Psoriatic Arthritis: Pathogenesis, Diagnosis & Management

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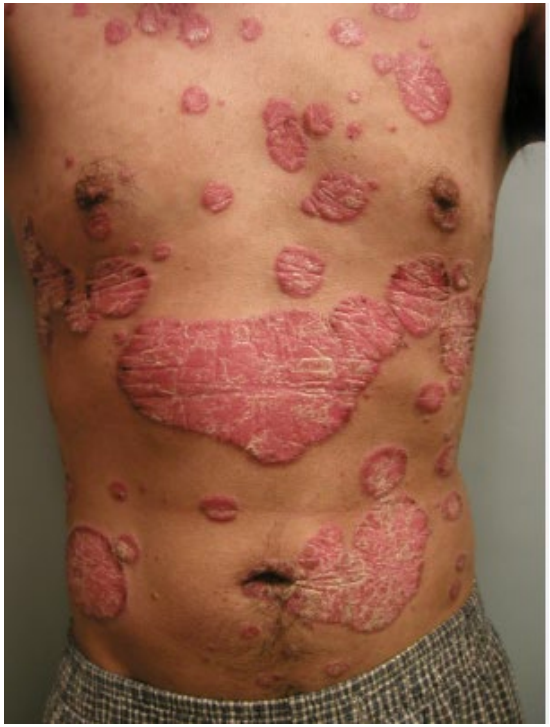
Psoriatic Arthritis (PsA)

- Rare, heterogeneous chronic inflammatory immune-mediated disease characterized by
  - arthritis
  - enthesitis
  - spondylitis
  - dactylitis

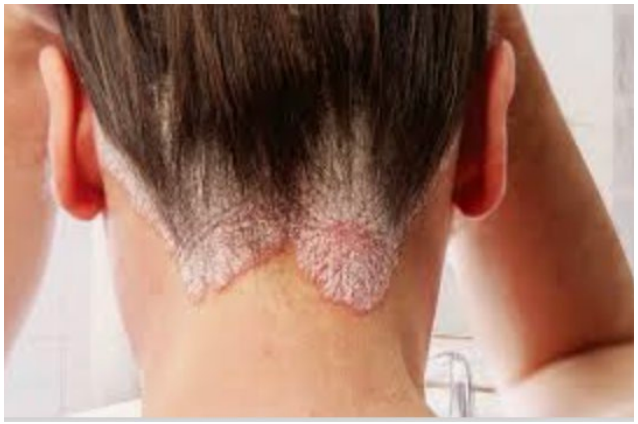
    Not always psoriasis!

- 0.3 – 1% population - ith psoriasis.
- Male female ratio 1:1
- Age 30-40
- Associated with obesity

Psoriasis

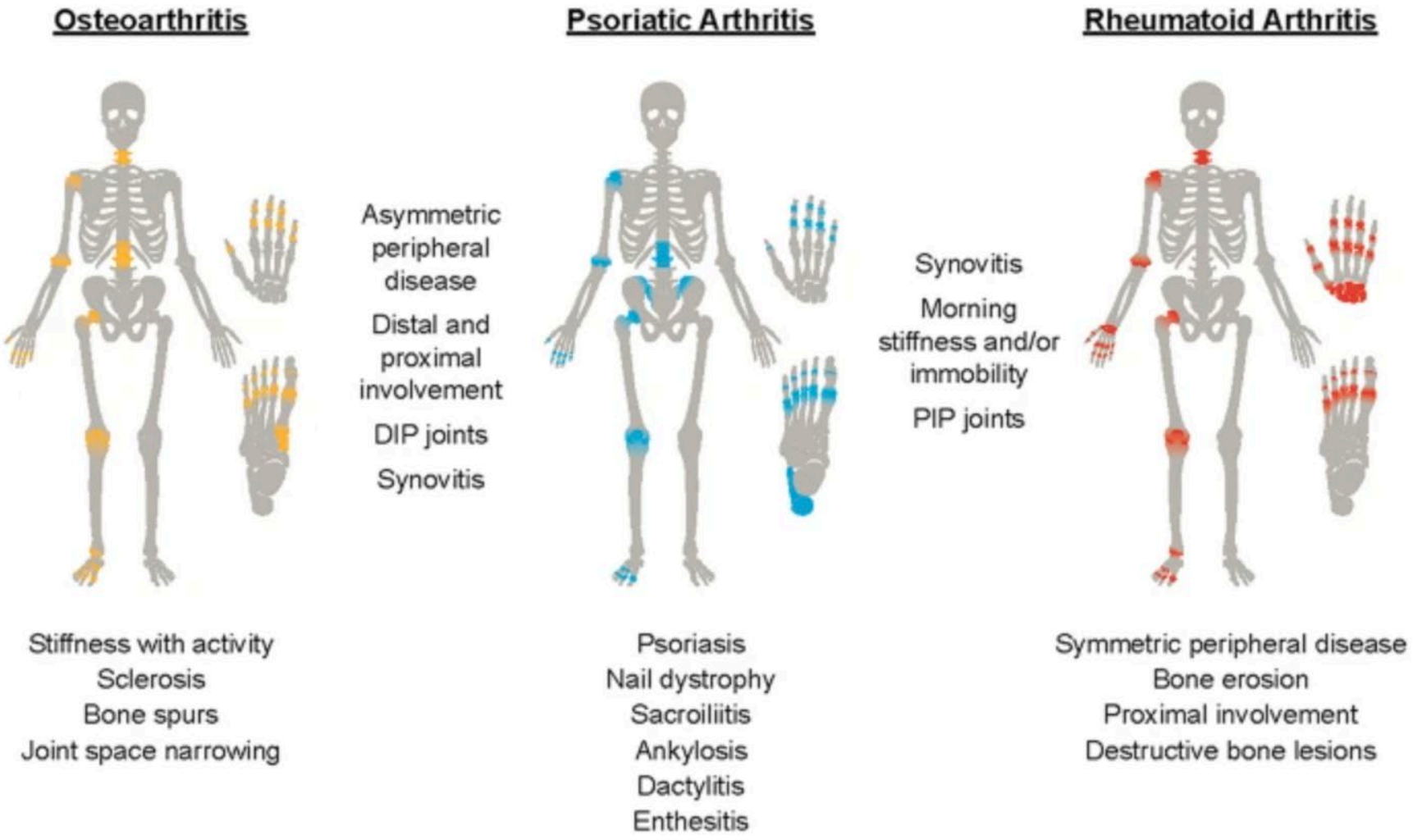


- Psoriasis (PsO) is a chronic inflammatory immune-mediated skin disease characterized by
  - erythematous and scaly plaque, but which also
  - frequently affects the scalp and nails .
  - 20-30% of patients with PsO may develop psoriatic arthritis (PsA), especially those with severe psoriasis or nail or scalp involvement
  - Skin disease usually presents before joints

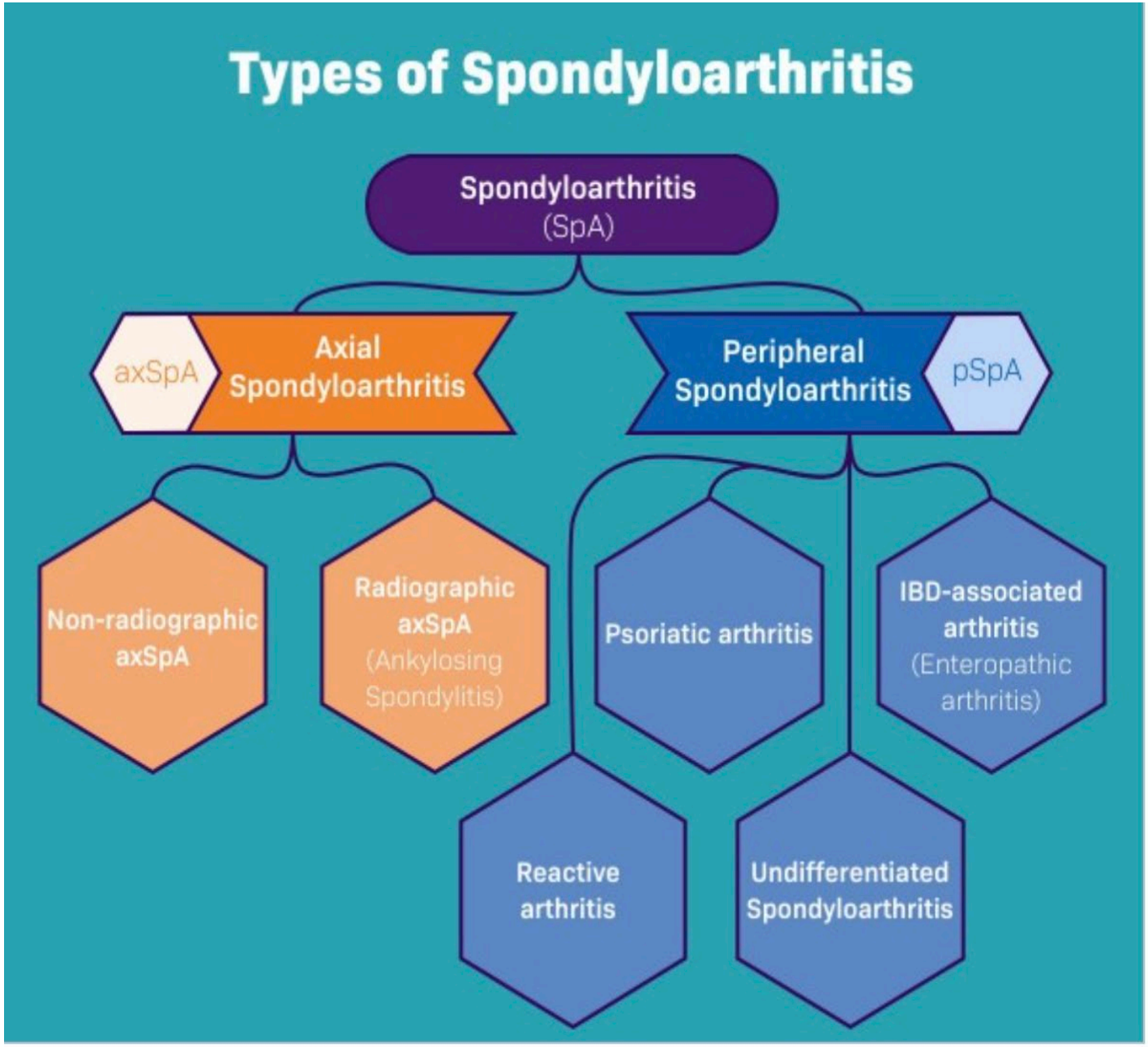


- Rapid progression in understanding of pathophysiology in recent times resulting in multiple new therapies for both skin and joint

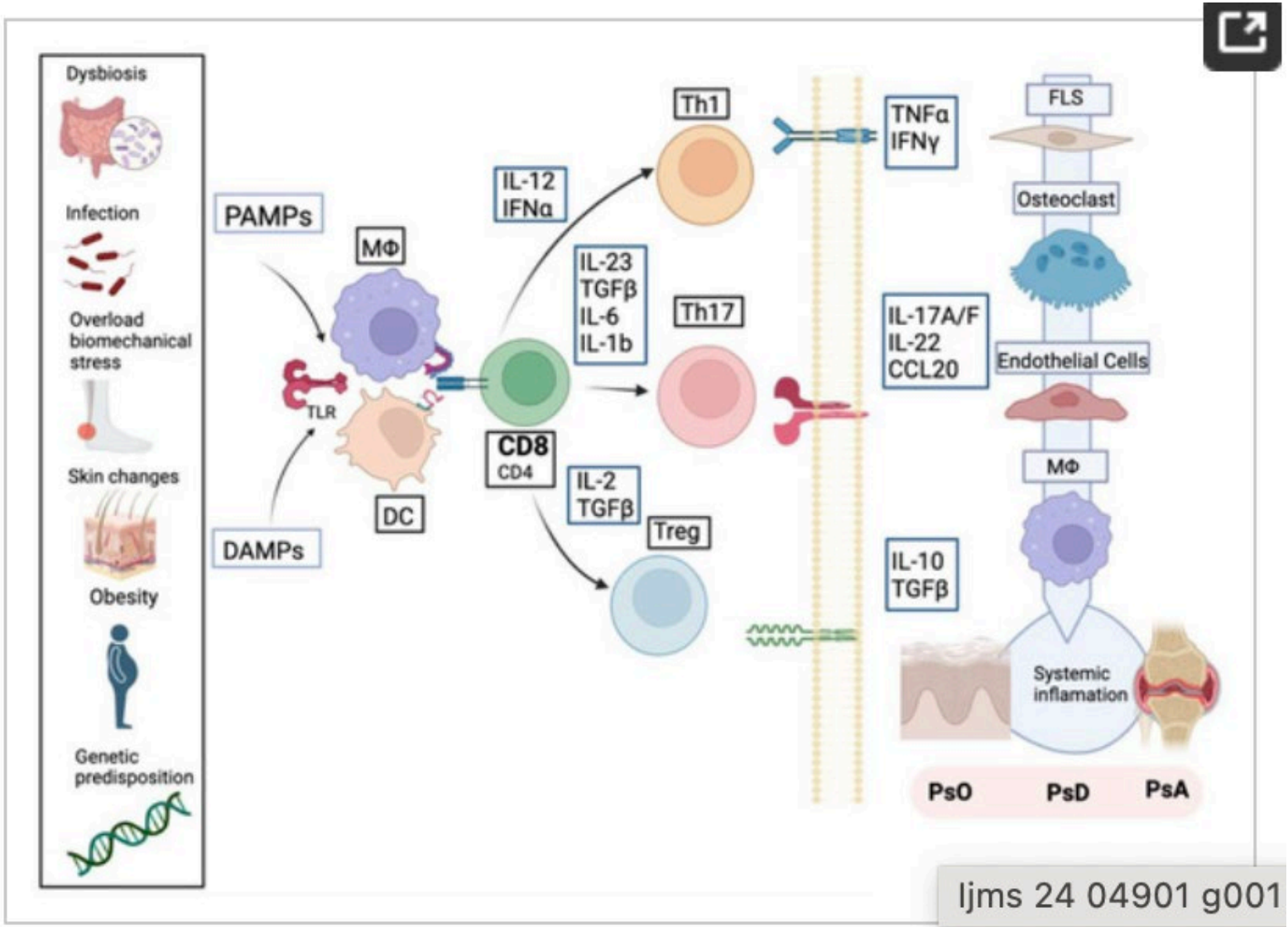
Fig. 2



Clinical manifestations characteristic of psoriatic arthritis to differentiate from characteristics of osteoarthritis and rheumatoid arthritis. DIP distal interphalangeal, PIP proximal interphalangeal


Types of Spondyloarthritis
Spondyloarthritis
(SpA)
axSpA
Axial
Spondyloarthritis
Peripheral
Spondyloarthritis
pSpA
Non-radiographic
axSpA
Radiographic
axSpA
(Ankylosing
Spondylitis)
Psoriatic arthritis
IBD-associated
arthritis
(Enteropathic
arthritis)
Reactive
arthritis
Undifferentiated
Spondyloarthritis

Pathogenesis



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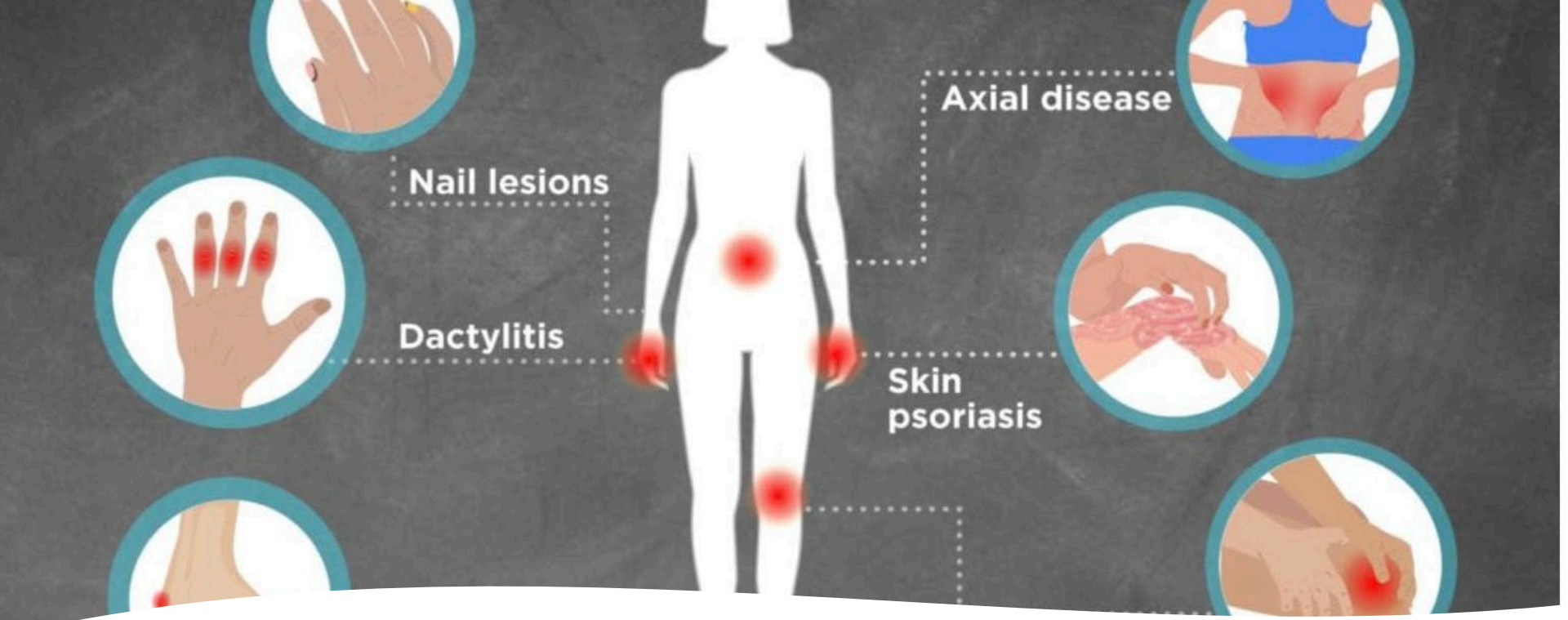
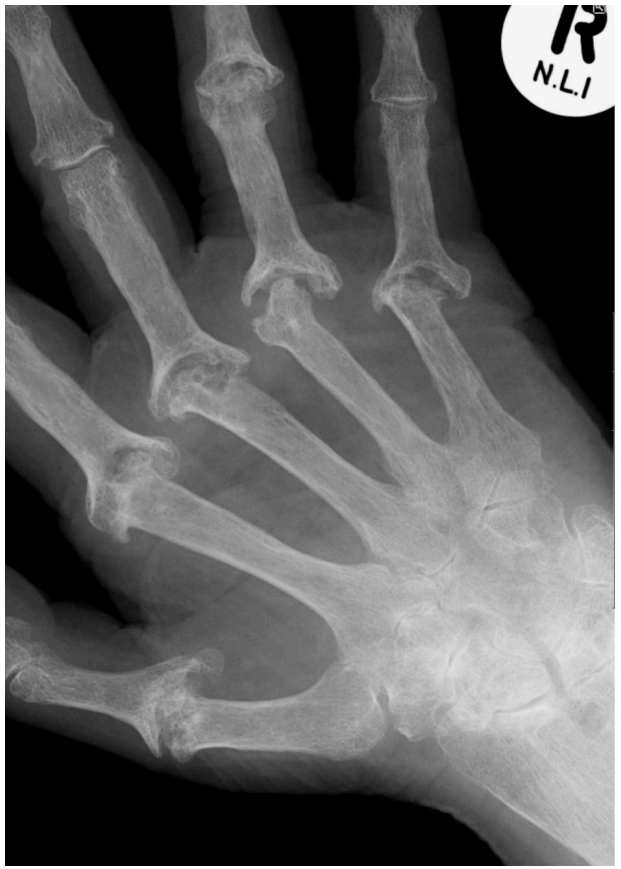


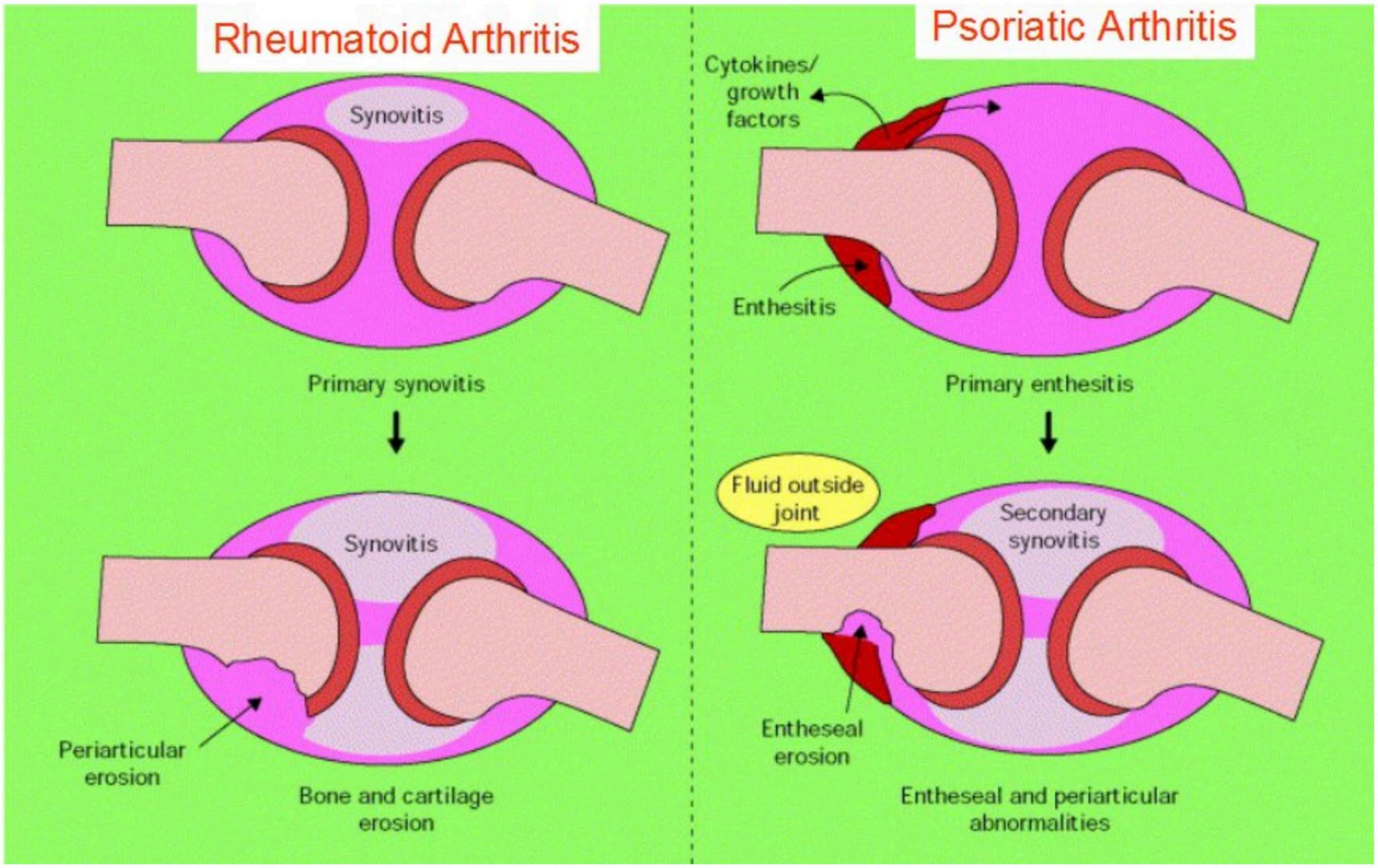
Presentatin of PsA

1. Peripheral synovitis – symmetrical v asymmetrical
2. Axial
3. Dactylitis
4. DIP prevalent
5. Enthesitis
6. Mutilans

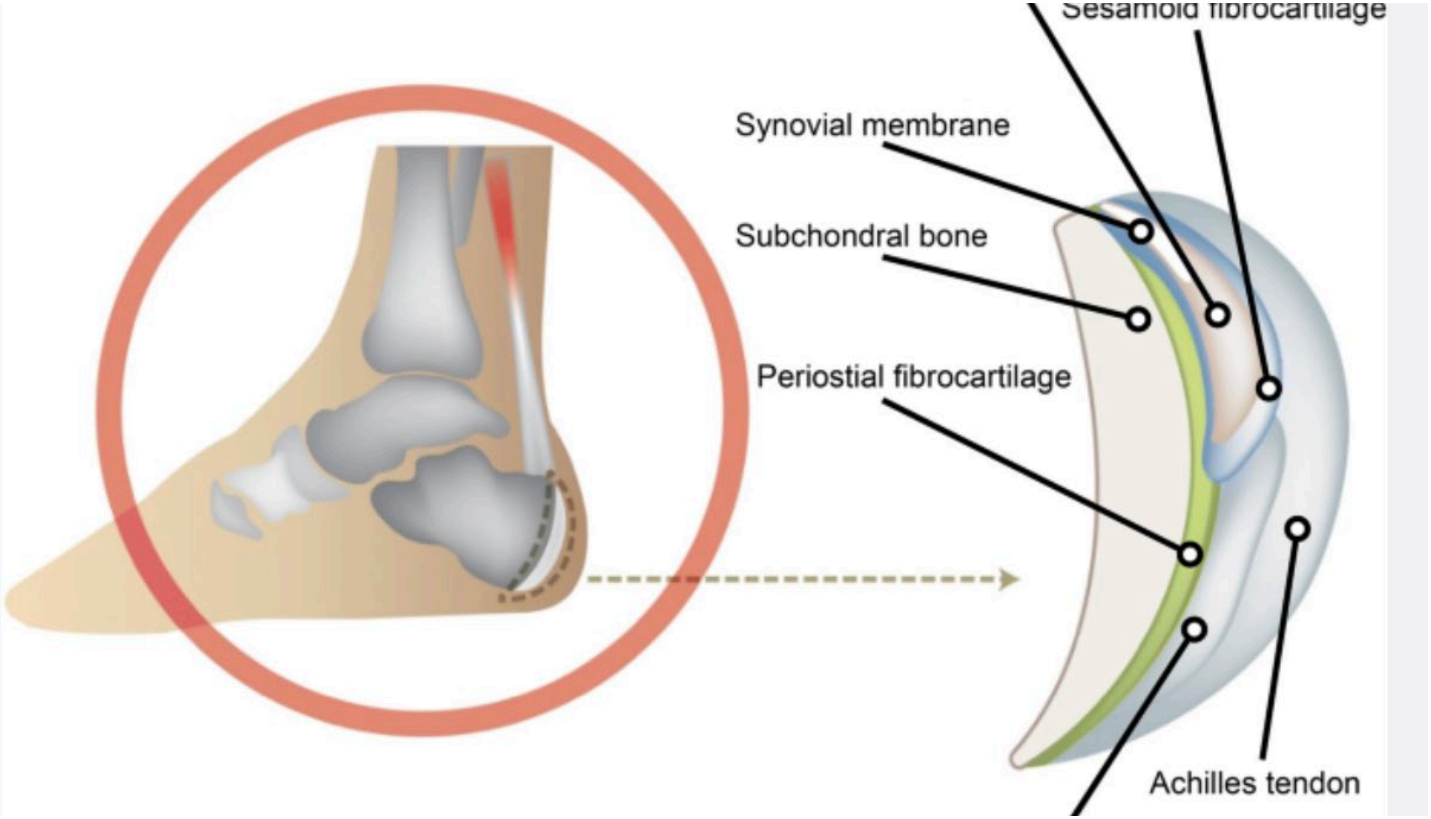
Synovitis in PsA

- Synovial angiogenesis, hypervascular pannus
- Bone erosion + new bone formation



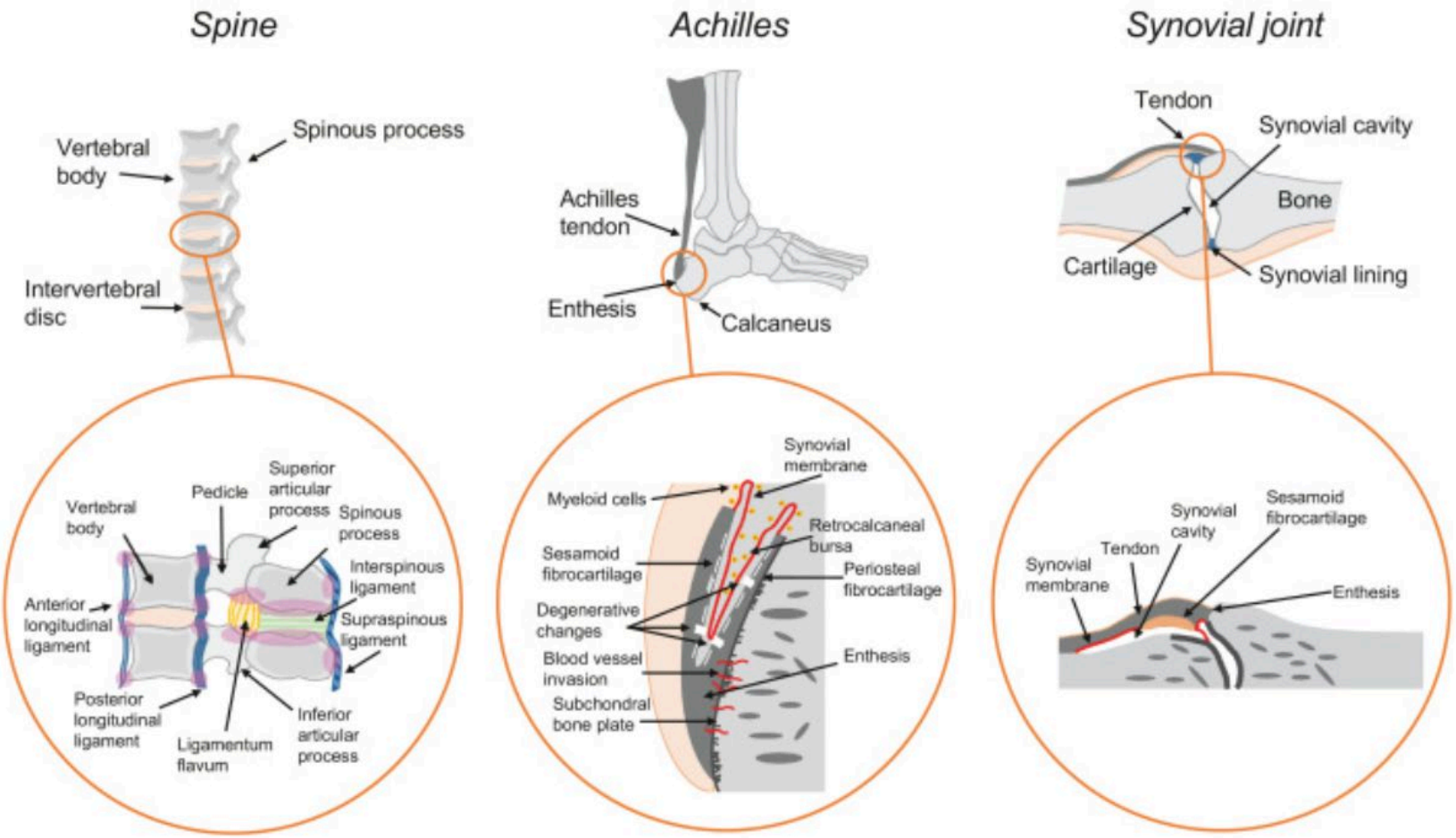


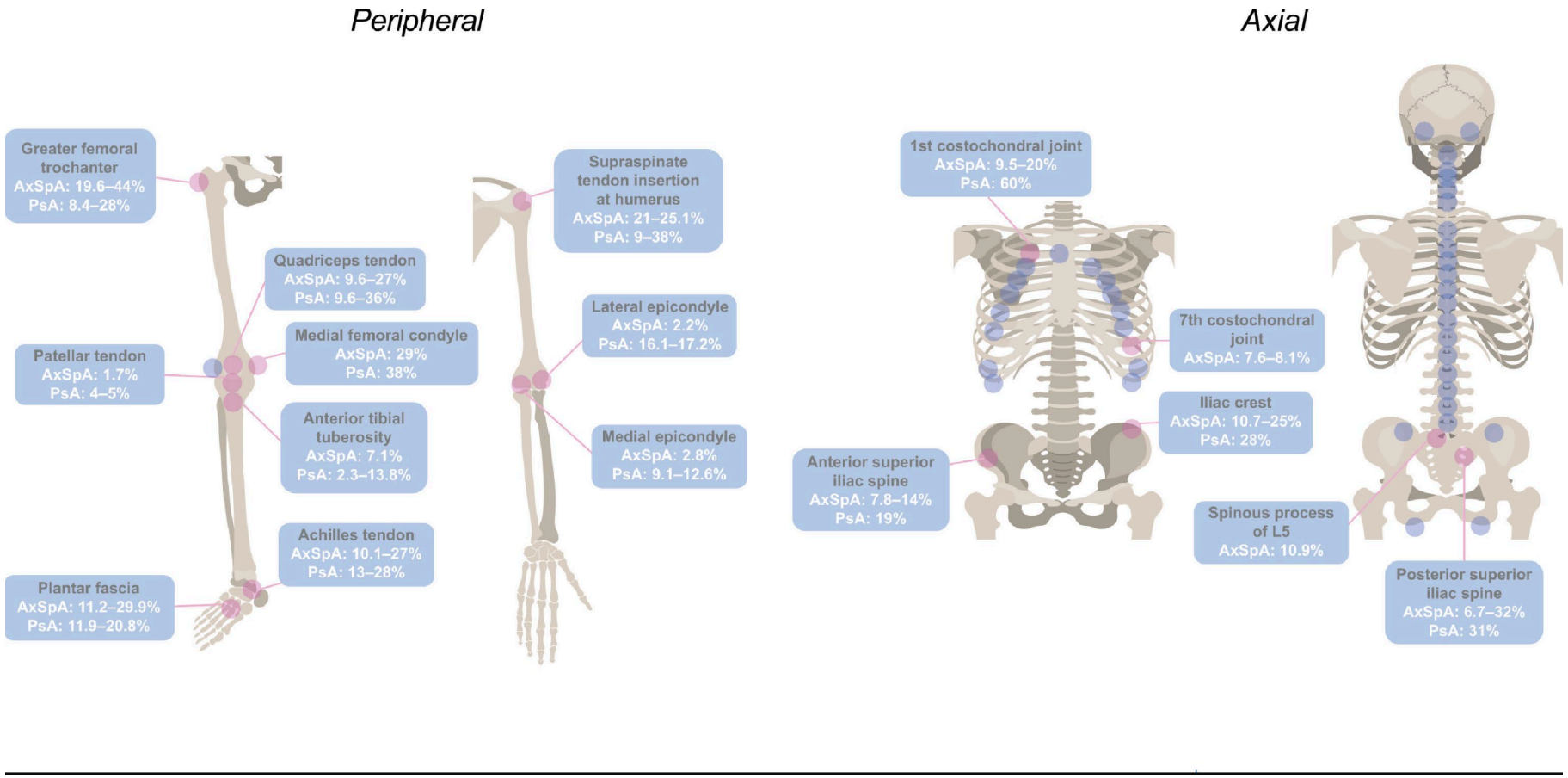
McGonagle et al Lancet 1998. In Rheumatoid Arthritis it is considered that inflammation starts in the joint lining which is called the synovium. In Psoriatic Arthritis it is recognised that the inflammaton may start at the enthesis and then spread to the adjacent bone and synovium and other tissues



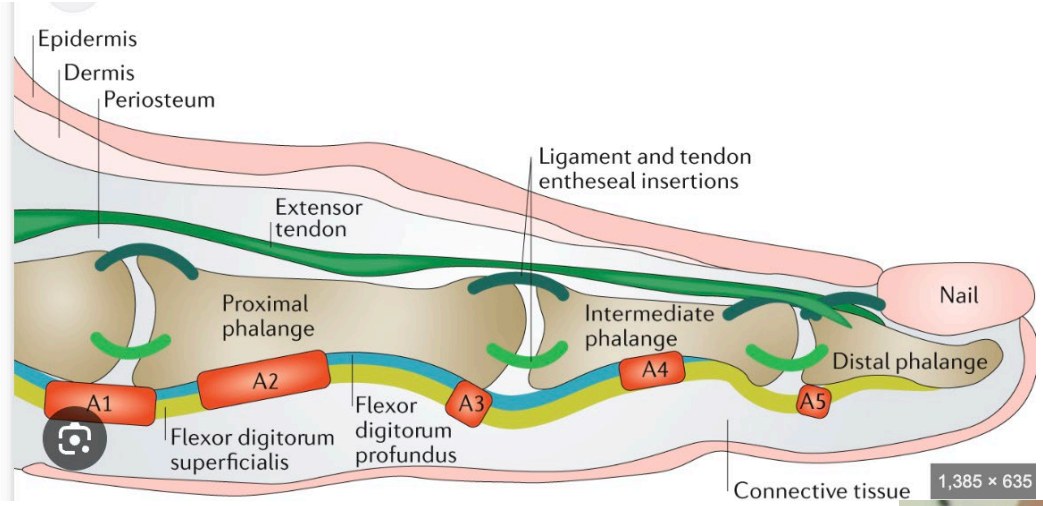
Enthesitis – The Hallmark

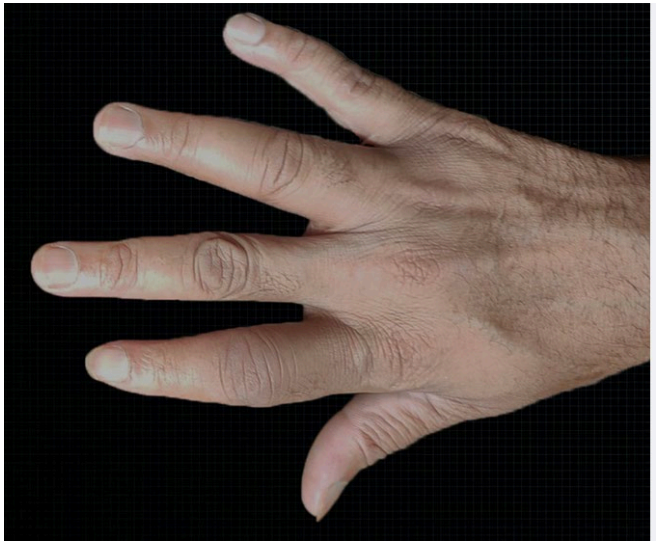
- Primary lesion hypothesis
- IL-23–responsive T cells at entheses
- Microdamage → inflammation → bone remodeling

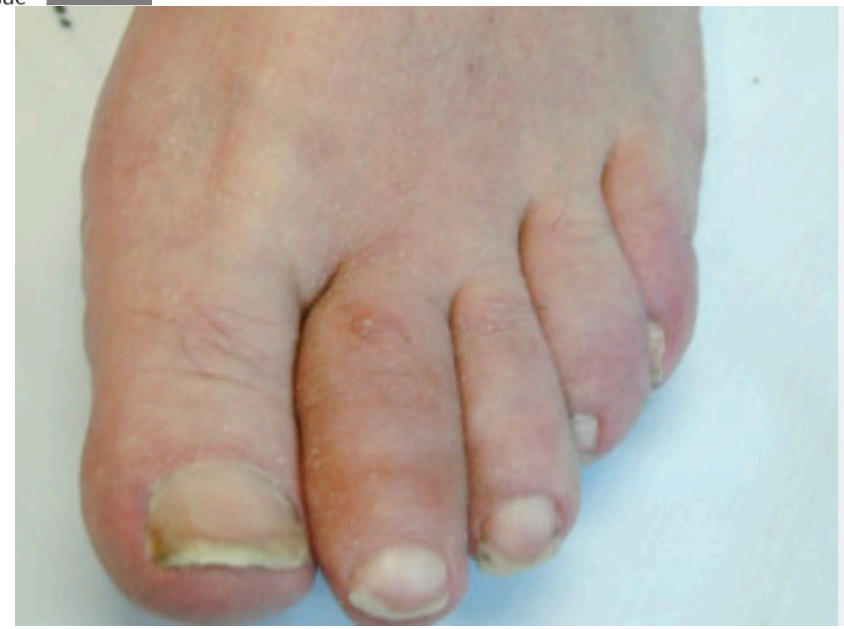

Spine
Vertebral body
Spinous process
Intervertebral disc
Vertebral body
Pedicle
Superior articular process
Spinous process
Interspinous ligament
Supraspinous ligament
Anterior longitudinal ligament
Posterior longitudinal ligament
Ligamentum flavum
Inferior articular process
Achilles
Achilles tendon
Enthesis
Calcaneus
Synovial membrane
Myeloid cells
Retrocalcaneal bursa
Sesamoid fibrocartilage
Periosteal fibrocartilage
Degenerative changes
Blood vessel invasion
Enthesis
Subchondral bone plate
Synovial joint
Tendon
Synovial cavity
Bone
Cartilage
Synovial lining
Synovial membrane
Tendon
Synovial cavity
Sesamoid fibrocartilage
Enthesis

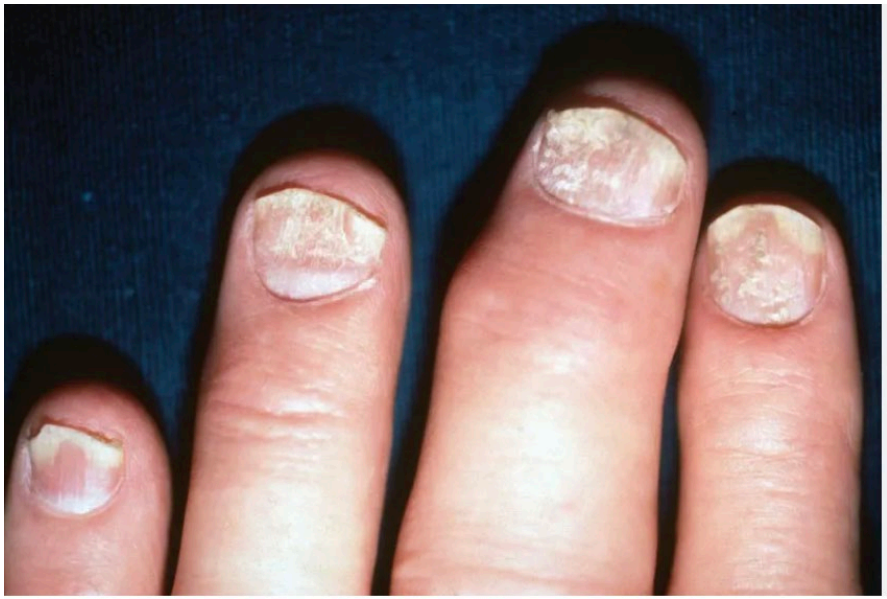

Peripheral
Axial
Greater femoral trochanter
AxSpA: 19.6–44%
PsA: 8.4–28%
Quadriceps tendon
AxSpA: 9.6–27%
PsA: 9.6–36%
Medial femoral condyle
AxSpA: 29%
PsA: 38%
Patellar tendon
AxSpA: 1.7%
PsA: 4–5%
Anterior tibial tuberosity
AxSpA: 7.1%
PsA: 2.3–13.8%
Achilles tendon
AxSpA: 10.1–27%
PsA: 13–28%
Plantar fascia
AxSpA: 11.2–29.9%
PsA: 11.9–20.8%
Supraspinate tendon insertion at humerus
AxSpA: 21–25.1%
PsA: 9–38%
Lateral epicondyle
AxSpA: 2.2%
PsA: 16.1–17.2%
Medial epicondyle
AxSpA: 2.8%
PsA: 9.1–12.6%
1st costochondral joint
AxSpA: 9.5–20%
PsA: 60%
7th costochondral joint
AxSpA: 7.6–8.1%
Iliac crest
AxSpA: 10.7–25%
PsA: 28%
Anterior superior iliac spine
AxSpA: 7.8–14%
PsA: 19%
Spinous process of L5
AxSpA: 10.9%
Posterior superior iliac spine
AxSpA: 6.7–32%
PsA: 31%

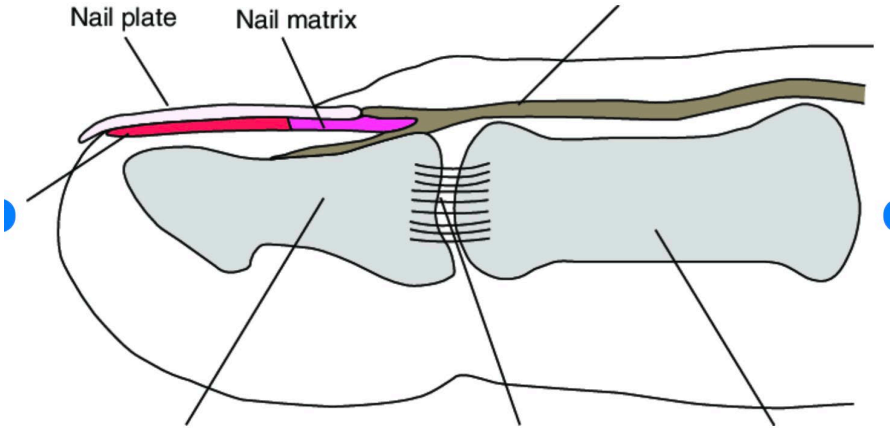
Dactylitis


Epidermis
Dermis
Periosteum
Ligament and tendon entheseal insertions
Extensor tendon
Proximal phalange
Intermediate phalange
Nail
Distal phalange
A1
A2
A3
A4
A5
Flexor digitorum superficialis
Flexor digitorum profundus
Connective tissue
1,385 × 635



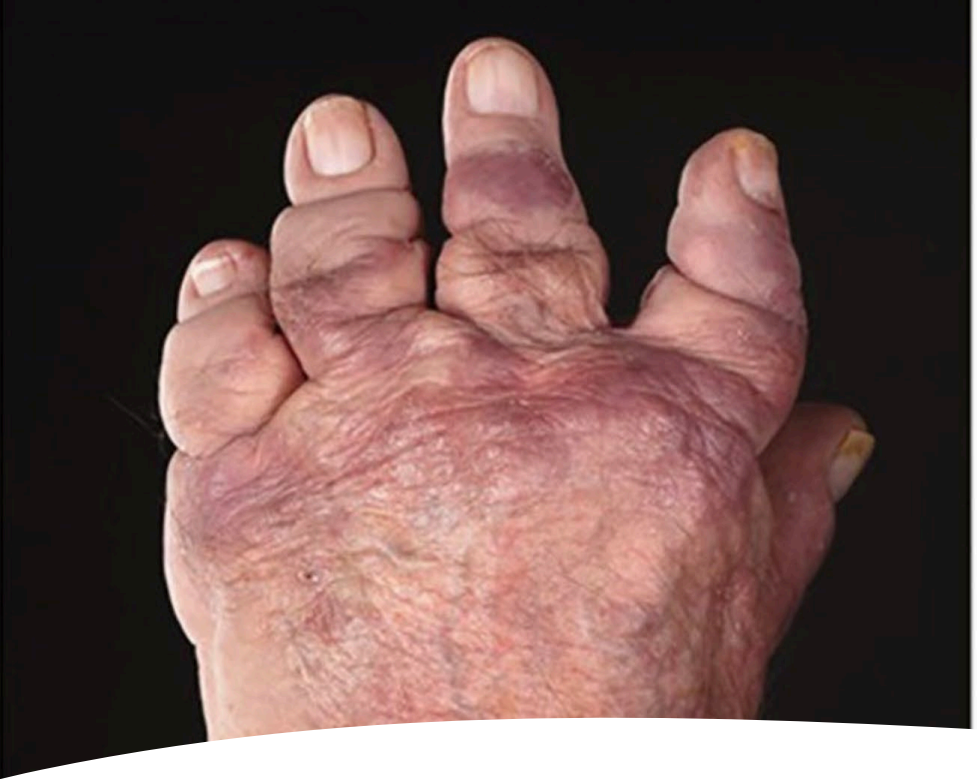


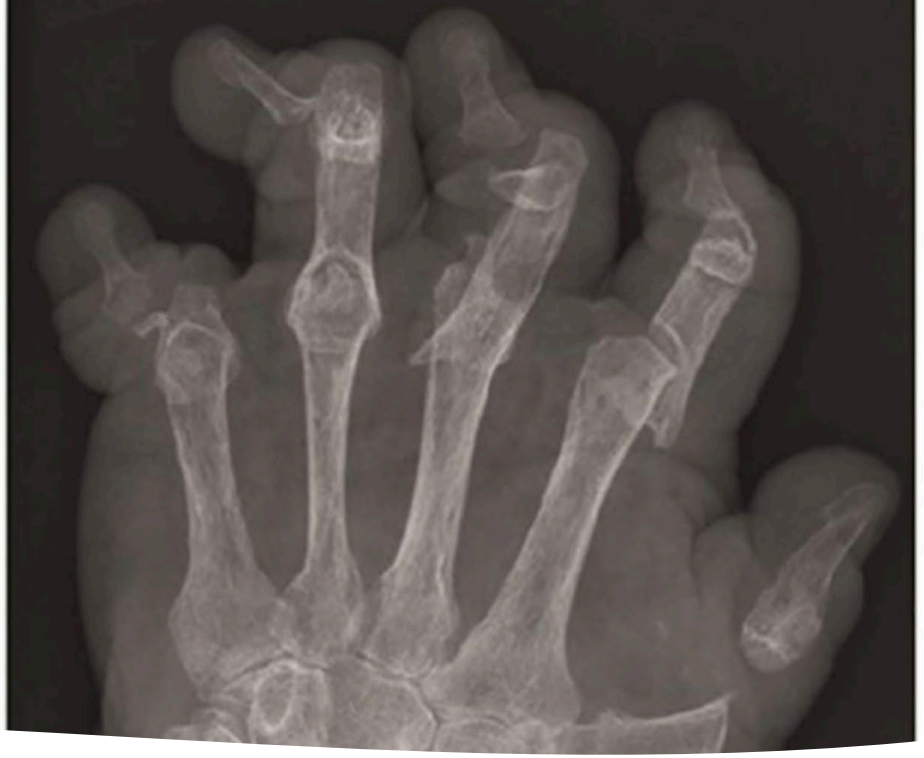




Intimate relationship between the nail apparatus, enthesis, and distal interphalangeal joint.

DIP predominant PSA





Arthritis Mutilans

- Arthritis mutilans: the most severe and least common form of psoriatic arthritis ,
- Characterized by digital shortening due to osteolysis and often associated with profound functional disability.
- AM typically presents in patients with distal interphalangeal joint involvement and is often linked to a history of dactylitis

Diagnostic Approach

- Is the joint pain inflammatory?
- Psoriasis, nail changes,
- Enthesitis, dactylitis
- CASPAR criteria ≥3 points

Entry criterion: Articular disease (joint, spine or entheseal)	
	Points
1. Evidence of psoriasis • Current psoriasis • Personal history of psoriasis • Family history of psoriasis	 2 or 1 or 1
2. Psoriatic nail dystrophy (pitting, onycholysis, hyperkeratosis)	1
3. Negative test result for rheumatoid factor	1
4. Dactylitis • Current dactylitis • History of dactylitis	 1 or 1
5. Radiologic evidence of juxta-articular new bone formation	1

Adapted from Taylor et al.[3]
CASPAR: Currently, the Classification Criteria for Psoriatic Arthritis; PsA: Psoriatic arthritis. To meet the CASPAR criteria for PsA, a patient must have inflammatory articular disease (joint, spine or entheseal) and score ≥3 points.

Investigations

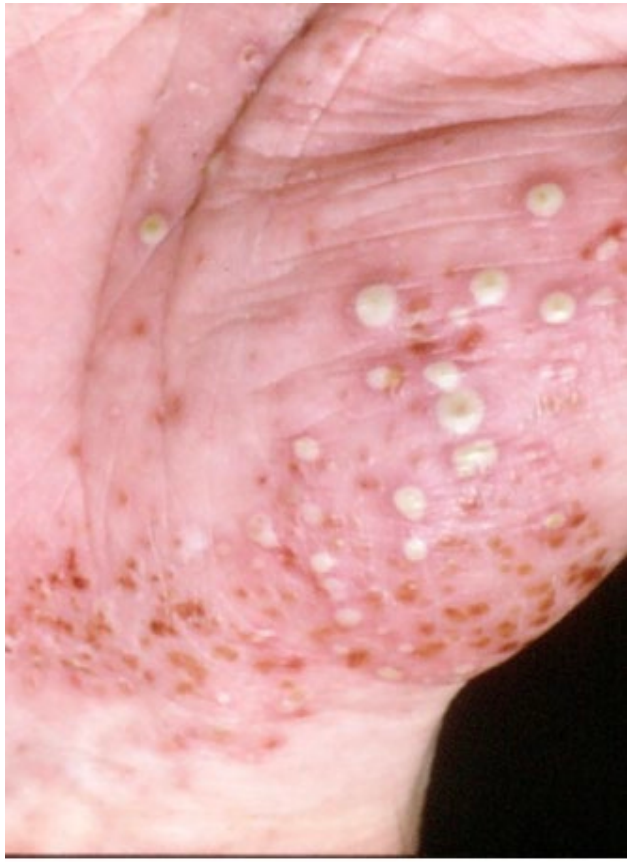
- RF/anti-CCP usually negative
- Imaging:
  - X-ray for erosions + new bone,
  - MRI/US for enthesitis/ tenosynovitis/synovitis
- CRP/ESR variable
- Screen for comorbidities
  - CV disease
  - Osteoporosis
  - Immunodeficiency
  - Chronic kidney/liver disease

Treatment Principles

- Treat-to-target: remission/low activity
- Screen for infection, comorbidities before DMARDs
- Choose the best treatment for the individual patient – precision medicine
- Skin v Joint trade off

csDMARDs (Synthetic)

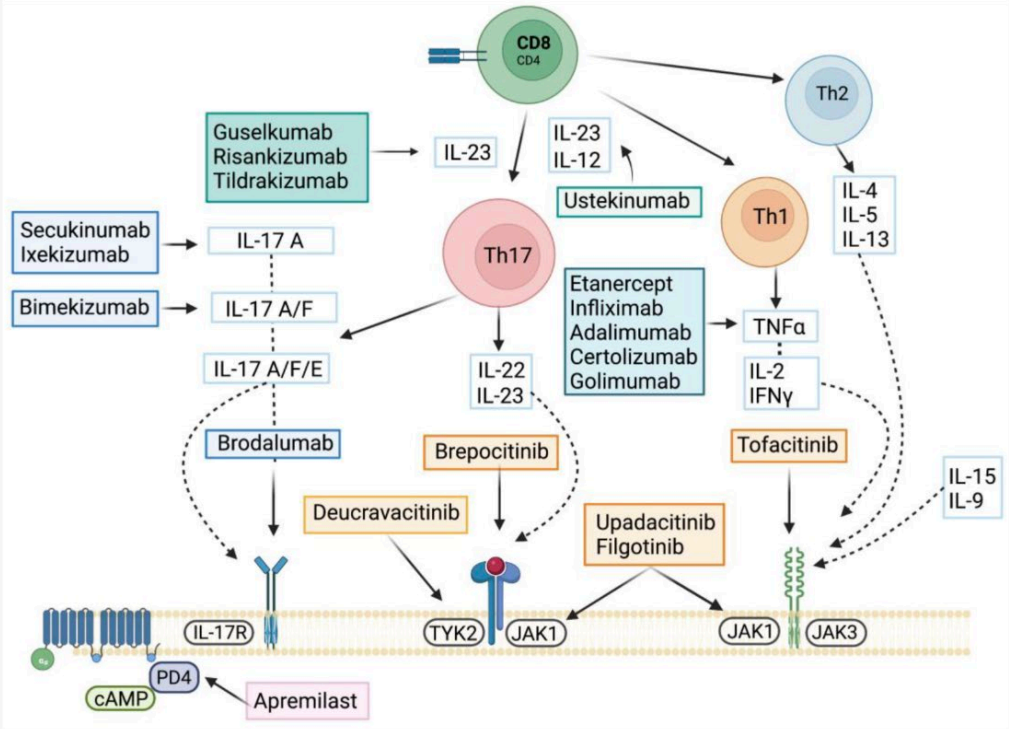
- Methotrexate, leflunomide, sulfasalazine
- Effective in peripheral arthritis and enthesitis
  - limited skin benefit
- No action on spine
  - Maybe SSZ
- Role of NSAIDs?



- The trouble with prednisolone.
  - Pustular psoriasis

Targeted therapies

Figure 2. Targeted therapies. Mechanism of action of the latest approved or in-development molecules for the treatment of PsA. Interleukin 17 (IL-17) and isoforms IL-17A/F/E and IL17 receptor (IL-17R); janus kinase 1, 2, 3 (JAK1, JAK2, JAK3) and tyrosine kinase 2 (TYK2).



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bDMARDs (Biologic)

- TNF inhibitors: joint and ? skin
  - Adalimumab
  - Infliximab
  - Certolizumab
  - Golimumab
  - Etanercept
- IL-17 inhibitors: joint + skin benefit
  - Secukinumab (IL 17 A)
  - Ixekizumab (IL 17 A)
  - Bimekizumab (IL17 A +F)
- IL-12/23, IL-23 inhibitors: strong skin efficacy
  - Ustekizumab (IL 12 +23)
  - Guselkumab (IL 12)
  - Risankizumab (IL 12)

tsDMARDs (Targeted Synthetic)

- JAK inhibitors: tofacitinib, upadacitinib
- Safety: infections, VTE risk, monitoring

Biologic DMARDS

- Advantages
  - Exceptional efficacy
- Disadvantages
  - Expensive
  - Onerous application process (rheumatologist only)
  - Increased risk of infection
  - Injection issues
    - Cold Chain /travel
    - Needle phobia

Things to remember about Biologics

Infection:

- cease until well +/- antibiotics completed

Shingles

- Eligible for free Shingrix
  - MTX, TNF JAK

Vaccines

- No live vaccines

Surgery

- Cease biologic 1 dosing interval prior and restart 2 weeks post op.

Non-Pharmacologic Management

- Exercise, physiotherapy, OT
- Weight reduction
- Smoking cessation
- Regular assessment of CV risk

Key Take-Home Messages

- PsA = systemic, heterogeneous
- Enthesitis as the primary lesion
- Subtypes: oligo, poly, DIP, axial, mutilans
- Early Dx + treat-to-target
- Every patient will have a different journey

Questions?