T, Bunker CB (2010) HIV-associated psoriasis: pathogenesis, clinical features, and management. *Lancet Infect Dis* **10**: 470–8
Mosmann TR, Coffman RL (1989) TH1 and TH2 cells: different patterns of lymphokine secretion lead to different functional properties. *Annu Rev Immunol* **7**: 145–73
Res PC, Piskin G, De Boer OJ, Van Der Loos CM, Teeling P, Bos JD, Teunissen MB (2010) Overrepresentation of IL-17A and IL-22 producing CD8 T cells in lesional skin suggests their involvement in the pathogenesis of psoriasis. *PLoS One* **5**: e14108 (doi: 10.1371/journal.pone.0014108)
Ritchlin C, Rahman P, Kavanaugh A et al (2014) Efficacy and safety of the anti-IL-12/23 p40 monoclonal antibody, ustekinumab, in patients with active psoriatic arthritis despite conventional non-biological and biological anti-tumour necrosis factor therapy: 6-month and 1-year results of the phase 3, multicentre, double-blind, placebo-controlled, randomised PSUMMIT 2 trial. *Ann Rheum Dis* **73**: 990–9 (doi: 10.1136/annrheumdis-2013-204655)
Suzuki E, Mellins ED, Gershwin ME, Nestle FO, Adamopoulos IE (2014) The IL-23/IL-17 axis in psoriatic arthritis. *Autoimmun Rev* **13**: 496–502 (doi: 10.1016/j.autrev.2014.01.050)
Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H, CASPAR Study Group (2006) Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum* **54**: 2665–73 (doi: 10.1002/art.21972)
Winchester R, Minevich G, Steshenko V, Kirby B, Kane D, Greenberg DA, Fitzgerald O (2012) HLA associations reveal genetic heterogeneity in psoriatic arthritis and in the psoriasis phenotype. *Arthritis Rheum* **64**: 1134–44 (doi: 10.1002/art.33415)