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RHEUMATOLOGY ADVANCED  
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**RHAPP NATIONAL CONFERENCE**

**SEPTEMBER 8-10, 2022**



# Introduction to Psoriatic Arthritis

## Scratching the Surface

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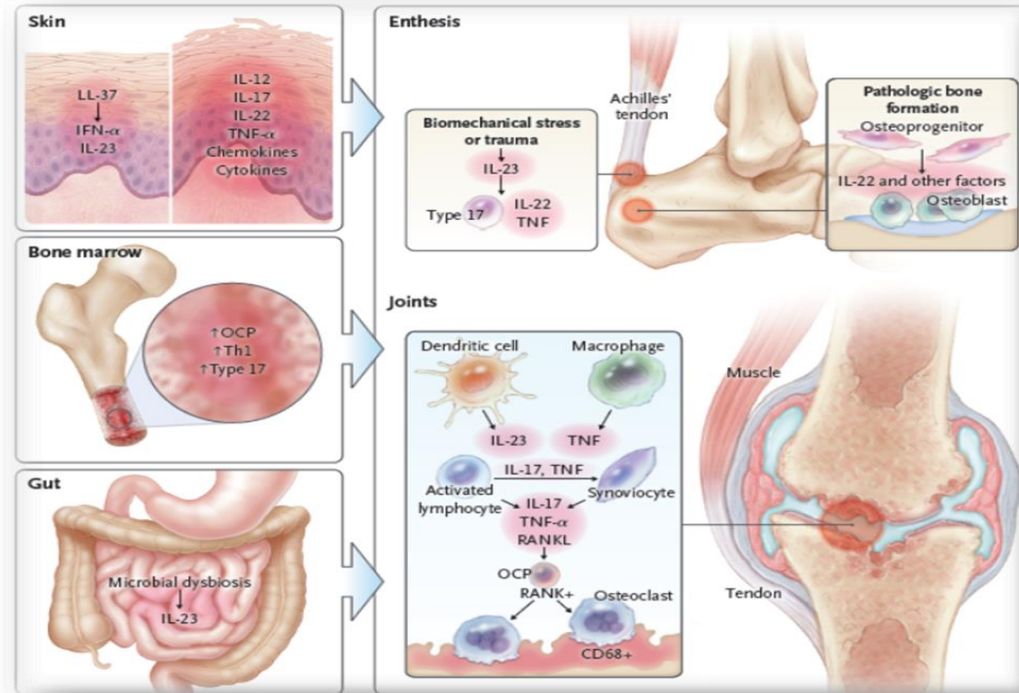
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Speaker: Lilly

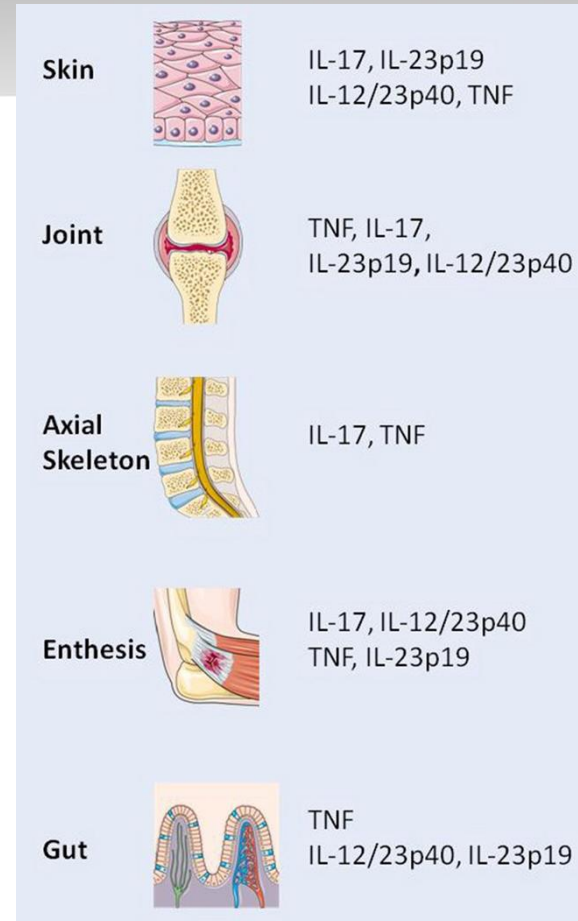
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# The organ, tissue and cellular and cytokine landscape in PsA



# Tissue Cytokine Hierarchy

- There is increasing evidence suggesting that different cytokines have distinct hierarchical roles in tissues across the spondyloarthritis spectrum
- Figure highlights pathways with demonstrable effects in each discrete tissues against those in which clinical responses were not observed
- Future analyses are required to ascribe formal within-tissue hierarchies

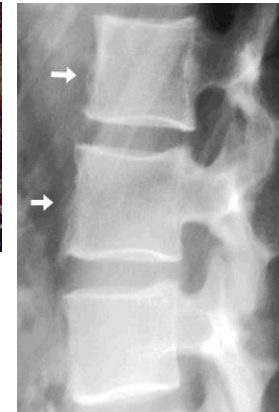
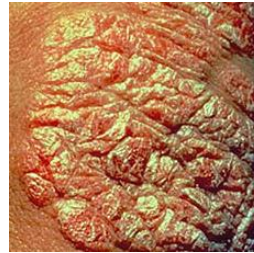
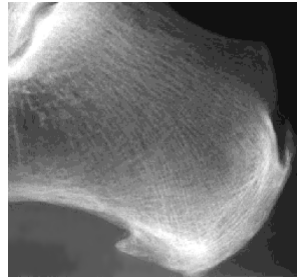




# Psoriatic Arthritis Clinical Features

# Psoriatic Disease

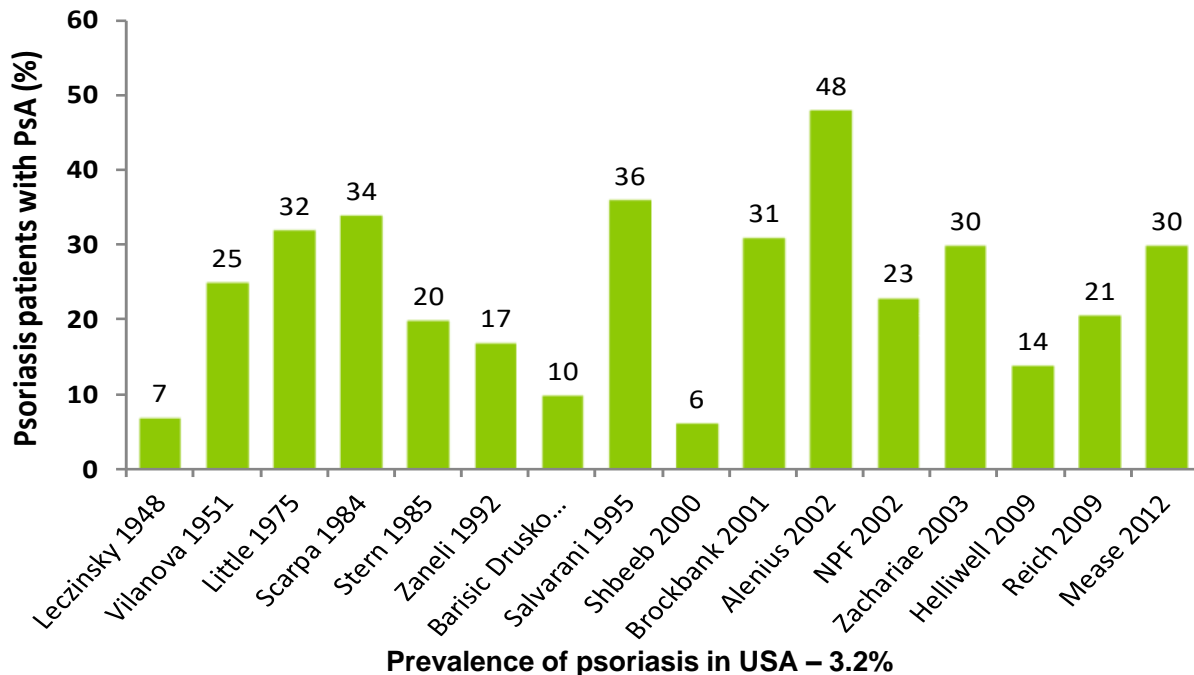
Complex, polygenic autoinflammatory disease with diverse clinical features



# Clues to Pathogenesis

- 40% have a positive family history
- In 60-70% of cases, psoriasis precedes joint disease
- Association with Class I MHC alleles – B13, B17, B27, B39 and Cw6 (HLA-B27 positive 15-50%, greater in PsA spondylitis (60%))
- Male/Female ratio approximately 1:1
- Age onset 30-50.
- Environmental triggers: trauma (Koebner phenomena), infection, stress, obesity

# Approximately 30% of PsO patients will develop PsA



Gladman DD. J Rheumatol 2009;36(Suppl. 83):4-8;

Mease PJ, et al. J Am Acad Dermatol 2013;69:729-735;

Reich K, et al. Br J Dermatol 2009;160:1040-1047

Rachakonda TD, et al. J Am Acad Dermatol. 2013;70:512-516.

# PsA has 5 Disease Domains

- Skin and nail: Apprx. 90% have skin involvement. 87% have nail changes. Only about 45% of patients w/psoriasis alone have nail changes.
- Articular Disease: Characteristic joint space narrowing and erosions.
- Dactylitis: present in 32-48% of individuals.
- Enthesitis: present in 25-53% of individuals.
- Spondylitis: Approximately 20-40% of patients w/peripheral joint disease have axial involvement.



# Skin and Nails

# Body Surface Area (BSA)

- Body surface area commonly used
- 1% BSA = 1 handprint
- PATIENT's hand! - Includes thumb
- Head and Neck = 10% (10 handprints)
  - Upper extremities = 20% (20 handprints)
  - Trunk (axillae and groin) = 30% (30 handprints)
  - Lower extremities (buttocks) = 40% (40 handprints)



# What is a **PASI** and why is it important?

- Psoriasis Area and Severity Index (PASI) is a mathematically derived score from 0-72 that includes plaque qualities (erythema, thickness, scaling score 0-4 over 4 different body areas), area of body (scored 0-6 based on percentage of coverage for each of 4 body areas).
- Although PASI did not start its “life” as a validated tool, it remains a widely used outcome measure in clinical trials.
- Comparisons across many clinical trials
- Can detect change

# Nails

- Features of the nail matrix
  - Pitting
  - Leukonychia
  - Red spots in lunula
  - Nail plate crumbling
- Features of the nail bed
  - Oil drop (salmon patch) discoloration
  - Onycholysis
  - Nail bed hyperkeratosis
  - Splinter hemorrhages

# Nail Matrix: Pitting



# Nail Matrix: Nail plate crumbling



# Nail bed: Onycholysis



## Nail Bed: Oil drop (salmon patch) discoloration



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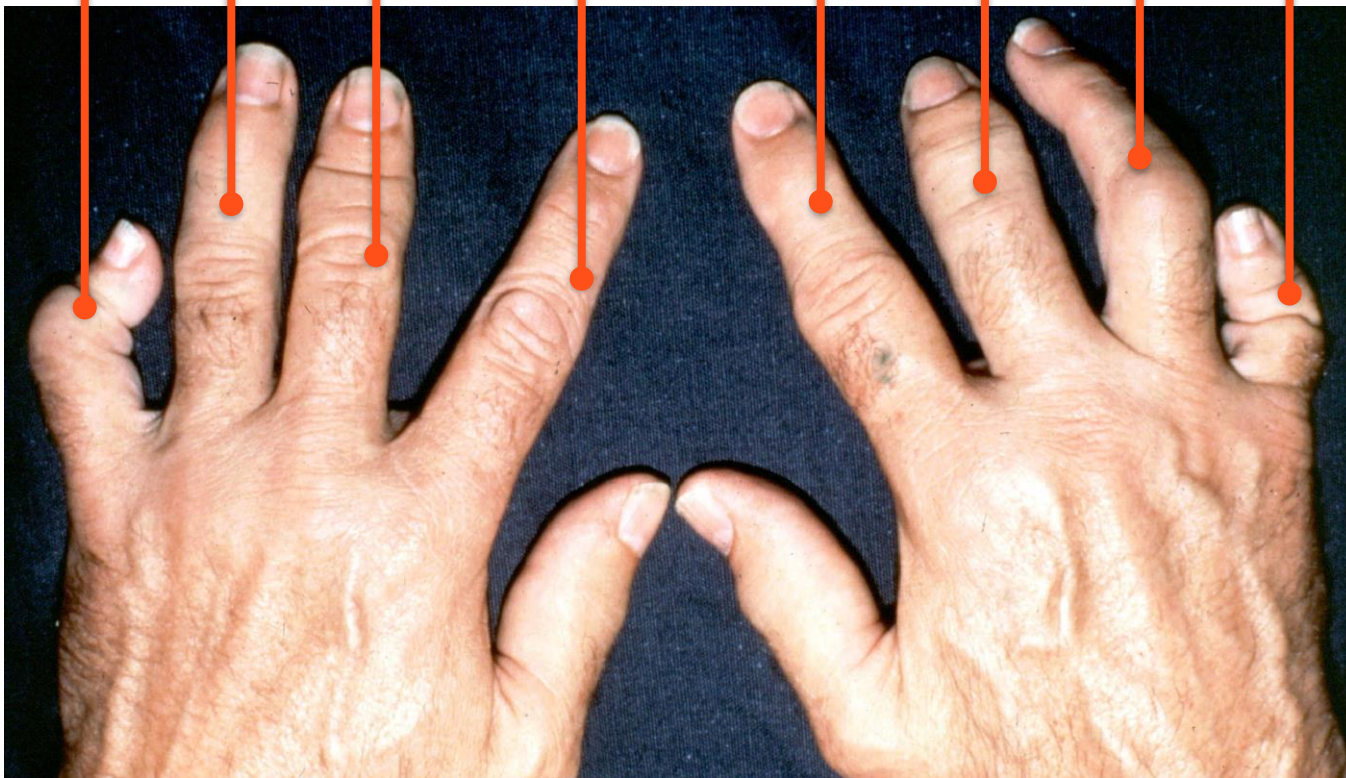
# Arthritis

# Arthritis

- Most frequently presents as polyarthritis but may be oligoarthritis.
- Asymmetric or symmetric.
- Distal arthritis, ie. DIP joints.
- Arthritis Mutilans (pencil and cup deformity)
- Radiographic changes can include erosions, new bone formation, periostitis, lysis of terminal phalanges, ankylosis. (many of these can occur in the same digit)

# Ray Diversity in PsA

Mutilans Dactylitis Mutilans Normal Synovitis Dactylitis Ankylosis Mutilans



# Assessing Structural Damage in PsA – Digit Diversity

Mutilans Dactylitis Mutilans

Normal

Synovitis

Dactylitis

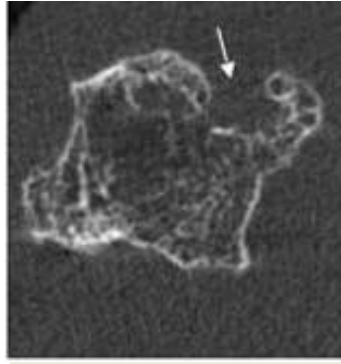
Ankylosis

Mutilans

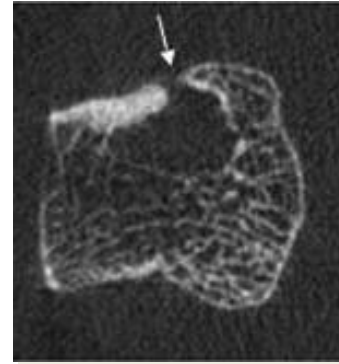


# Morphology of Erosions in RA and PsA

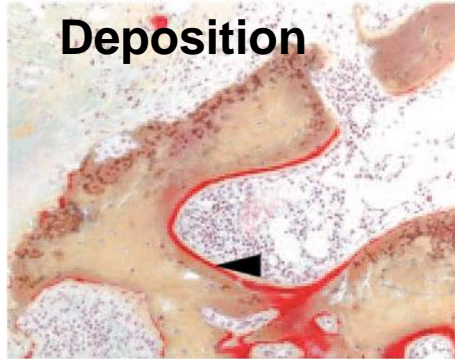
**RA**



**PsA**



**Osteoid  
Deposition**



Finzel S et al Ann Rheum dis.  
Jan 2011;70:122

Jimenez-Bos et al. JI, 2005;175

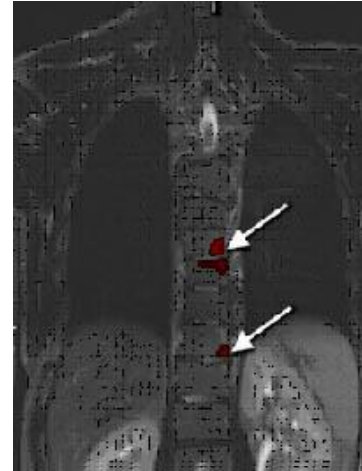
# Sites of Joint Inflammation



**RA-synovium**



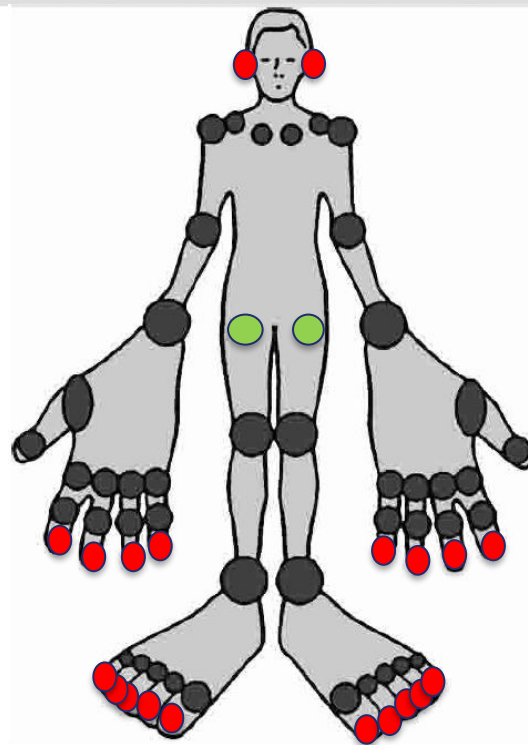
**PsA-bone,  
entheses and  
synovium**



**AS-bone,  
entheses**

# Joint Counts

- Joint Count
  - 46/44 in AS
  - 68/66 in PsA
  - 28 in RA





# Dactylitis

# Dactylitis in PsA

- Diffuse swelling of a digit, also referred to as “sausage digit”<sup>1</sup>
- One of the cardinal features of PsA, occurring in up to 40% of patients<sup>1,2</sup>
- Feet commonly affected<sup>1</sup>
- Associated with increased radiological damage<sup>1</sup>



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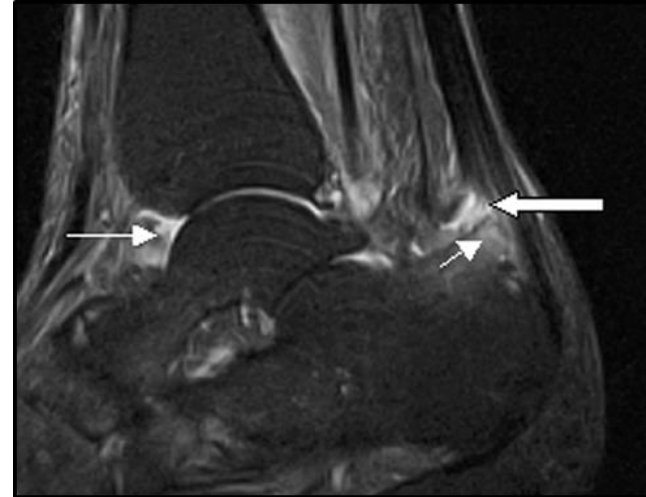
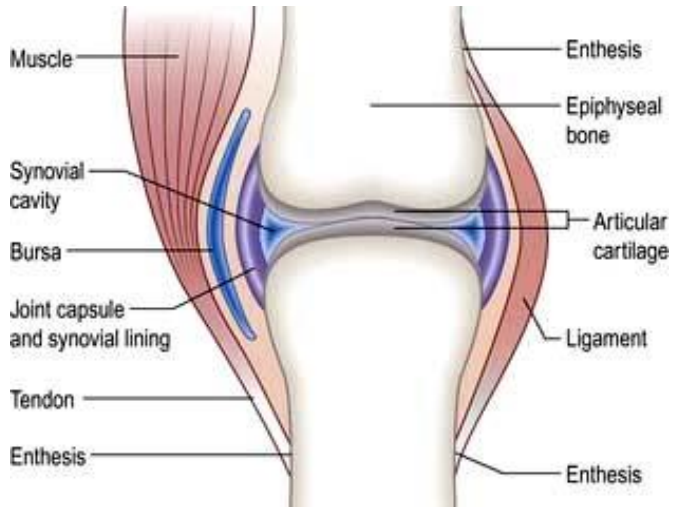
1. Brockbank J, et al. Ann Rheum Dis. 2005;64:188-90.  
2. Veale D, et al. Br J Rheumatol. 1994;33:133-8.



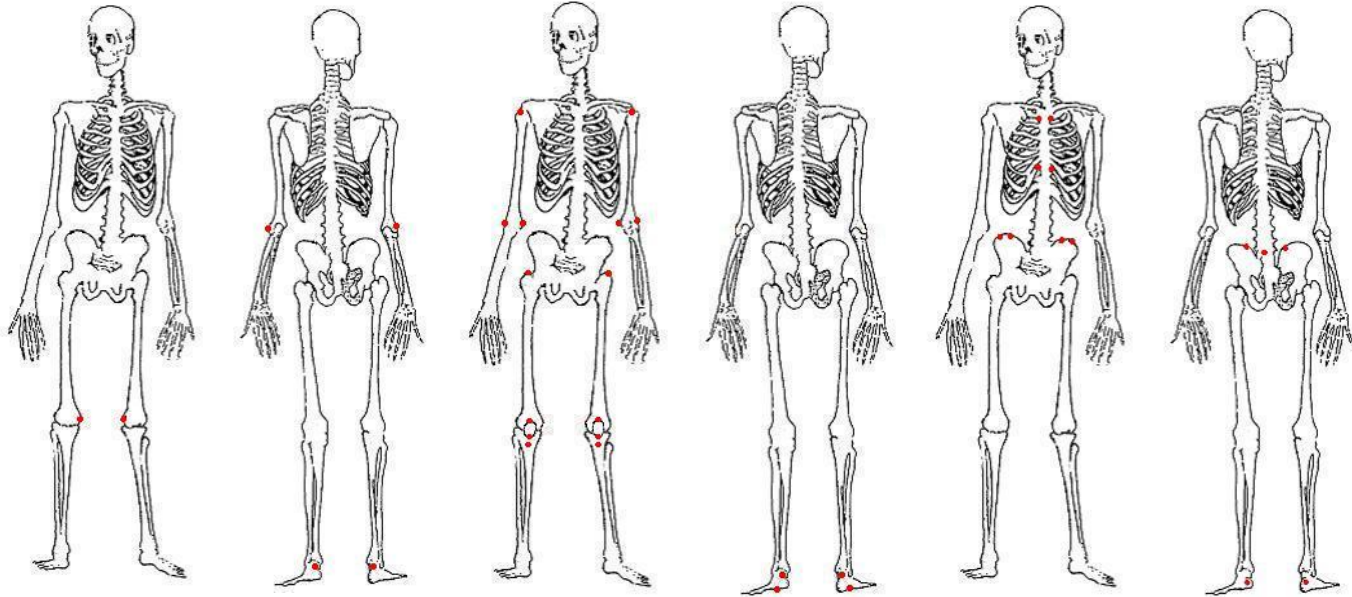
# Enthesitis

# Enthesitis

"**Enthesis**" from the Greek word, "ένθεσις" or "ένthesis," meaning insertion. The site of attachment of tendons, ligaments or joint capsule fibers to bone.



# Enthesitis Indices



**LEI**  
6 sites

**SPARCC**  
18 sites; score of 16

**MASES**  
13 sites

# Enthesitis- Onset and Prevalence

- In registry studies, up to 35% of PsA patients present with enthesitis
- Primary lesion that precedes the diverse skeletal manifestation of PsA in subjects with psoriasis
- Isolated peripheral enthesitis may be the only Rheumatologic sign of PsA in a subset of patients.
- Subclinical enthesitis is common in subjects with psoriasis and may predict development of PsA
- The enthesial architecture is abnormal in early SpA with increased vascularity and cellular infiltration
- In clinical trials, 56–79% of PsA subjects present with enthesitis at baseline

1. Simon et al., *Ann Rheum Dis* 2016;75:660-6, 2. Takata T, et al. *J Dermatol*. 2016;43:650–4; 3. Ozçakar L, et al. *Int J Dermatol*. 2005;44:930-2; 4. Tinazzi I et al. *J Rheumatol*. 2011;38:2691–2; 5. McGonagle D, et al. *Ann Rheum Dis*. 2002;61:534–7; 6. Benjamin M, et al. *Arthritis Rheum*. 2007;56:224–33; 7. Mease P, et al. *N Engl J Med*. 2015;373:1329-39; 8. McInnes IB, et al. *Lancet*. 2015;386:1137-46; 9. McInnes IB, et al. *Lancet*. 2013;382:780-9; 10. Kavanaugh A, et al. *Arthritis Rheum*. 2009;60:976-86; 11. Mease P, et al. *Ann Rheum Dis*. 2014;73:48-55; 12. Kavanaugh A, et al. *Ann Rheum Dis*. 2014;73:1020-6; 13. Polachek A, et al. *Arthritis Care Res (Hoboken)*. 2016 Dec 20

## Enthesitis and Dactylitis as Markers of Greater Disease Activity and Negative Patient Impact

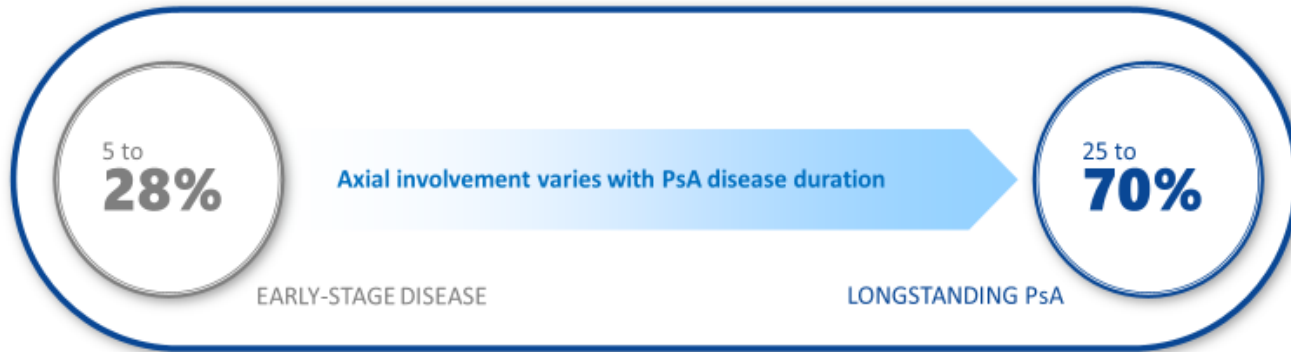
In Corrona PsA-SpA registry (N=1567)

- Enthesitis and/or dactylitis (N=648)
- Presence of dactylitis and enthesitis correlated with
  - Worse measures of disease activity (eg.CDAI, CRP)
  - Worse function (HAQ)
  - Worse pain, fatigue, work productivity
  - Less likely to achieve Minimal Disease Activity state



# Spondylitis

# Prevalence of Axial Disease in PsA



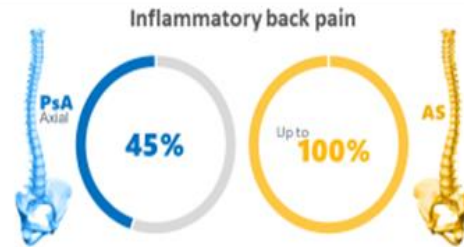
An estimated **15%** of patients with PsA who didn't have axial involvement at presentation could have developed axial PsA over 10 years of follow-up

# Spondylitis: PsA vs. AS

## PsA Axial Disease vs AS: Differing Clinical Presentations

**Inflammatory back pain** is reported by patients with PsA and by patients with AS, and includes<sup>1</sup>:

- Pain in the hips or buttocks that improves with activity and worsens with rest
- Pain that occurs at night
- Pain that is responsive to NSAIDs
- Axial morning stiffness that lasts for more than 30 minutes



**Compared to AS<sup>1-2</sup>:**

- Can be asymptomatic
- Asymmetrical sacroiliitis
- Worse degree of peripheral arthritis
- Spondylitis (w/ or w/o sacroiliitis)



**Compared to PsA axial disease<sup>1-2</sup>:**

- Male
- Younger
- More limitation of spinal mobility
- More back pain

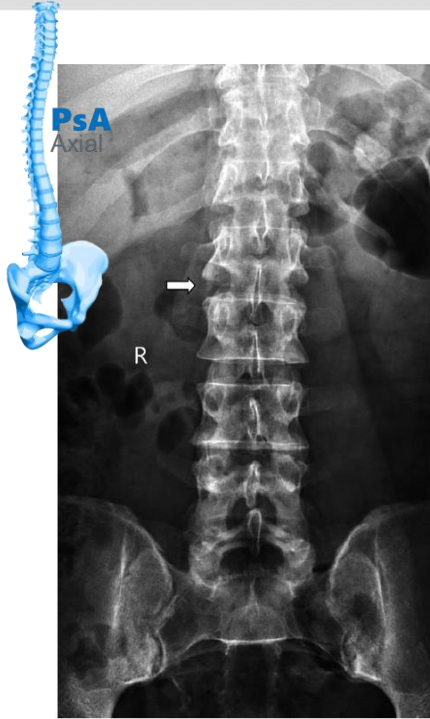
Similar levels of self-perceived health status, which reflects pain, disease activity and quality of life, were reported for both diseases.

AS=ankylosing spondylitis; NSAIDs=nonsteroidal anti-inflammatory drugs; PsA=psoriatic arthritis.

1. Feld J, et al. *Nat Rev Rheumatol*. 2018;14:363–371.

2. Helliwell PS. *Rheumatol* 2019; doi.org/10.1093/rheumatology/kez629.

# PsA Axial Disease vs AS—Differing Radiographic Presentations



Spinal disease in PsA is more frequently (compared to AS)<sup>1</sup>:

- Unilateral
- Syndesmophytes show a larger volume
- Do not follow exactly the course of the anterior longitudinal ligament
- Do not appear in consecutive vertebrae

Symmetrical erosion and ankylosis of the sacroiliac joints; “Bamboo spine”<sup>1,2</sup>



Baraliakos X, et al. *Clin Exp Rheumatol*. 2015; 33 (Suppl. 93): S31-S35.

Baraliakos X, et al. *Clin Exp Rheumatol*. 2015; 33 (Suppl. 93): S31-S35.

AS=ankylosing spondylitis; PsA=psoriatic arthritis.

1. Baraliakos X, et al. *Clin Exp Rheumatol*. 2015;33(Suppl.93):S31-S35.
2. Ostergaard M, Lambert RG. *Ther Adv Musculoskelet Dis*. 2012;4(4):301-311.

# Classification criteria for PsA (CASPAR)

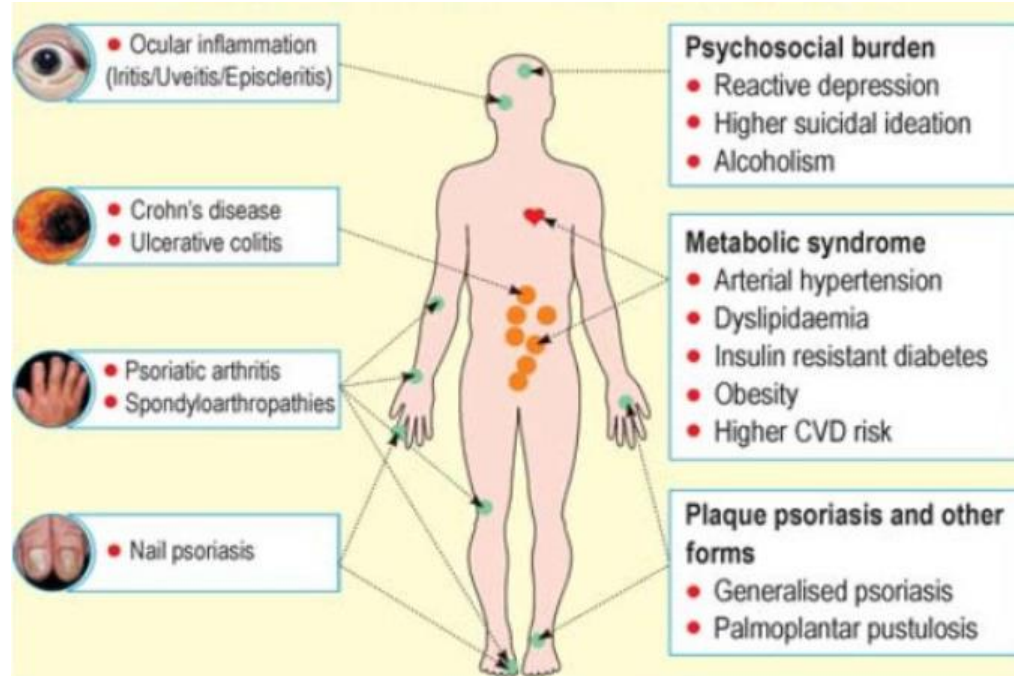
Established inflammatory musculoskeletal disease (joint, spine, or enthesal)		
With 3 or more of the following		
1. Psoriasis	(a) Current*	Psoriatic skin or scalp disease present today as judged by a qualified health professional
	(b) History	A history of psoriasis that may be obtained from patient, or qualified health professional
	(c) Family history	A history of psoriasis in a first or second degree relative according to patient report
2. Nail changes		Typical psoriatic nail dystrophy including onycholysis, pitting and hyperkeratosis observed on current physical examination
3. A negative test for RF		By any method except latex but preferably by ELISA or nephelometry, according to the local laboratory reference range
4. Dactylitis	(a) Current	Swelling of an entire digit
	(b) History	A history of dactylitis recorded by a qualified health professional
5. Radiological evidence of juxta-articular new bone formation		Ill-defined ossification near joint margins (but excluding osteophyte formation) on plain x-rays of hand or foot

\*Current psoriasis awarded 2 points  
Criteria specificity 98.7%, sensitivity 91.4%.



# Comorbidities

# Comorbidities to consider in PSA





# Treatment Recommendations

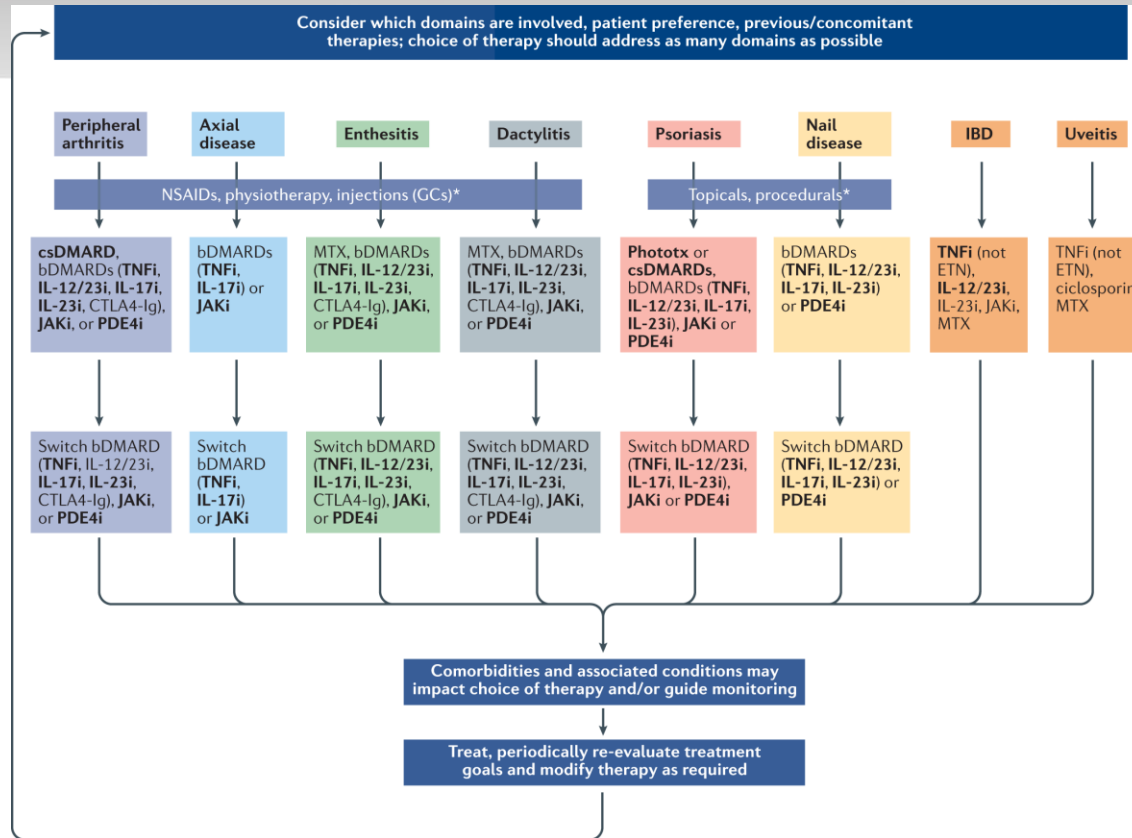
# How do you approach Treatment of PsA

- Consideration of prominent domains.
- Think about Comorbidities.
- Disease activity/severity.
- Safety.
- Patient preference?
- Unfortunately.....Insurance preference.

# PsA Therapeutic Groups

- Conventional synthetic DMARDs (cs-DMARDs)
  - Methotrexate, Sulfasalazine, Leflunomide
- TNF inhibitors (TNFi)
  - Etanercept (Enbrel), infliximab (Remicade), adalimumab (Humira), golimumab (Simponi), certolizumab (Cimzia)
- IL17i
  - Secukinumab (Cosentyx), ixekizumab (Taltz), [Bimekizumab](#)
- IL12/23i
  - Ustekinumab (Stelara)
- IL23i
  - Guselkumab (Tremfya), Risankizumab (Skyrizi), [Tildrakizumab \(Ilumya\)](#)
- T cell modulator
  - Abatacept (Orencia)
- Targeted synthetic DMARDs (ts-DMARDs)
  - PDE4i (Apremilast (Otezla))
  - JAKi (tofacitinib (Xeljanz), [Baricitinib \(Olumiant\)](#) , Upadacitinib (Rinvoq), [filgotinib](#))
  - [Tyk2i \(Deucravacitinib\)](#)

## Fig. 2: GRAPPA 2021 treatment schema.



# GRAPPA 2021 Tx Recommendations: Comorbidities

Comorbidity	NSAIDs	GCs	MTX and/or LEF	TNF inhibitor	IL-17 inhibitor	IL-12/23 inhibitor, IL-23 inhibitor	JAK inhibitor	PDE4 inhibitor
Elevated risk of CVD	Caution	–	–	–	–	–	Caution	–
Congestive heart failure <sup>a</sup>	–	Caution	–	Avoid	–	–	–	–
Elevated risk for VTE	–	–	–	–	–	–	Caution	–
Obesity	–	–	Caution	–	–	–	–	–
Fatty liver disease	–	–	Avoid	–	–	–	–	–
Active hepatitis B or C	–	–	Avoid	Caution	Caution	Caution	Caution	Caution
HIV	–	–	–	Caution	Caution	Caution	Caution	Caution
Tuberculosis	–	–	–	Caution	Caution	Caution	Caution	Caution
History of recent malignancy	–	–	–	Caution	Caution	Caution	Caution	Caution
MS and/or demyelinating disease	–	–	–	Avoid	–	–	–	–
Depression and/or anxiety	–	–	–	–	–	–	–	Caution

# In Summary

- In summary PsA often has a pleomorphic presentation and can be associated with a wide spectrum of comorbidities.
- Domains as well as comorbidities are important in selecting treatment.

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