




PSORIASIS ARTHRITIS

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5 things to know about PsA

- Diagnosis is almost entirely clinical (there are no useful biomarkers) so look hard for psoriasis – it can be hidden; dactylitis is also an important clue to diagnosis and prognosis
- Affects men and women equally; 1:400 population prevalence
- Non-biologic DMARDS are commonly used and recommended but not as well supported by evidence as biologics
- Biologics that are effective include anti-TNF inhibitors, ustekinumab (anti-IL12/23) and secukinumab (anti IL-17)
- There is an increased risk of co-morbidities especially cardiovascular disease and depression

Mr PS

- 34 year old man, presenting with recurrent heel pain and recent onset swollen knee

What would a good evaluation include?

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- Is there a history of trauma or over-use (eg running)?
- Are the symptoms typically inflammatory (prolonged morning stiffness, improvement with activity)?
- Is there a personal or family history of psoriasis, inflammatory back pain, iritis, inflammatory bowel disease or recent GI/GU infection?
- Examine the skin, joints and nails carefully.
- What is the functional impact?
- US heel might be useful
- CRP might be useful (but normal values do not exclude PsA)
- Consider STI evaluation (esp. chlamydia and HIV tests) in appropriate clinical context



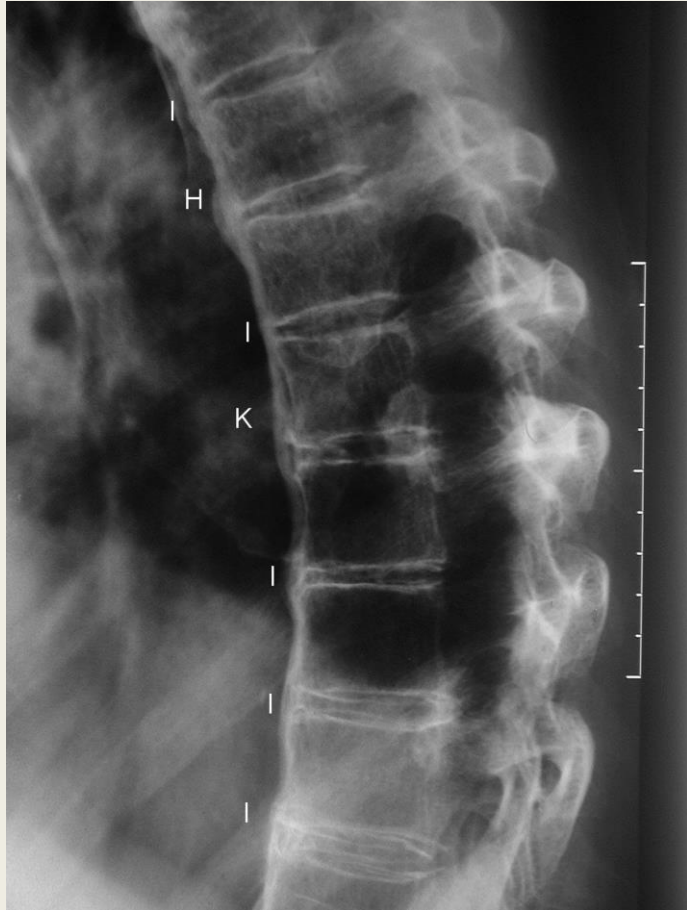
How else can PsA present?

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Peripheral oligo- or poly-arthritis that might look a bit like rheumatoid arthritis

How else can PsA present?



Inflammatory back disease that looks a lot like ankylosing spondylitis

How else can PsA present?



Arthritis mutilans – marked bony resorption and ‘telescoping’ of the digit

Mr PS

- No history of trauma; some possible nail dystrophy and a family history of psoriasis
- Tenderness and swelling at L Achilles insertion; definite R knee effusion
- CRP 14
- Walking distance limited to 150m; too painful to go the gym

Initial management options?

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- NSAIDs are a reasonable first-line therapy; worth trying 2 or 3 if necessary in view of individual differences in response
- Local glucocorticoids (injections) are effective in the short to medium term
- Systemic glucocorticoids are effective but ...
<https://www.dermnetnz.org/topics/erythrodermic-psoriasis/>

Mr PS

- Is prescribed celecoxib 200mg bd and referred for US-guided peri-tendon glucocorticoid injection of L Achilles tendon
- Returns 2 weeks later with improvement in symptoms and return to normal activities but persisting swelling of the R knee

Longer term management?

Considerations

Treatment risk

- Risks of long term NSAID use (mainly CVS, GI, renal)
- Risks of csDMARD use
- Risks of biologic DMARDS (mainly infection)

Disease risk

- 'One size does not fit all'
- Chronic pain, depression, functional loss
- Risk of irreversible joint damage, which has its own consequences
- Risk of cardiovascular comorbidity

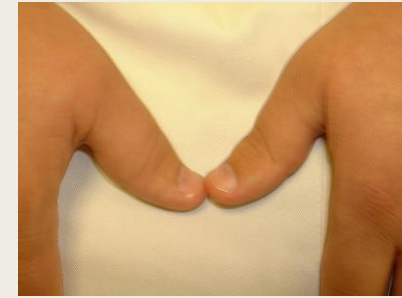
Clinical sub-groups of psoriatic arthritis



Symmetric Polyarticular
resembling RA - 15%



Arthritis mutilans -
5%



Dactylitis - 40%



Spinal disease - 5%



Oligoarthritis - 70%



Distal interphalangeal
predominant - 5%



Enthesitis - 50%

*Moll and Wright. Sem Arthr Rheum 1973;3:58;
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All RCT in PSA enrol patients on the basis of peripheral polyarthritís



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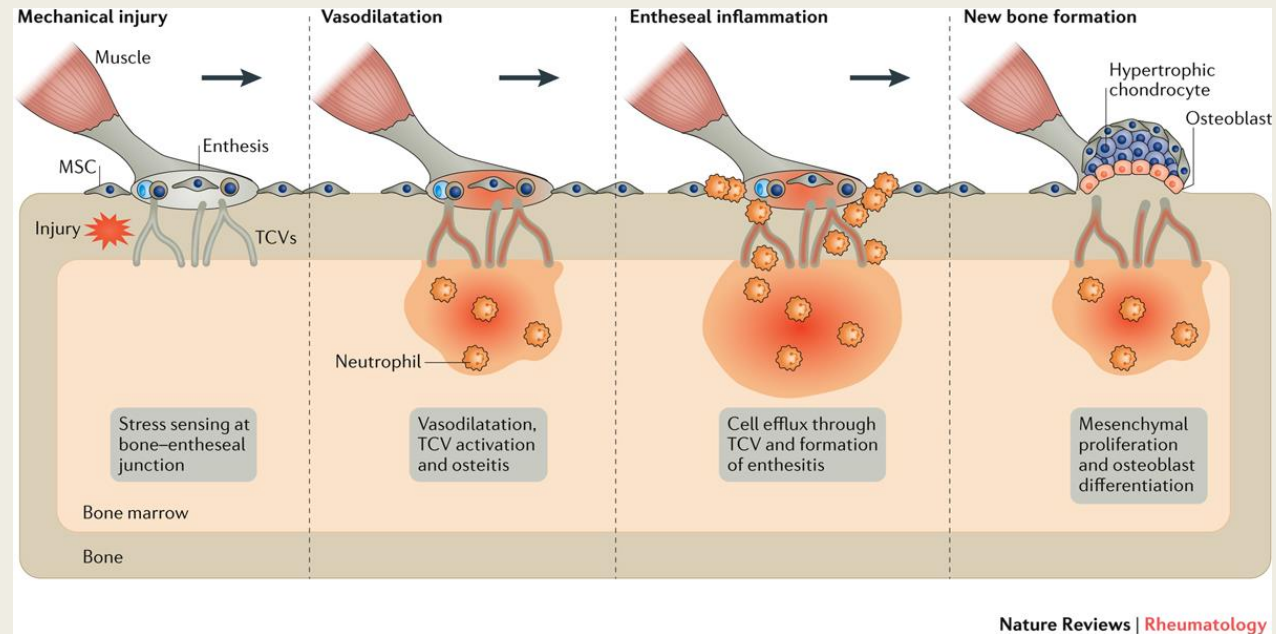
Distal interphalangeal predominant - 5%



Enthesitis - 50%

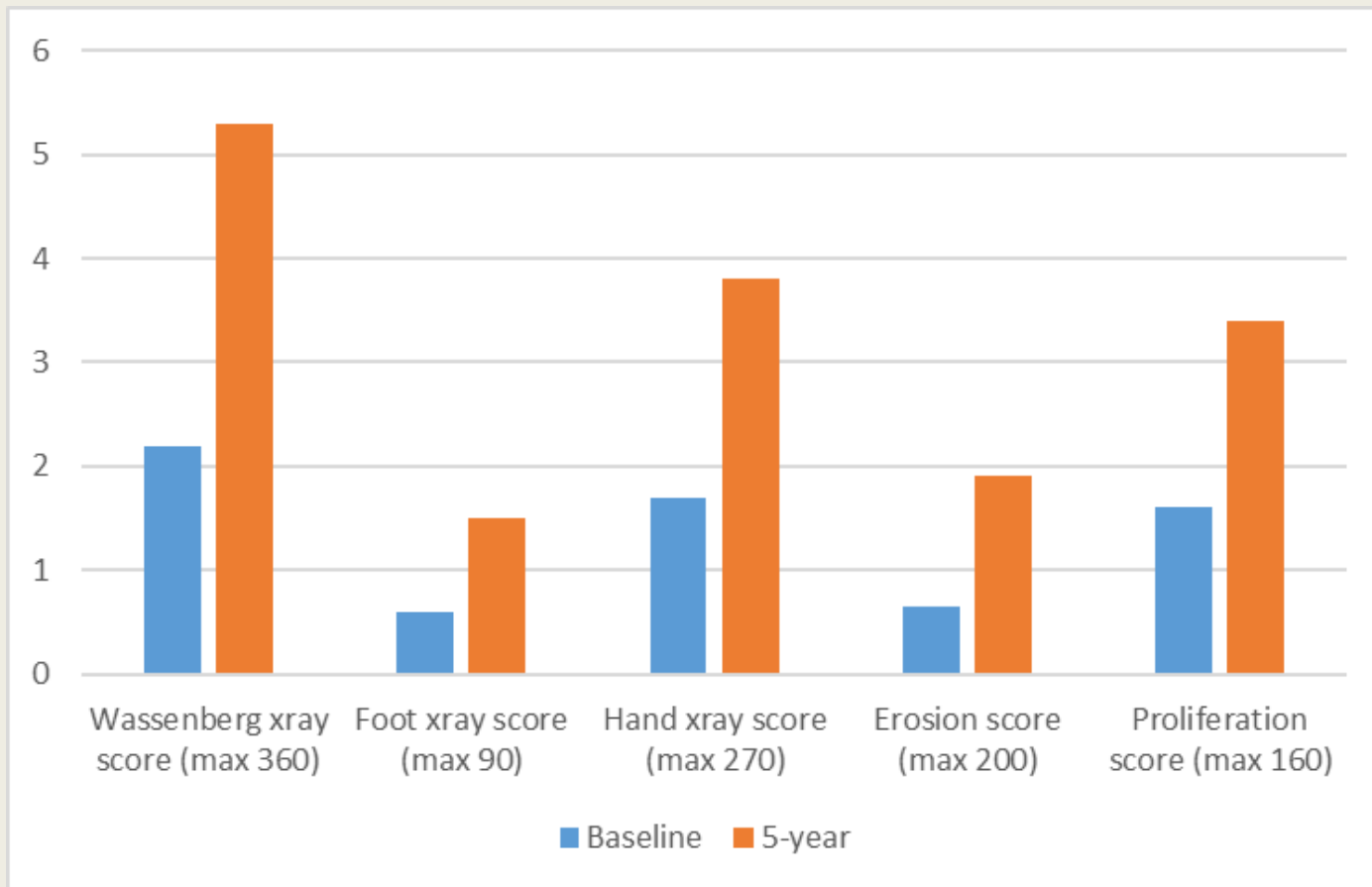
*Moll and Wright. Sem Arthr Rheum 1973;3:58;
Images reproduced, with permission, from P Helliwell.

Figure 3 Microanatomical changes in enthesitis



Schett, G. *et al.* (2017) Enthesitis: from pathophysiology to treatment
Nat. Rev. Rheumatol. doi:10.1038/nrrheum.2017.188

Risk of irreversible joint damage



- 0 xray score in **45%** (baseline) to **14%** (5-years)
- Predictors of xray progression were
 - Male sex
 - Dactylitis
 - High disease activity
- Achieving remission or 'minimal disease activity' protected against xray damage

Geijer M, Lindqvist U, Husmark T, Alenius G, Marie, Larsson PT, et al. The Swedish Early Psoriatic Arthritis Registry 5-year Followup: Substantial Radiographic Progression Mainly in Men with High Disease Activity and Development of Dactylitis. The Journal of Rheumatology. 2015;42(11):2110.

Mr PS

- Manages with intermittent celecoxib for 2 years then re-presents with pain and swelling of both knees and painful swelling of two toes
- Would like to explore other options since he worries that celecoxib is becoming less and less effective

Next steps?

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csDMARDs

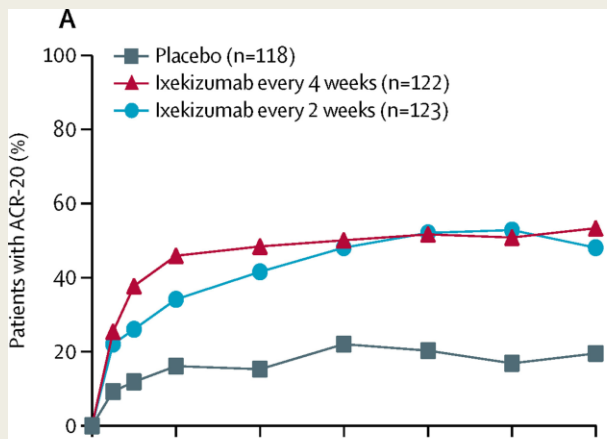
- Methotrexate 10-25mg weekly
- Sulphasalazine 1000mg bd
- Leflunomide 20mg daily
- (Azathioprine 100mg daily)
- (Cylosporine 5-10mg/kg daily)
- (Apremilast 30mg bd) NS

bDMARDs

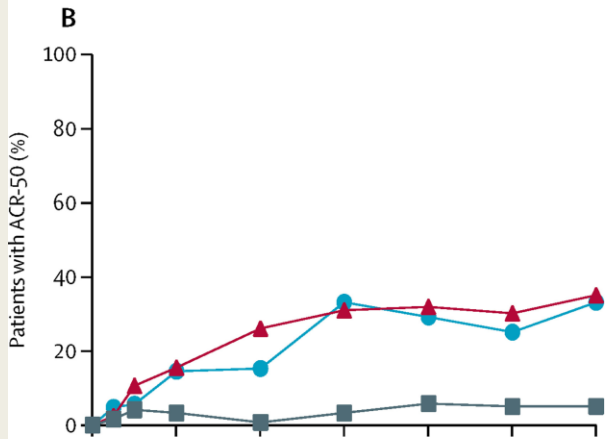
- Adalimumab 40mg SC eow
- Etanercept 50mg SC w
- Infliximab 5-10mg/kg IV 8w
- Secukinumab 150-300mg SC 4w
- Ustekinumab 45-90mg SC 12w NS

General principles of DMARD use

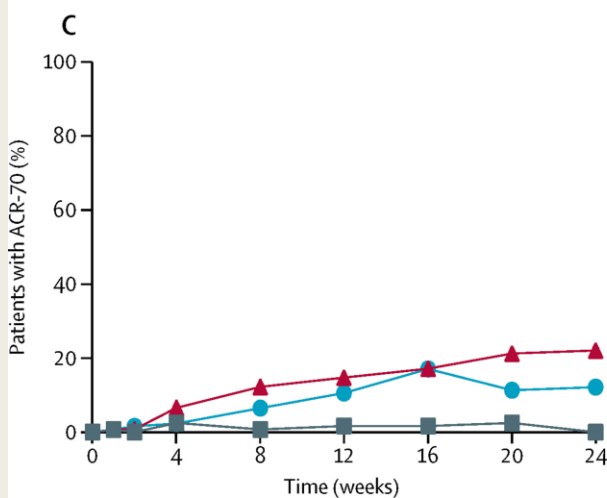
- Slow acting so assessment of response needs to wait for 6 to 8 weeks
- Most of these drugs require some kind of blood test monitoring (risk of bone marrow toxicity and/or liver toxicity)
- Immuno-active drugs so live attenuated virus vaccinations should be avoided
- Infection risk is mainly seen with bDMARDs; early antibiotic use; discontinue prior to elective surgery
- Each drug has its own AE profile



Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	0.0012	0.0057
2	<0.0001	0.0055
4	<0.0001	0.0017
8	<0.0001	<0.0001
12	<0.0001	<0.0001
16	<0.0001	<0.0001
20	<0.0001	<0.0001
24	<0.0001	<0.0001



Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	>0.99	0.28
2	0.06	0.77
4	0.0031	0.0030
8	0.0003	<0.0001
12	<0.0001	<0.0001
16	<0.0001	<0.0001
20	<0.0001	0.0001
24	<0.0001	<0.0001

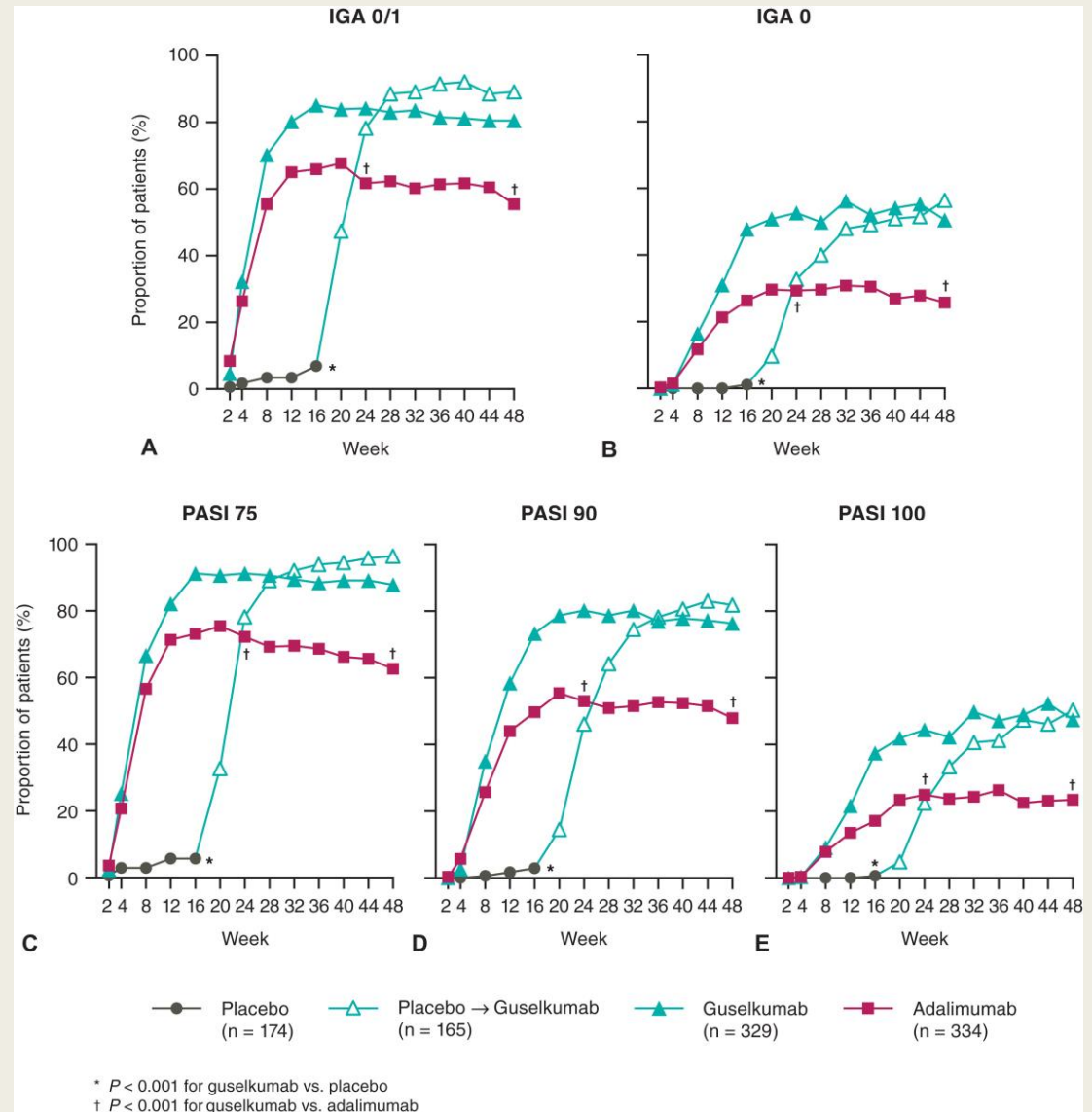


Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	>0.99	>0.99
2	>0.99	0.50
4	0.22	>0.99
8	0.0065	0.0360
12	0.0020	0.0059
16	<0.0001	<0.0001
20	0.0002	0.0146
24	<0.0001	<0.0001

Ixekizumab is an interleukin-17A specific monoclonal antibody for treatment of psoriasis and PsA

Nash P, Kirkham B, Okada M, Rahman P, Combe B, Burmester G, et al. **Ixekizumab** for the treatment of patients with active psoriatic arthritis and an inadequate response to tumour necrosis factor inhibitors: results from the 24-week randomised, double-blind, placebo-controlled period of the SPIRIT-P2 phase 3 trial. *The Lancet*;389(10086):2317-27.

VOYAGE 1: Guselkumab is a 'pure' IL-23 inhibitor 100mg q8w



Blauvelt A, Papp KA, Griffiths CEM, Randazzo B, Wasfi Y, Shen Y, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. Journal of the American Academy of Dermatology. 2017;76(3):405-17.

Mr PS

- Is established on MTX 20mg weekly and symptoms improve after several weeks; some initial nausea settles
- On a general check-up, BP taken as 150/90; he is a non-smoker, normal HbA1C, no family history of early CVS disease and TC:HDL-C ratio is 5 (estimated 5-year CVS risk based on traditional algorithm is no more than 5%)

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- In RA, it is recommended that CVS risk scores be multiplied by 1.5 to account for the increased risk attributed to RA itself.
- In Ps and PsA, there is a similar increased risk of CVS disease but the magnitude of the increased risk and whether it is attributable to inflammatory disease or an increased rate of conventional CVS risk factors is less clearcut.
- Main recommendation is to monitor and treat conventional CVS risk factors more diligently

5 things to know about PsA

- Diagnosis is almost entirely clinical (there are no useful biomarkers) so look hard for psoriasis – it can be hidden; dactylitis is also an important clue to diagnosis and prognosis
- Affects men and women equally; population prevalence is about 1 in 400
- Non-biologic DMARDs are commonly used and recommended but not as well supported by evidence as biologics
- Biologics that are effective include anti-TNF inhibitors, ustekinumab (anti-IL12/23) and secukinumab (anti IL-17)
- There is an increased risk of co-morbidities especially cardiovascular disease and depression