

The Enthesopathies: Ankylosing Spondylitis, Psoriatic Arthritis, Reactive Arthritis, and Arthritis of IBD

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A 23-year-old male with a 2-year history of left buttock pain and 1 hr. AM stiffness. No trauma or injury. Worked as a house framer- off work for 6 months because of “back strain”. Has had episodes of right Achille’s tendinitis and has developed a rash on the soles of his feet.

Rx- some benefit from NSAIDs.

HLA B27-positive and CRP-normal.

- The pelvic radiograph is unremarkable.
- T1W MRI scan- erosion of the left sacrum and ilium (arrows).
- STIR MRI scan-BME in the left sacrum (arrow).



THE SPONDYLOARTHROPATHIES:

- Ankylosing Spondylitis
- Non-radiographic Axial spondyloarthropathies
- Psoriatic Arthritis
- Inflammatory Bowel Disease Associated (Enteropathic)- Crohn's and ulcerative colitis
- Reactive Arthritis

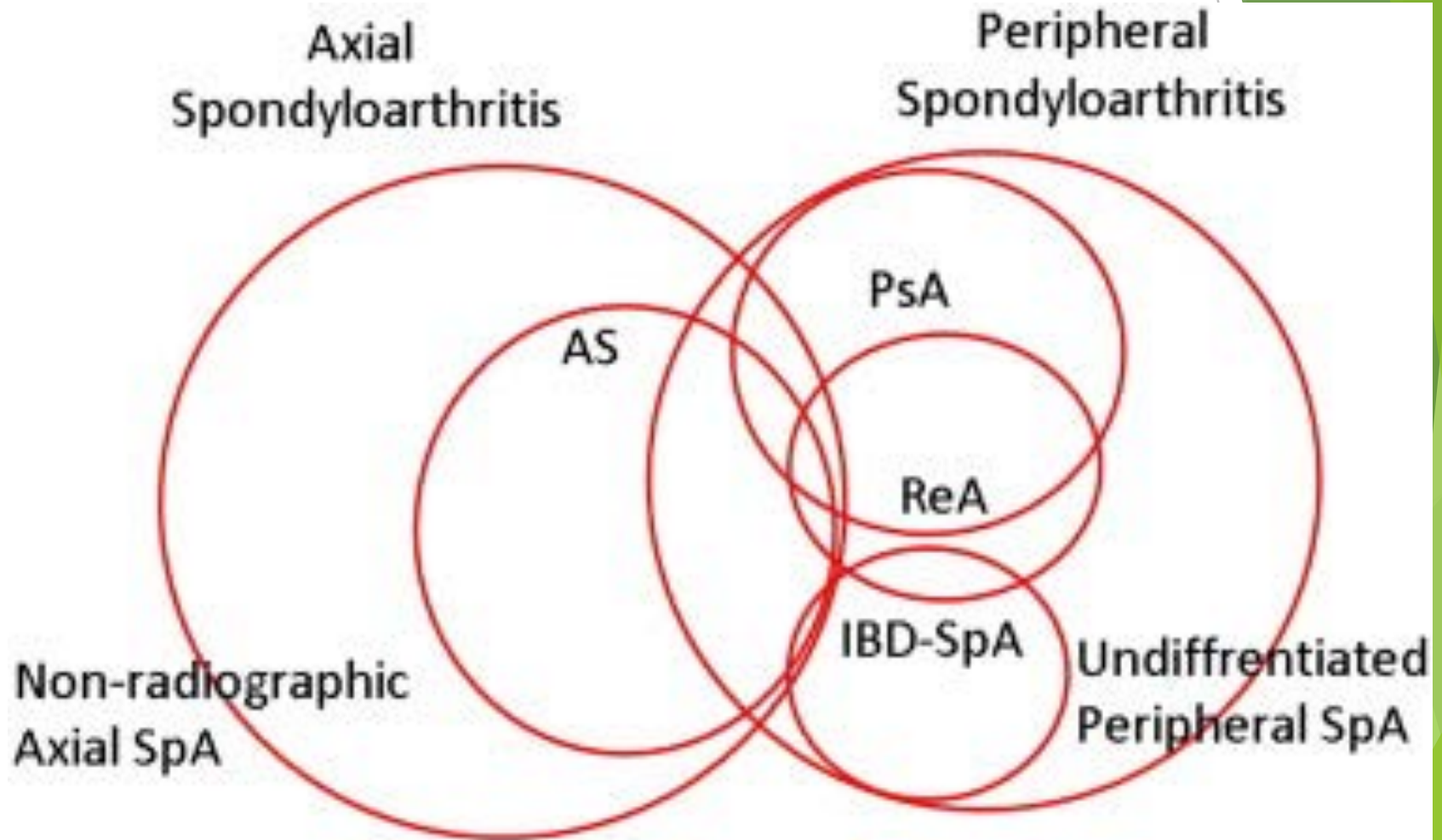
A Disease of Antiquity: Ankylosing Spondylitis

- ▶ Amenhotep II (1439-1413 BC)¹
- ▶ Rameses the Great (1298-1232 BC)¹
- ▶ Marie Strumpell spondylitis
- ▶ Rheumatoid “variants”
- ▶ Ankylosing spondylitis, HLA B27(1973)
- ▶ Spondyloarthropathies-“enthesopathies”



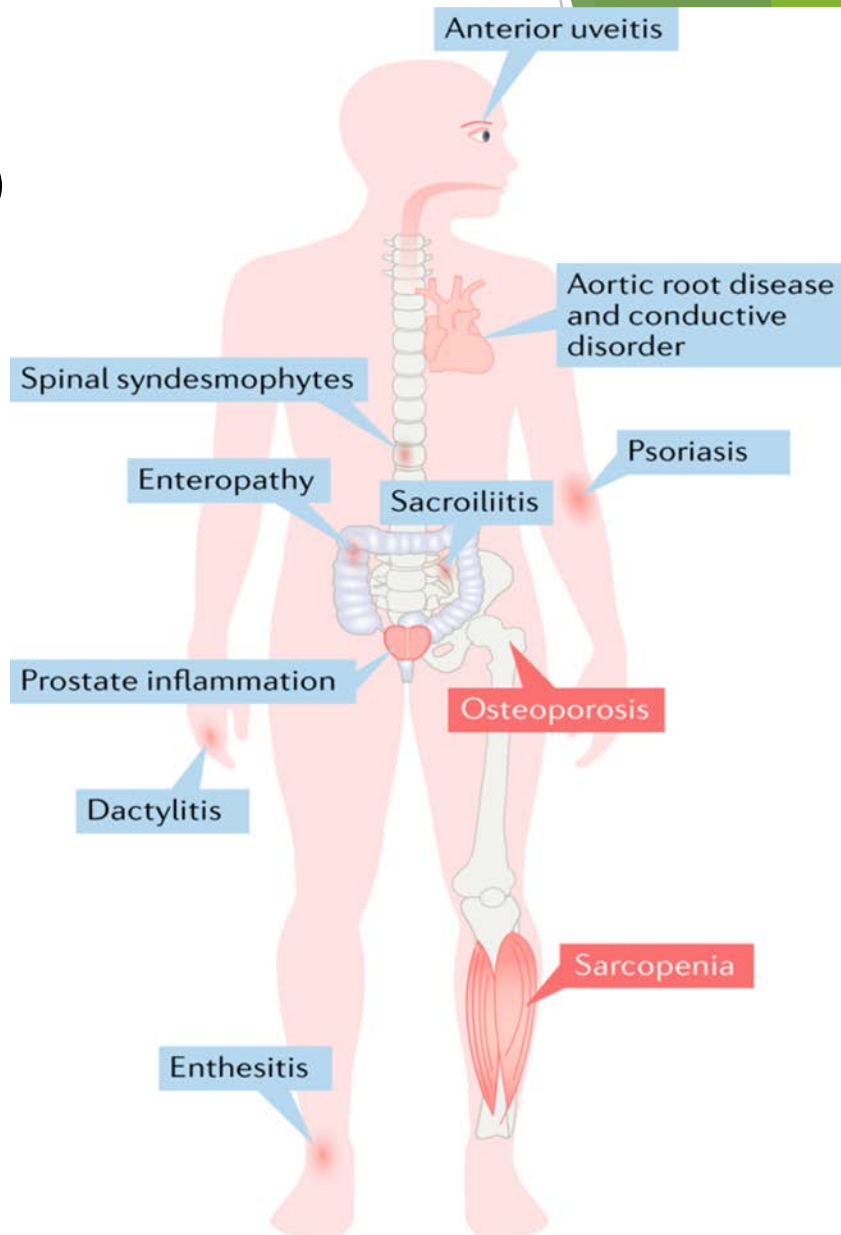
¹Rheumatol Int. 2003; 23:1-5.

THE SPONDYLOARTHRITIS:



SHARED CLINICAL FEATURES:

- Axial joint disease (esp. SI joints)
- Asym. oligoarthritis (2-4 jts.)
- Dactylitis (sausage digits)
- Enthesitis
- Syndesmophytes
- Associations with infections
- Eye inflammation
- Bowel inflammation
- Mucocutaneous features
- HLA-B27+ and FHx
- Responsible Interleukins: IL-12, IL17, IL-22, and IL23.



SHARED CLINICAL FEATURES:

- Inflammatory Back Pain:

Chronic back pain better **with exercise** but not with rest and pain at night, **AM stiffness**

Insidious onset with more than 3 months in duration

Usual onset **<45** years of age

Male prominence

Marked **improvement w/ NSAIDs**

- Peripheral Arthritis:

Acute in onset

Lower extremities esp. knees and ankles

Asymmetrical, Oligoarticular

ASAS Classification Criteria for Axial Spondyloarthritis (SpA)

In patients with ≥ 3 months back pain and age of onset < 45 years

Sacroiliitis on imaging
AND
 ≥ 1 SpA feature

OR

HLA-B27 positive
AND
 ≥ 2 other SpA features

SpA features

- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's / colitis
- good response to NSAIDs
- family history of SpA
- HLA-B27
- elevated CRP

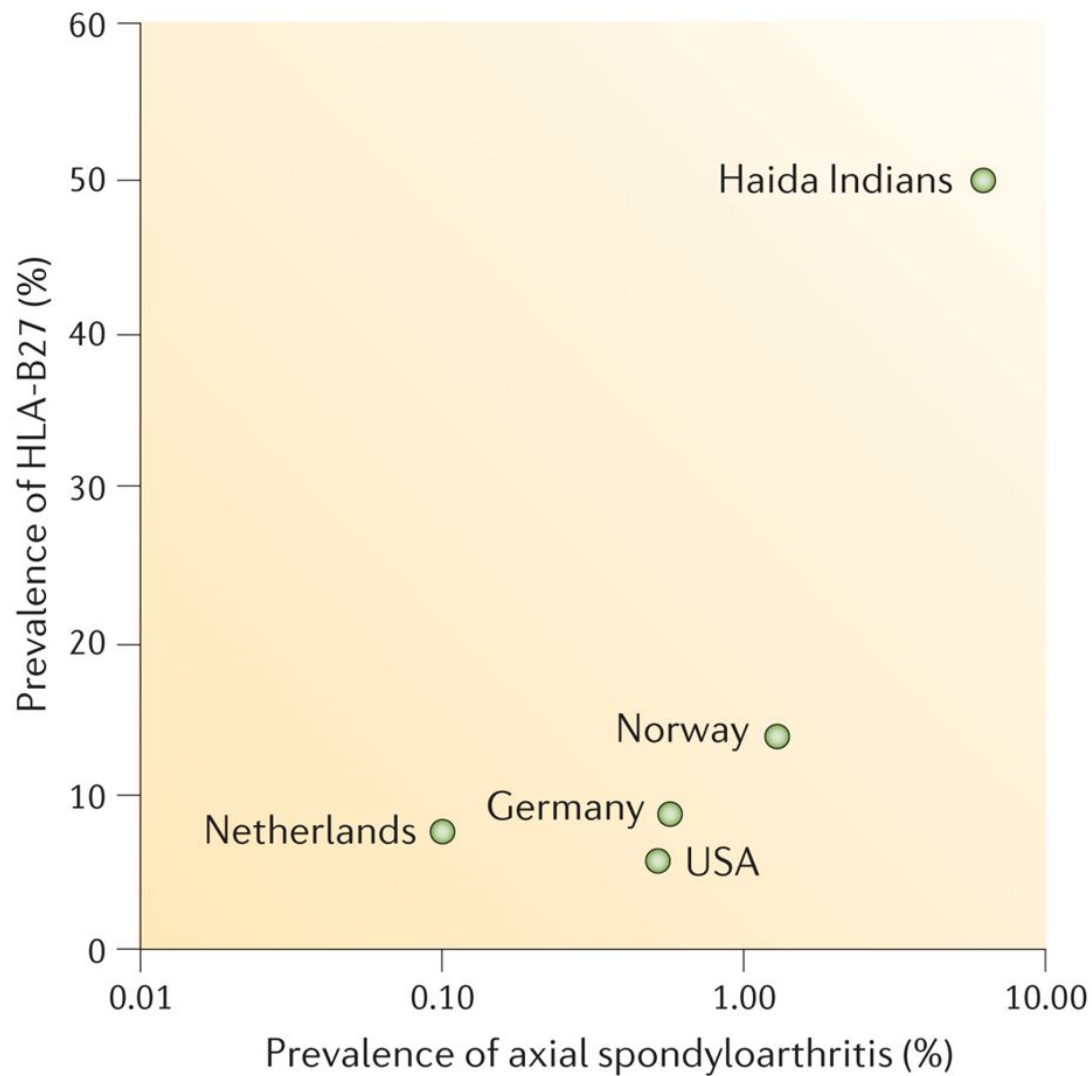
Sacroiliitis on imaging

- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- definite radiographic sacroiliitis according to modified New York criteria

Sensitivity 82.9% Specificity 84.4%

Epidemiology of AS

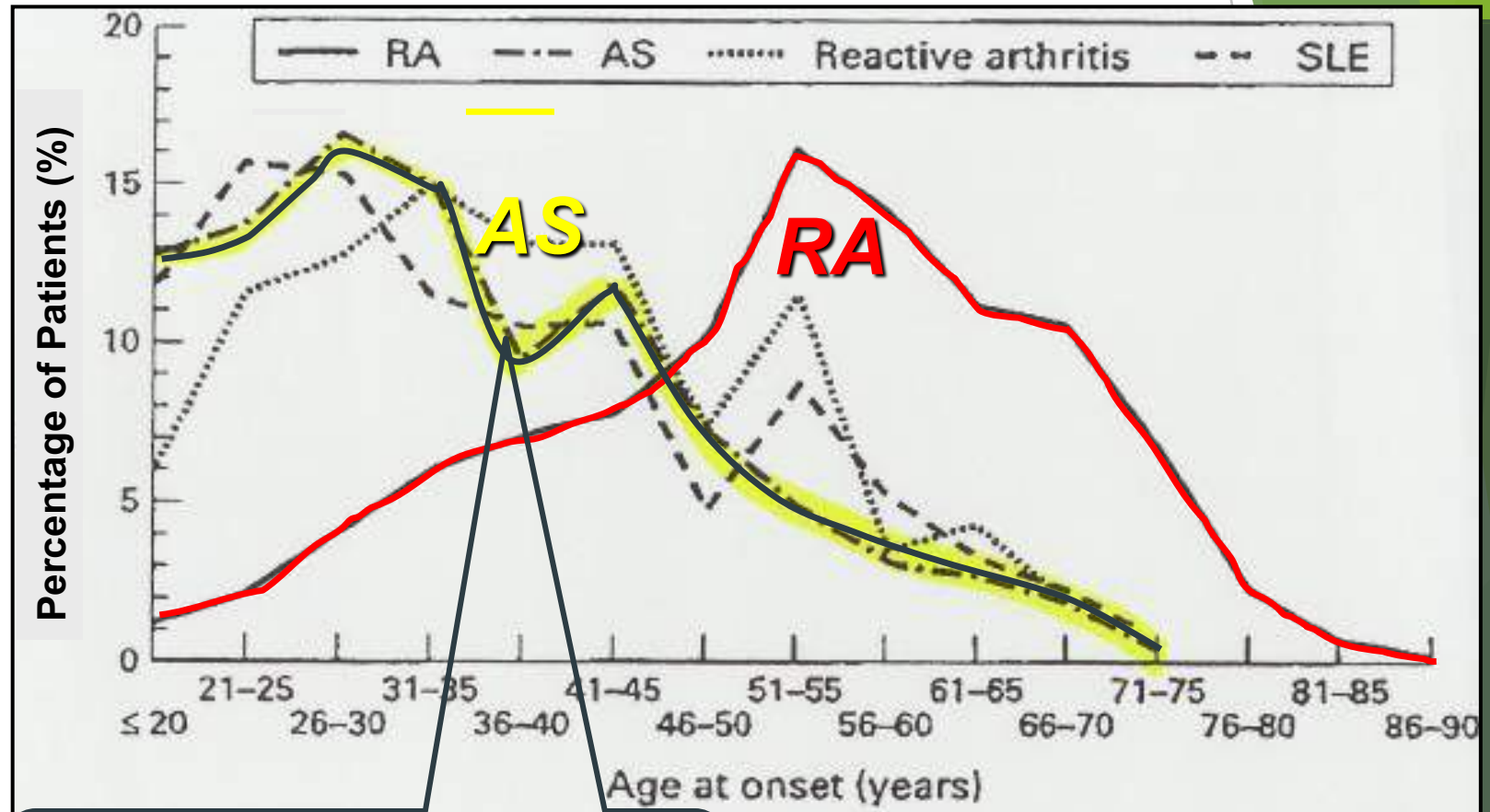
- ▶ 2.4 million adults in the US have SpA (RA-1.3 million)
- ▶ The incidence of AS may be underestimated due to unreported cases
- ▶ HLA-B27 gene is associated with AS
- ▶ Age of onset typically between 15 and 35 years
- ▶ 2-3 times more frequent clinically in men than in women



Nature Reviews | **Disease Primers**

The prevalence of axial spondyloarthritis in different populations depends, in part, on the prevalence of HLA-B27.

Age at Onset Distribution of AS and Rheumatoid Arthritis (RA)

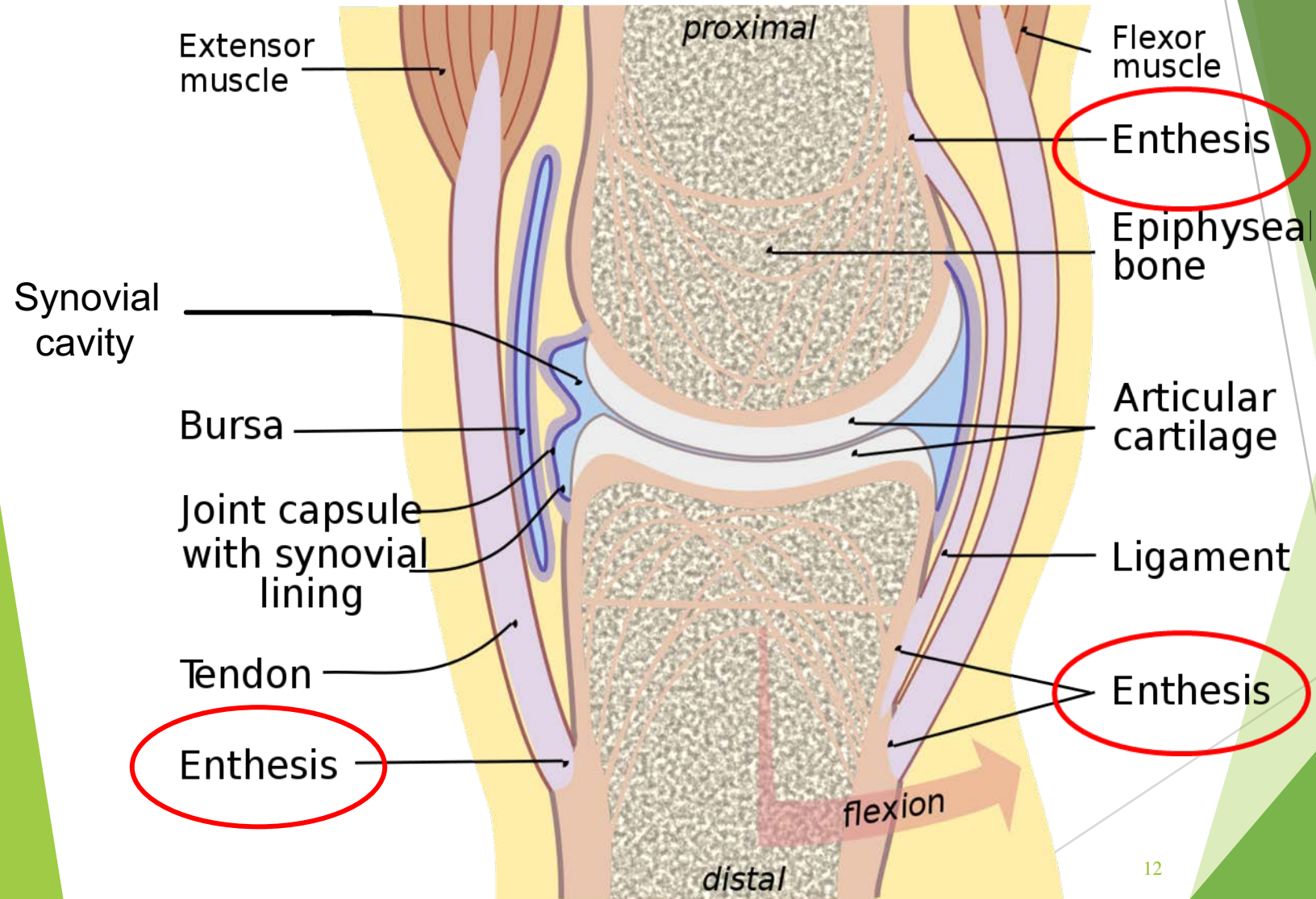


**Economically active individuals
with a major impact on their ability
to work¹**

¹Barkham N et al. Rheumatology 2005;44:1277-1281

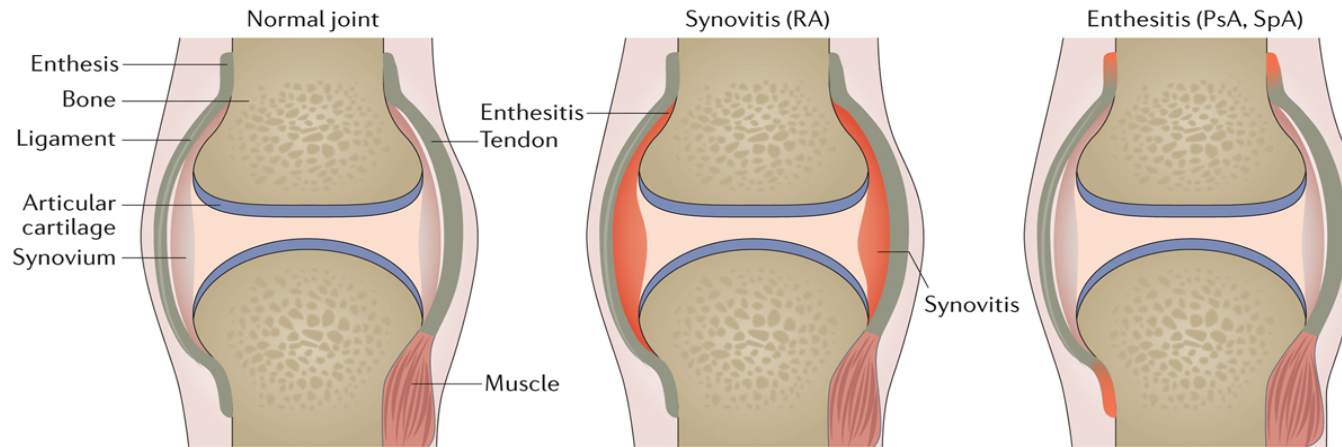
²Zink A et al. Ann Rheum Dis 2001;60:199-206

Diarthrodial joint

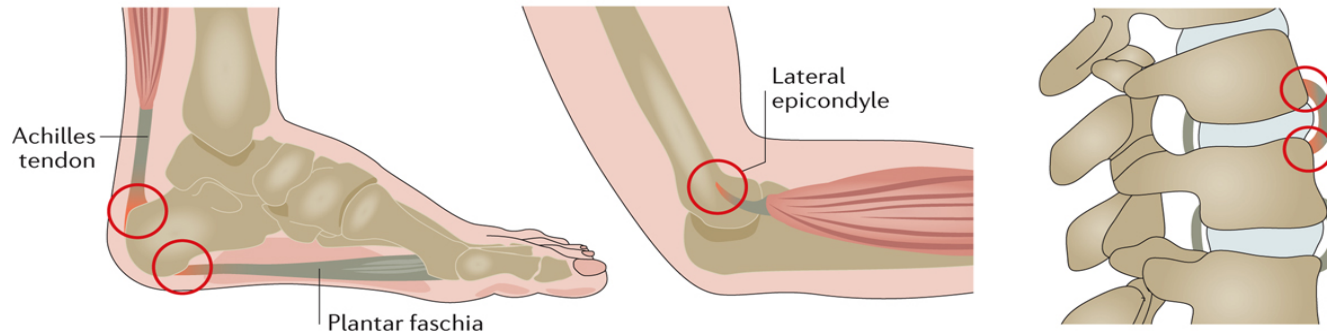


Enthesitis versus synovitis

a Synovial and enthesal structures in the joints



b Enteses distant from joints

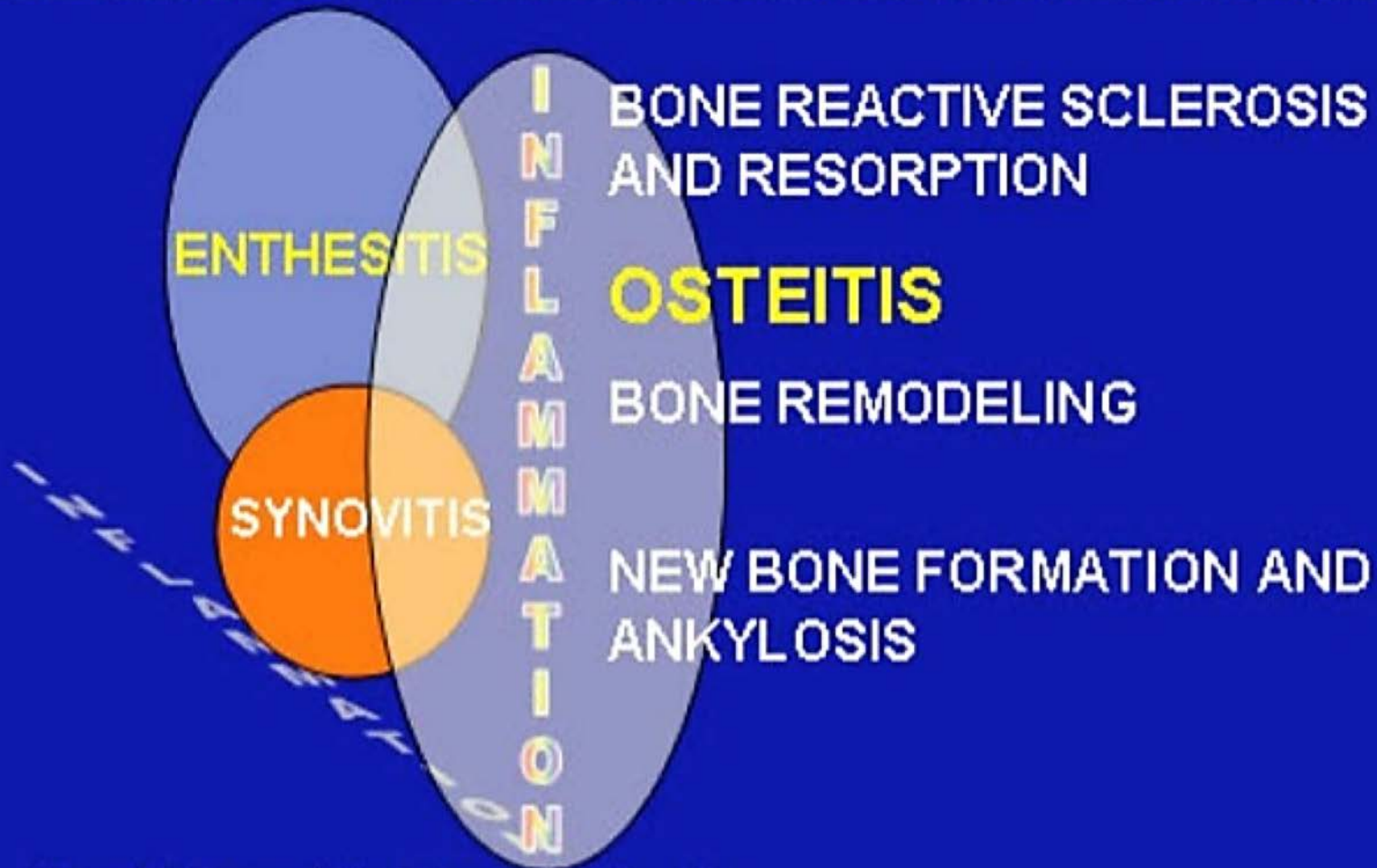


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Diarthrodial joint showing the joint capsule with the synovial membrane and tendons inserting into periosteal bone. **Synovitis** is characterized by inflammation of the synovial membrane. **Enthesitis** is defined as inflammation of the **entheses**, the insertion sites of tendons and ligaments to the bone surface. Enthesitis can occur with secondary synovitis.

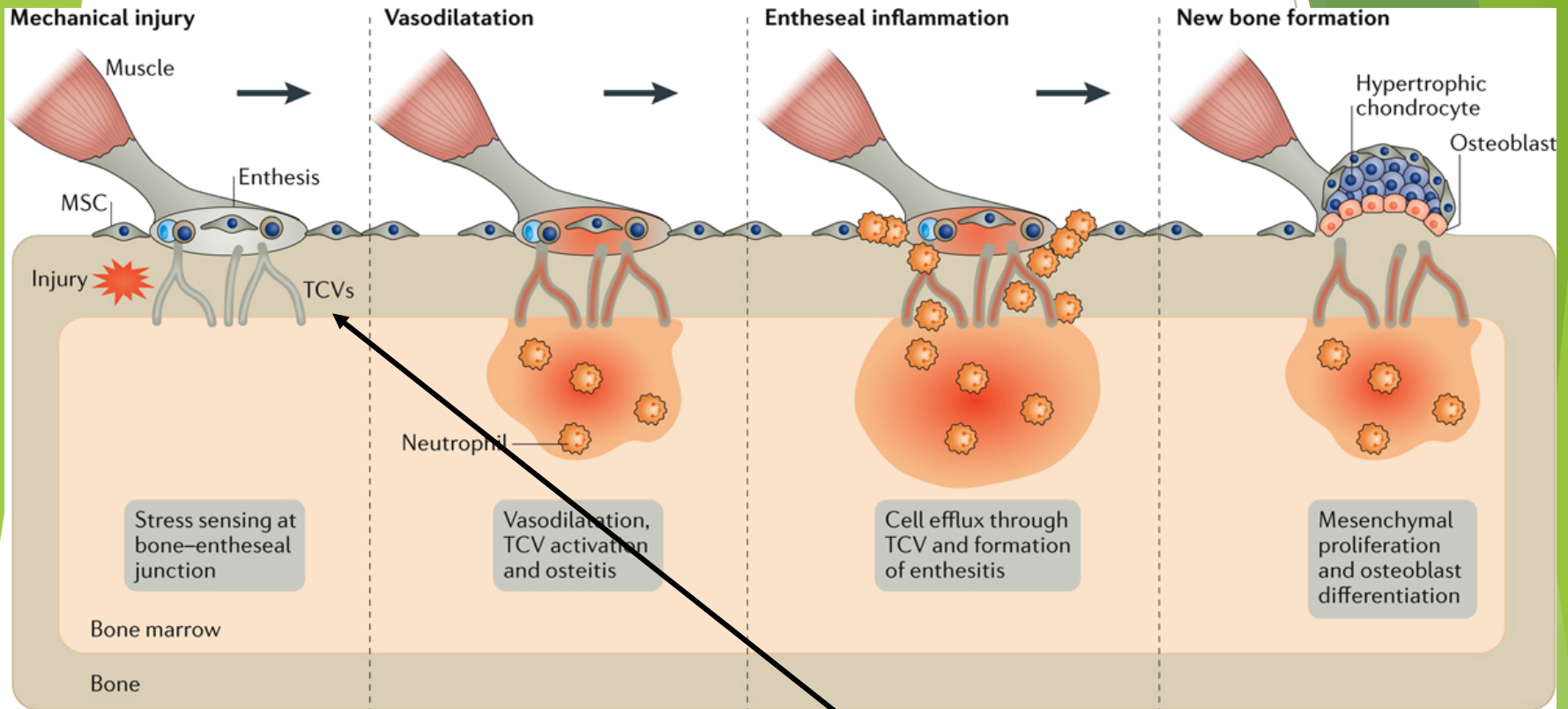
Pathology of AS / SpA

Enthesitis, Arthritis, Tenosynovitis, Periostitis, Dactylitis, Spondylitis, Ankylosis



AS = ankylosing spondylitis; SpA = spondyloarthritis.

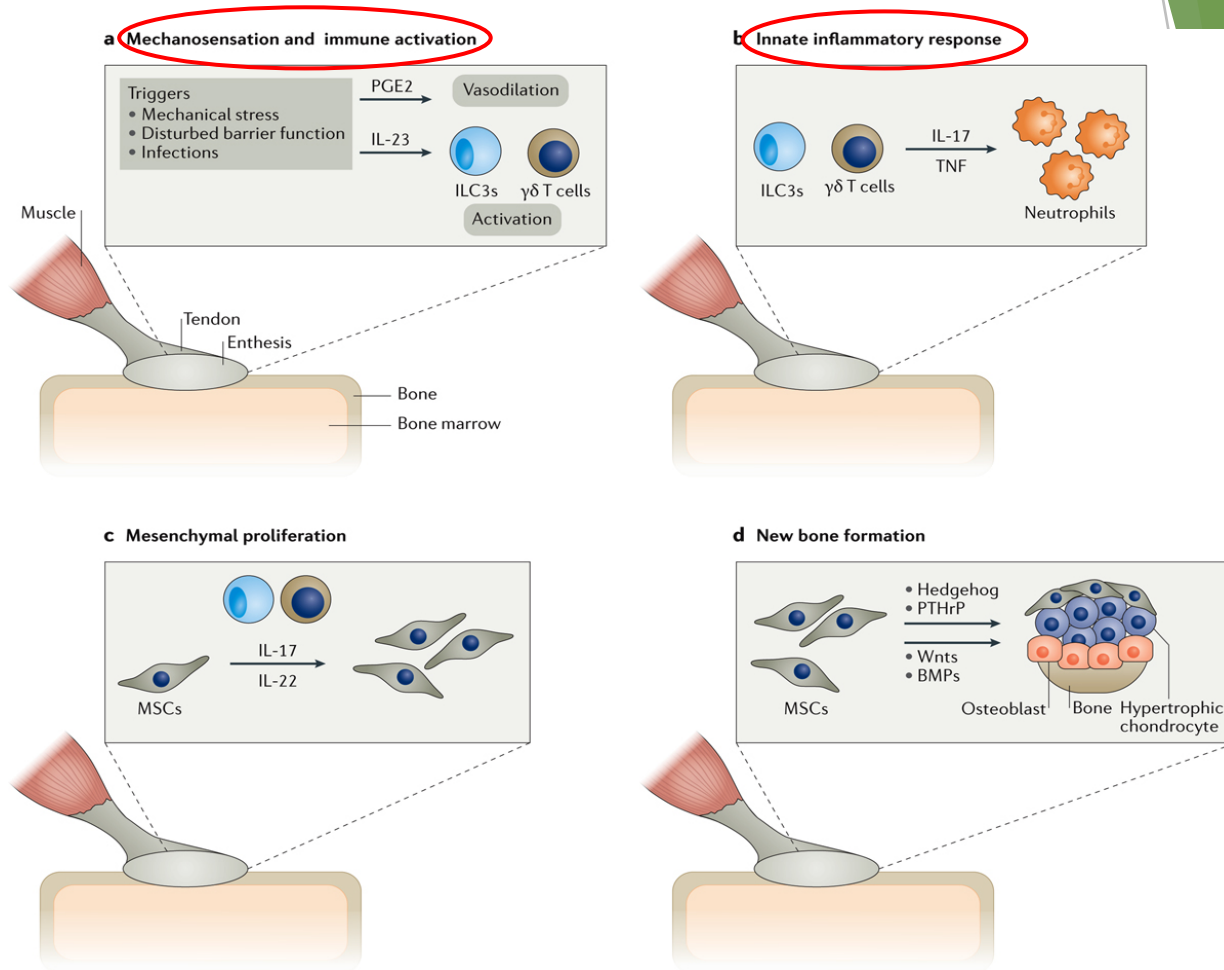
Microanatomical changes in enthesitis



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Following **mechanical stress** at the enthesion, transcortical microvessels are activated and an **inflammatory reaction**, (osteitis) forms in the adjacent bone marrow. TCV widening via vasodilatation facilitates the efflux of immune cells (such as neutrophils) from the perientheseal bone marrow **into the enthesion**.

Functional model of enthesitis

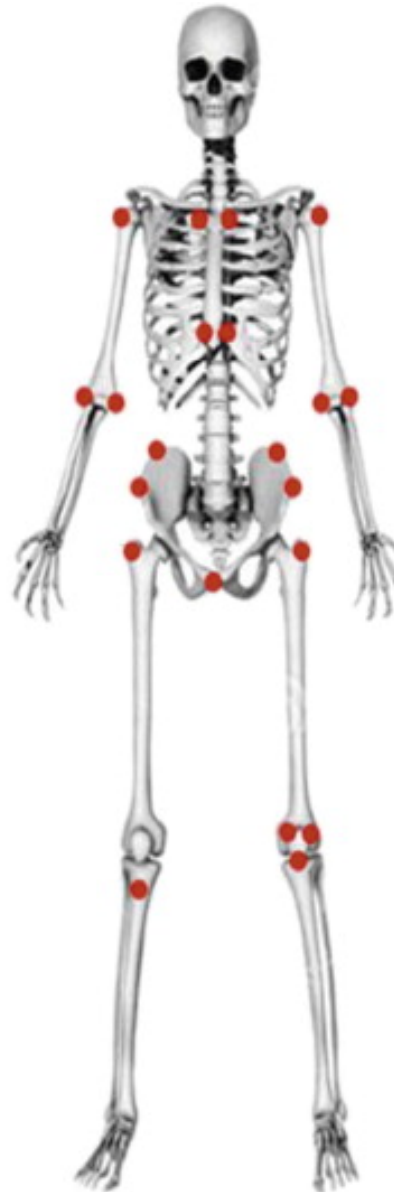


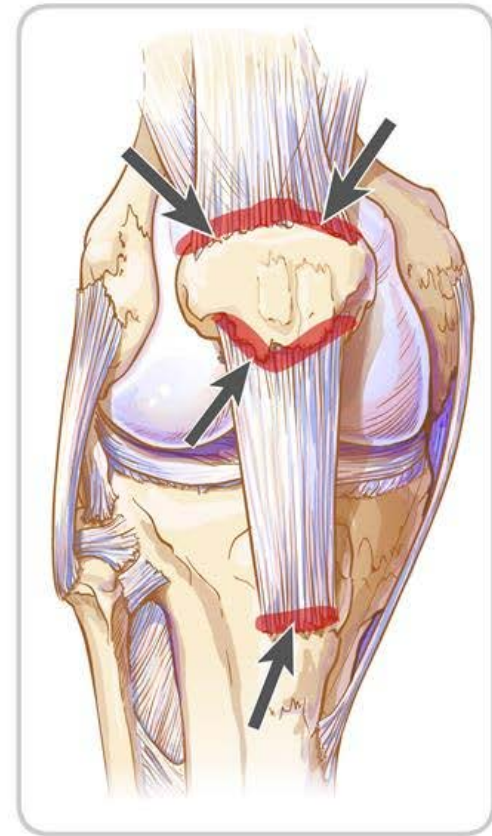
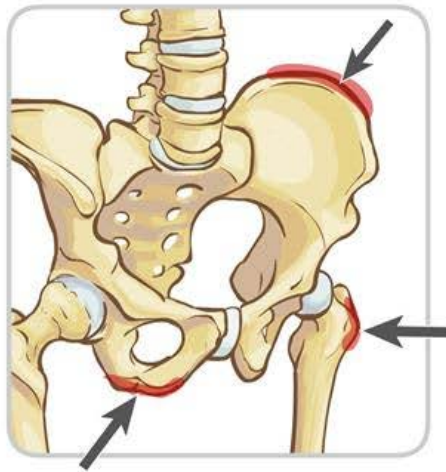
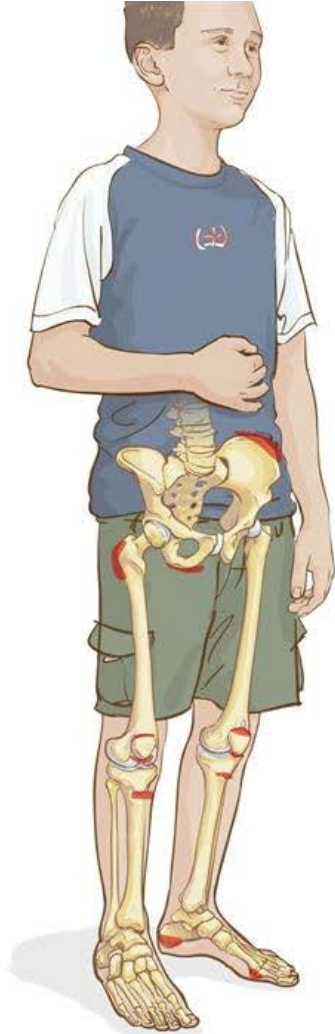
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Enthesitis is initiated during a **mechanosensation** and by **innate immune activation** involving **mechanical** and/or **infectious** stress that leads to the activation of prostaglandin E2 (PGE2) and IL-23, followed by release of TNF and IL-17, leading to the influx of immune cells such as polymorphonuclear neutrophils.

Local and systemic enthesopathies

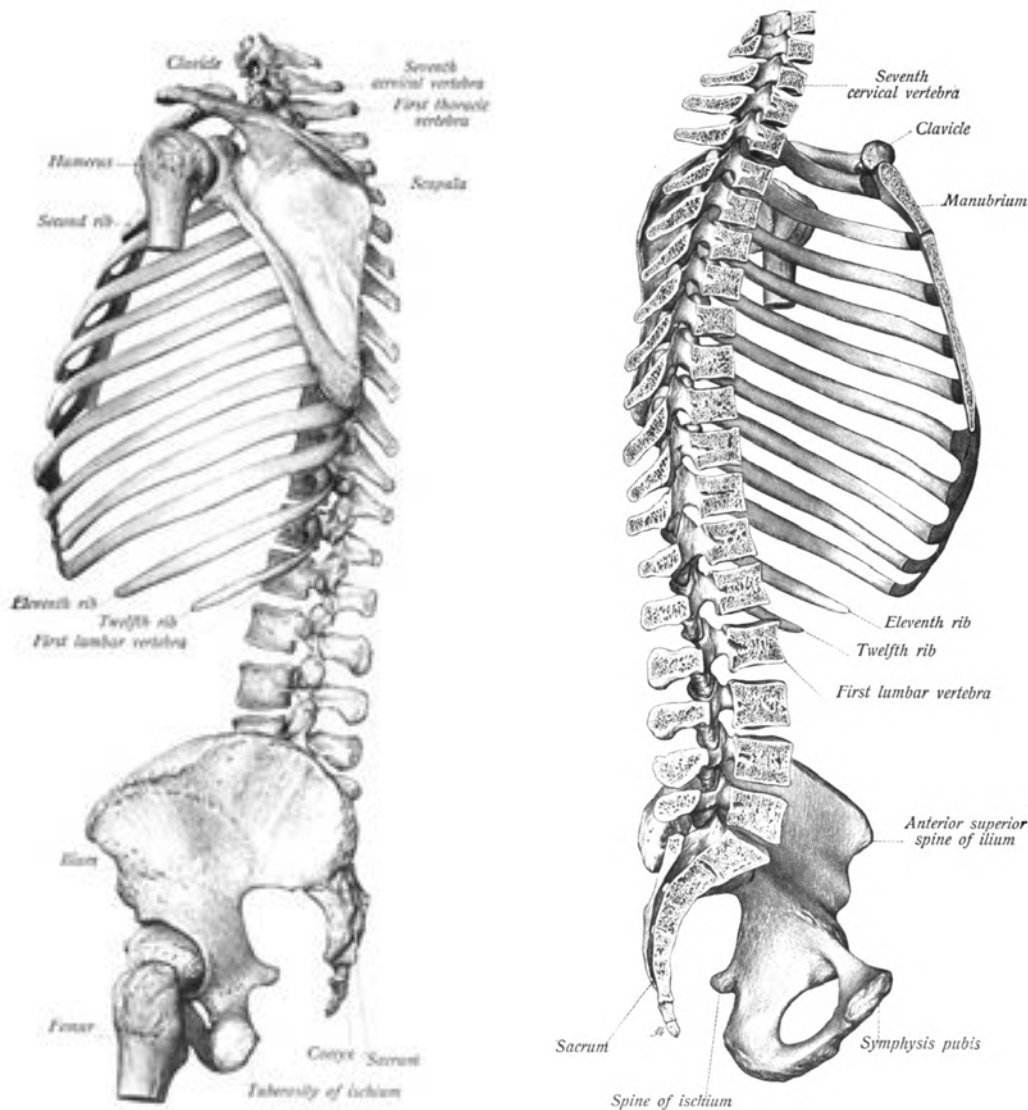
Anatomic region	Enthesitis exam
Foot and ankle	Achilles tendon insertion to calcaneus Plantar fascia insertion to calcaneus Plantar fascia insertion to metatarsal heads Plantar fascia insertion to base of fifth metatarsal
Knee	Quadriceps tendon insertion to patella (2 and 10 o'clock) Infrapatellar ligament insertion to patella (6 o'clock) and tibial tuberosity
Pelvis	Hip extensor insertion at greater trochanter of femur Sartorius insertion at anterior superior iliac spine Posterior superior iliac spine Abdominal muscle insertions to iliac crest Gracilis and adduction insertion to pubis symphysis Hamstrings insertion to ischial tuberosity
Spine	5th lumbar spinous process
Upper extremity	Common flexor insertion at medial epicondyle of humerus Common extensor insertion at lateral epicondyle of humerus Supraspinatus insertion into greater tuberosity of humerus
Chest	Costosternal junctions (1st and 7th)





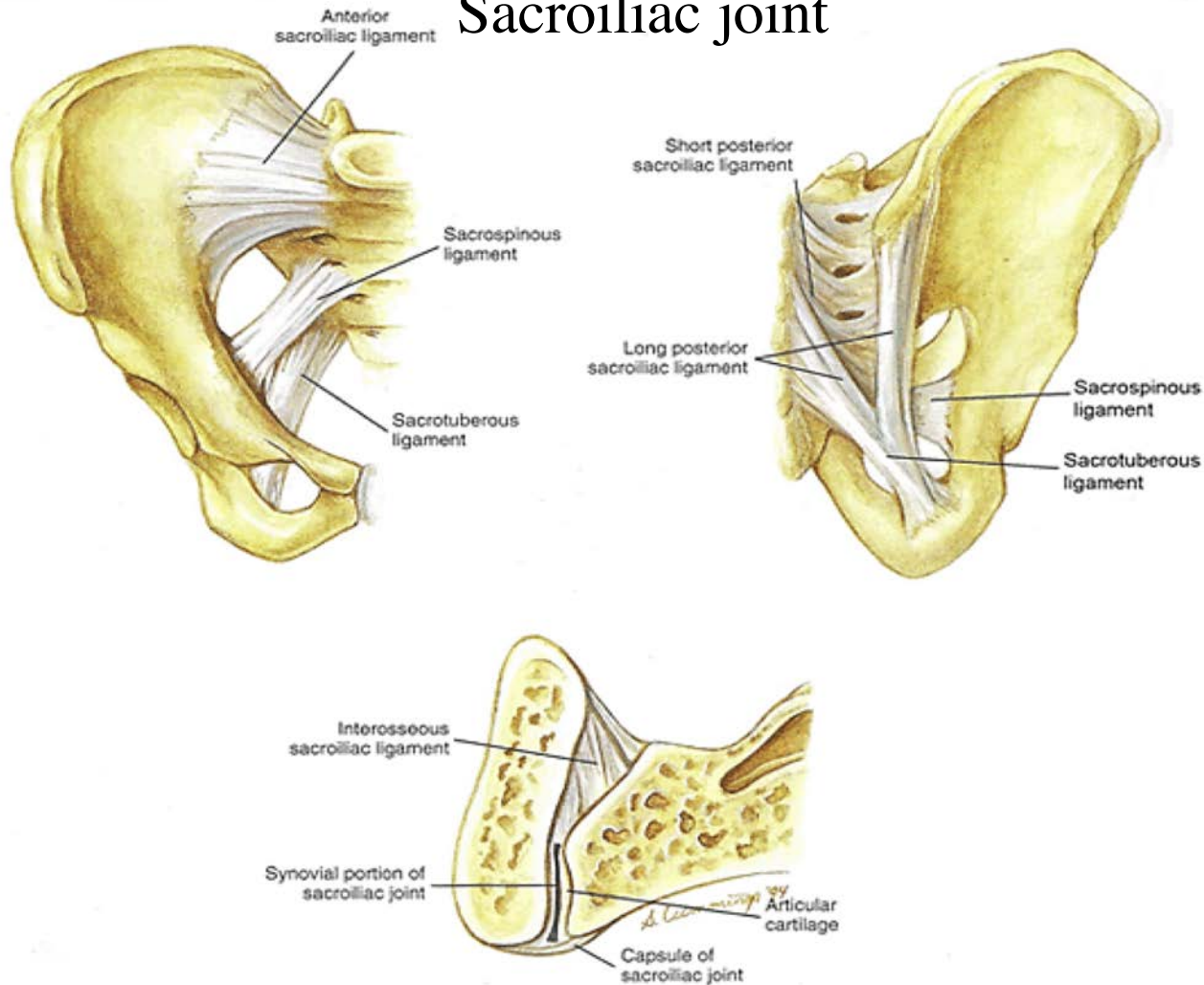
© AboutKidsHealth.ca

Enthesitis can result from repeated **mechanical overloading**, such as that which occurs during sporting activities, in otherwise healthy individuals. 'Tennis elbow' or 'golfer's elbow' is a typical example of an **isolated enthesitis** resulting from mechanical overload. In such cases, enthesitis usually affects only one enthesis, also involves the body of the tendon and usually resolves spontaneously. However, **enthesitis** is also a pathognomonic feature of PsA and SpA, where it occurs frequently, often affects more than one enthesis and shows a remarkable degree of chronicity



Axial (from the word "**axis**"-central) **skeleton** consists of the bones including the vertebrae, sacrum, coccyx, ribs, and sternum.

Sacroiliac joint



The **upper portion** of the joint, the sacrum and the ilium are not in contact- connected with powerful posterior, inter-osseous, and anterior **ligaments**. The **anterior** and the **lower half** of the joint is a typical **synovial joint** with hyaline cartilage on the joint surfaces.

The SI joint is an axial joint with an approximate surface of 17.5 square cm. The joint surface is smooth in juveniles and becomes irregular.

SACROILIITIS:

Causes of sacroiliitis:

- Inflammatory: SpAs, infection (bacteria, fungal, mycobacterial).
- Traumatic: fracture, OA
- Generalized Disease: Gout, Hyperparathyroidism, Paget's disease, paraplegia, neoplastic mets.
- Involves the lower 2/3rd synovial-lined portion.
- In **A.S. and IBD** it is **symmetric and bilateral**.
- In **psoriatic arthritis** and **reactive arthritis** is **asymmetric and unilateral**.
- Earliest x-ray change: erosions of the iliac side of the SI joint where the cartilage is thinner.
- Early on: “pseudo-widening” of the SI joints, then sclerosis and ankyloses/fusion.



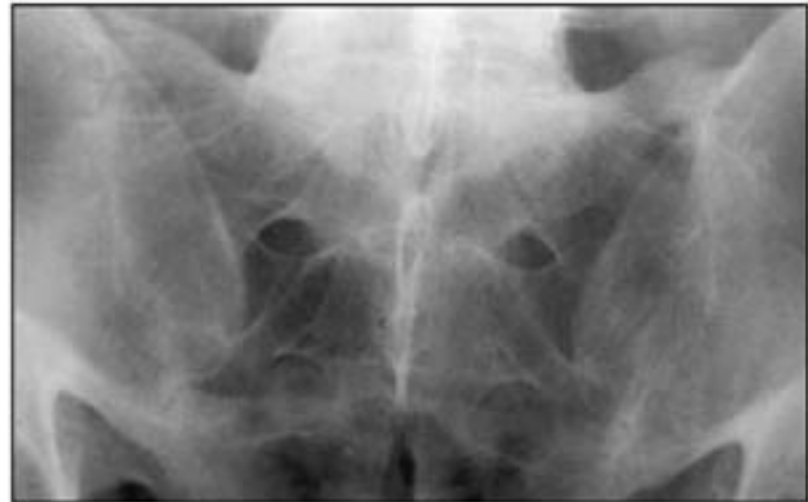
A



B



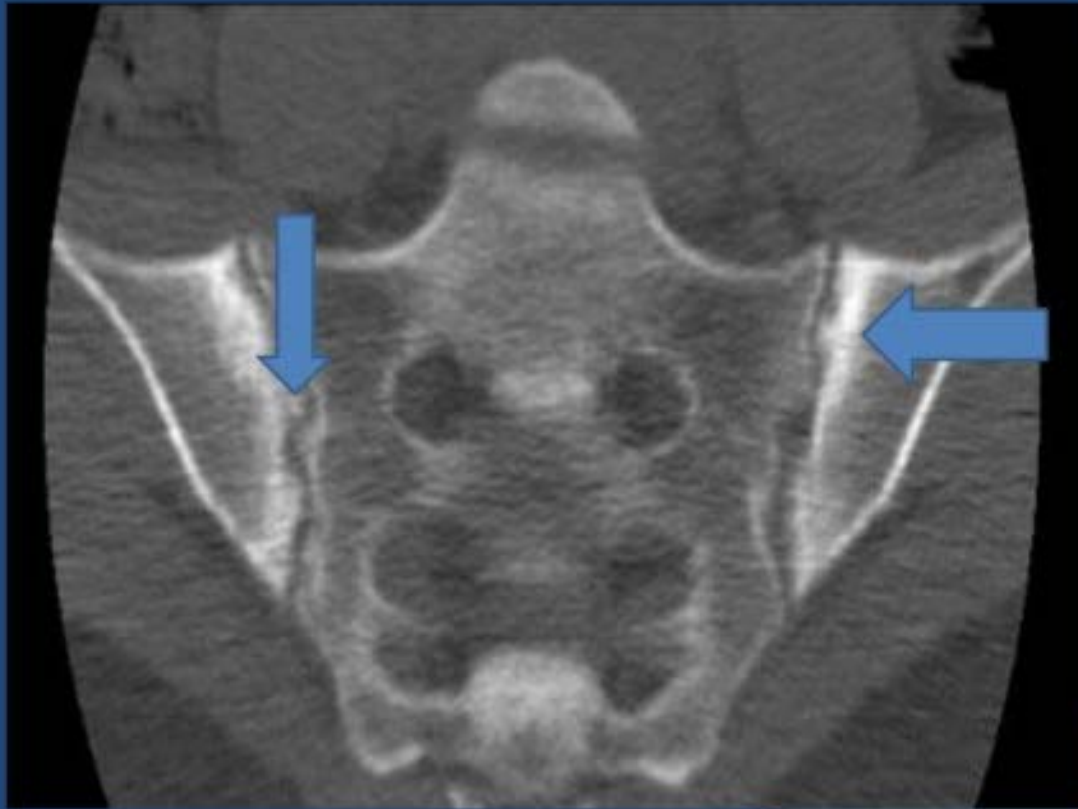
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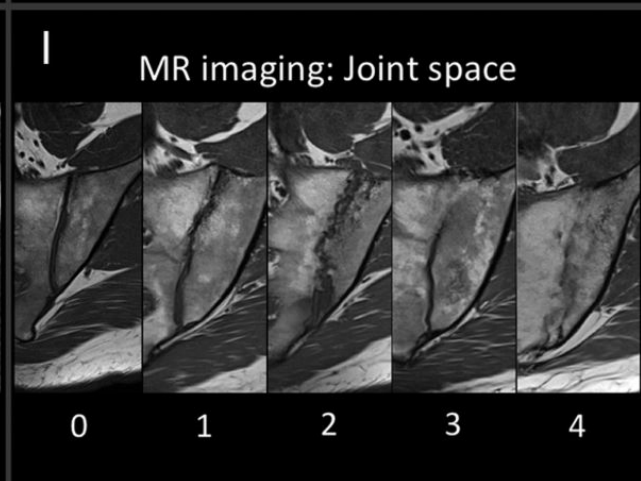
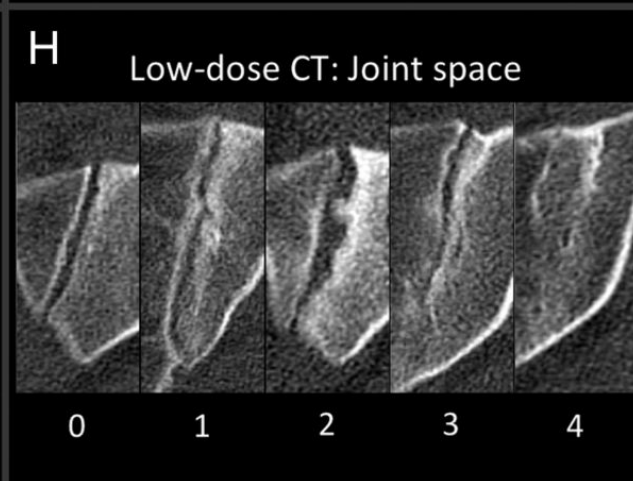
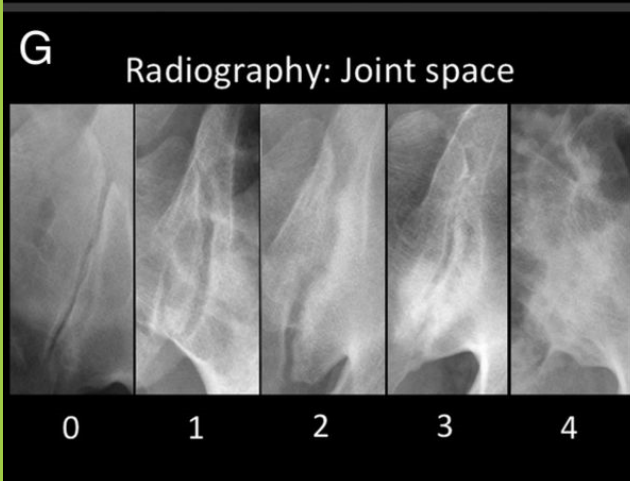
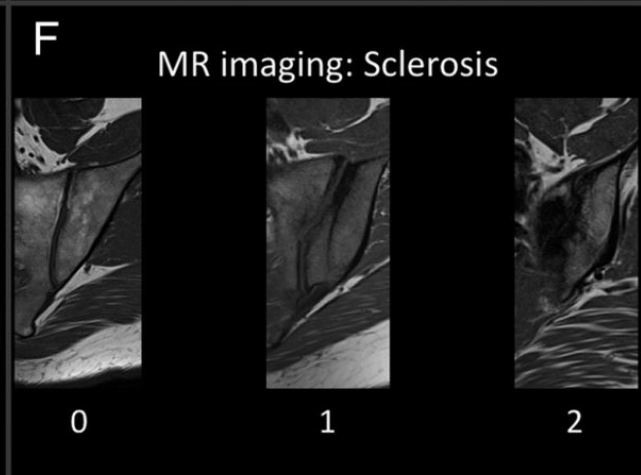
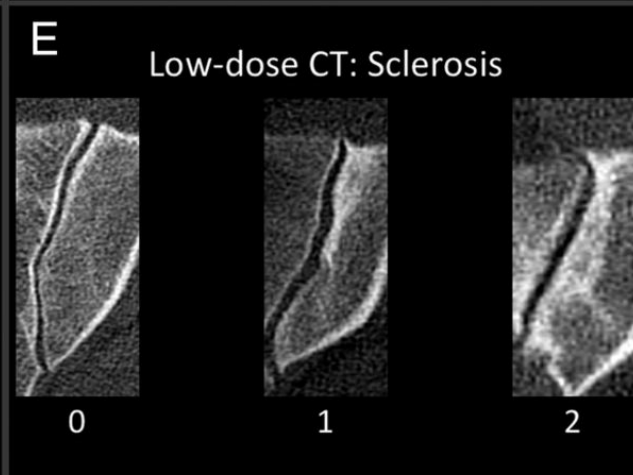
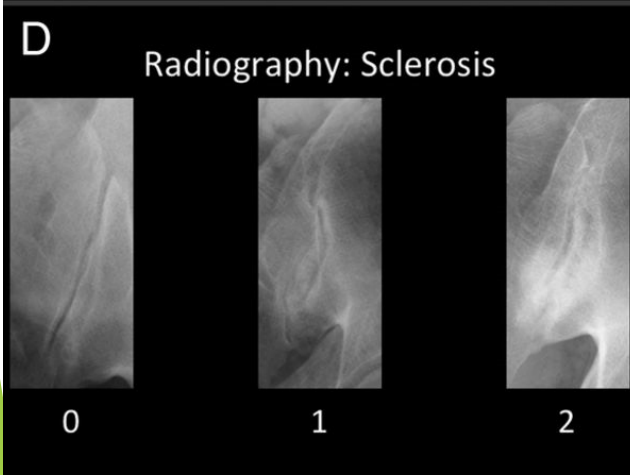
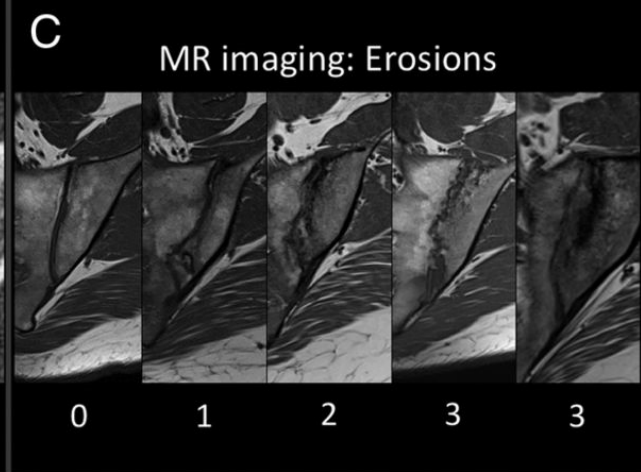
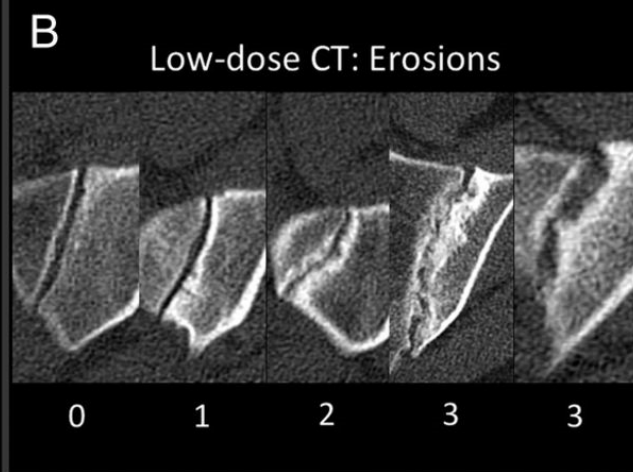
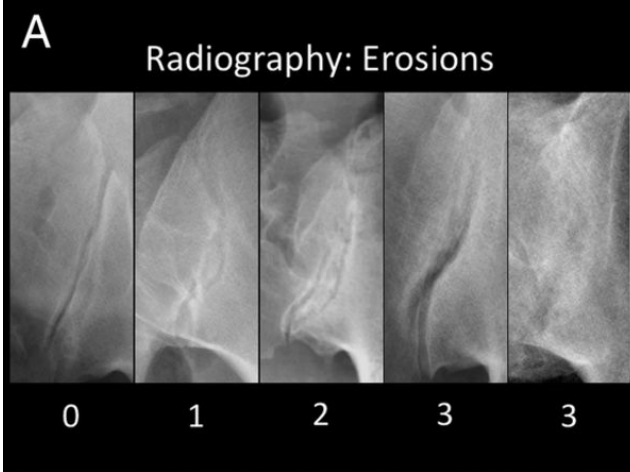


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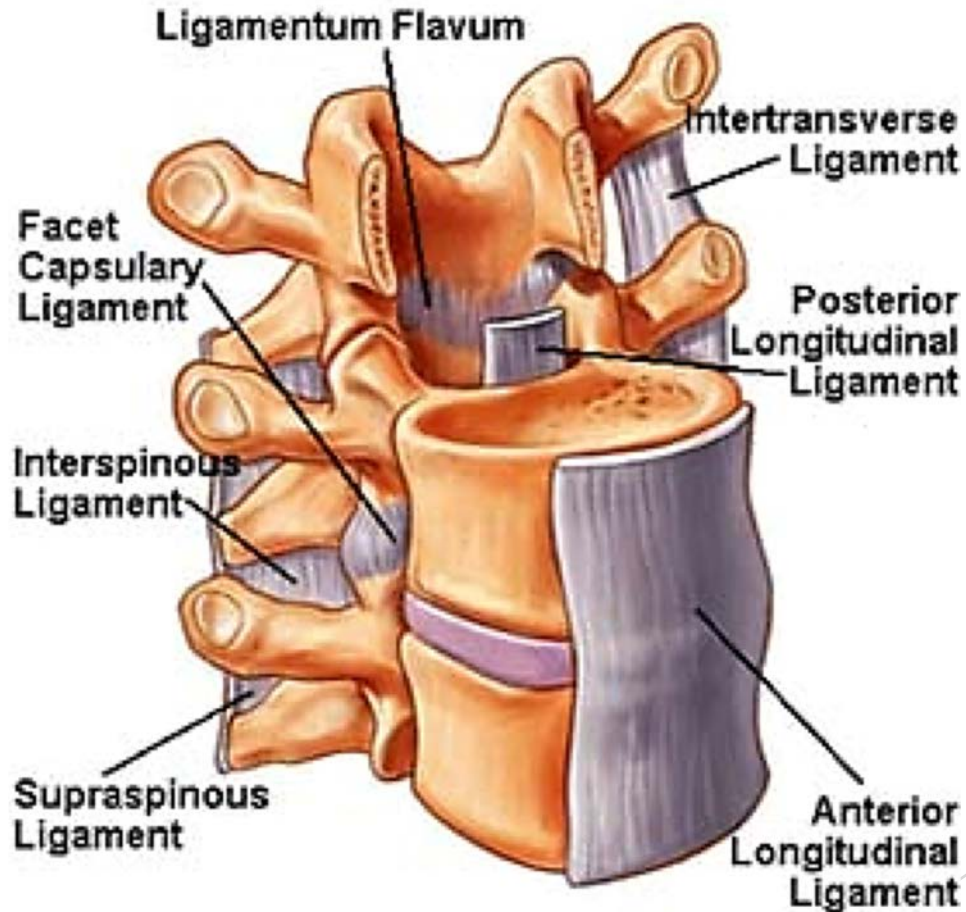
Figure 4. Radiographic classification in the evaluation of sacroiliac joints. Grade 0 – normal (**A**); grade I – suspicious; grade II – mild irregularity and sclerosis of articular surfaces, with preserved joint space (**B**); grade III – joint space narrowing, besides intense irregularity and subchondral sclerosis (**C**); grade IV – bilateral ankylosis (**D**).

MRI – Early changes





Spinal ligaments



Spinal ligaments

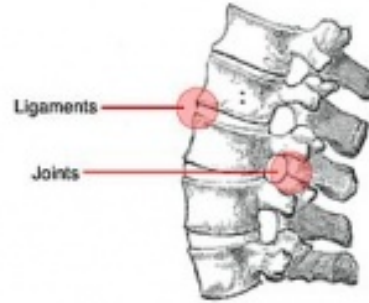
- The reparative process forms vertical linear bone ossification along the outer fibers of the annulus fibrosus of the disc, called **syndesmophyte** formation.
- Ossification of anterior longitudinal ligament and annulus – “bamboo spine”
- Vertebral bodies tend to become osteoporotic (dorsal spine appears to become wedge-shaped)



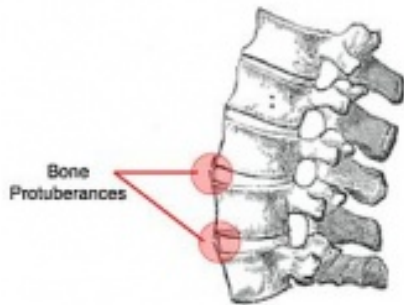
1. Normal Spine



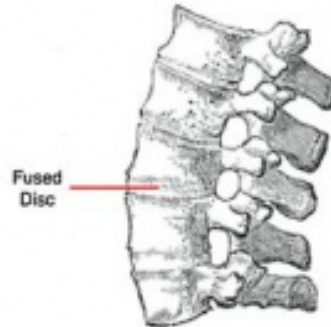
2. Inflammation



3. Formation of Syndesmophytes



4. Fusion



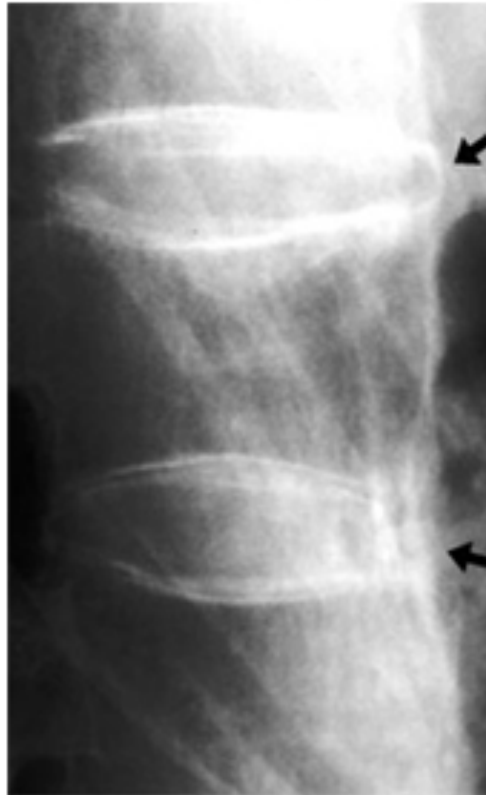
Syndesmophyte formation



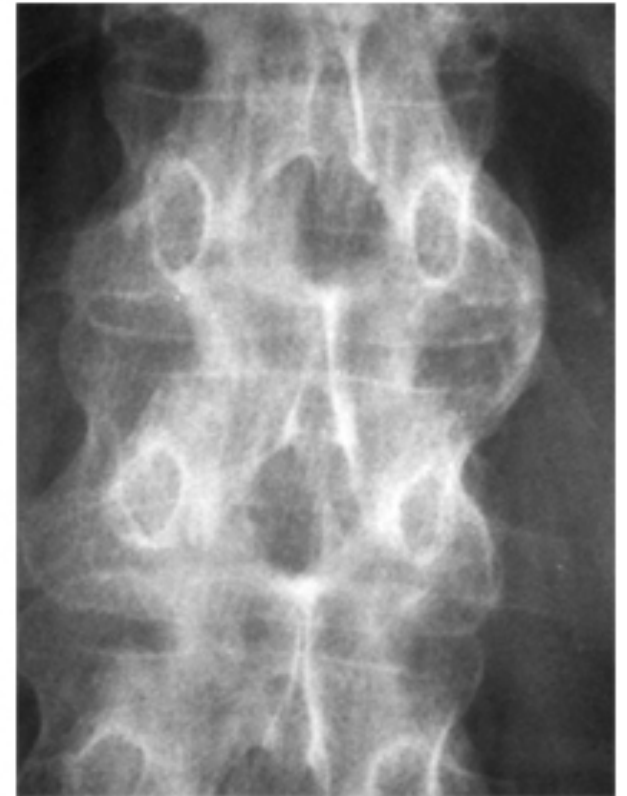
Osteophytes



Marginal syndesmophytes (AS)



Nonmarginal syndesmophytes



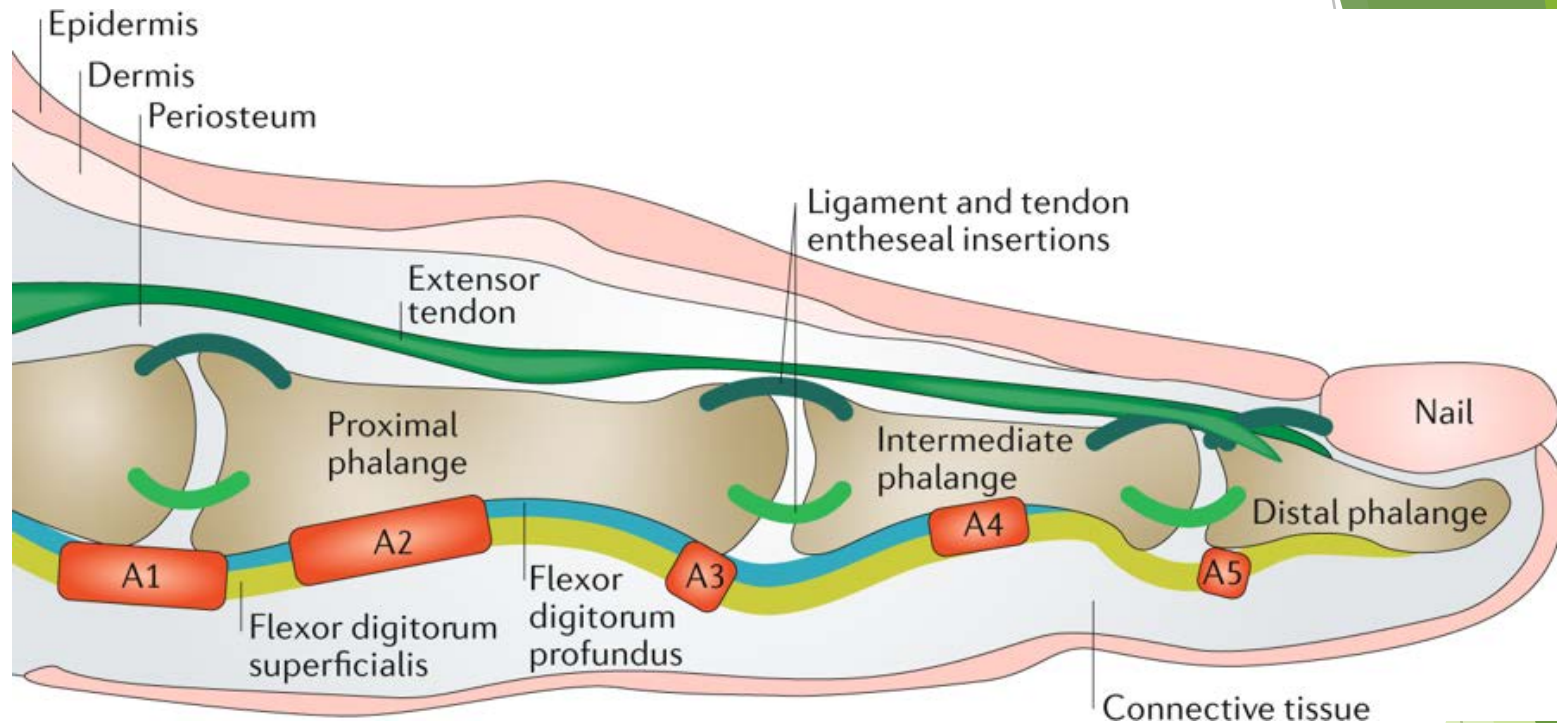
Ankylosing spondylitis
IBD

Reactive arthritis
Psoriatic arthritis



Dactylitis
“Sausage digit”

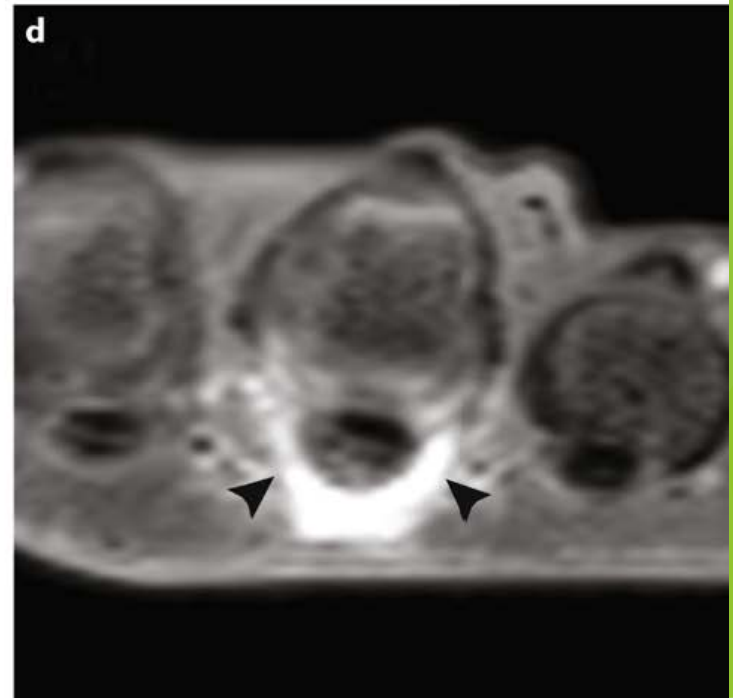


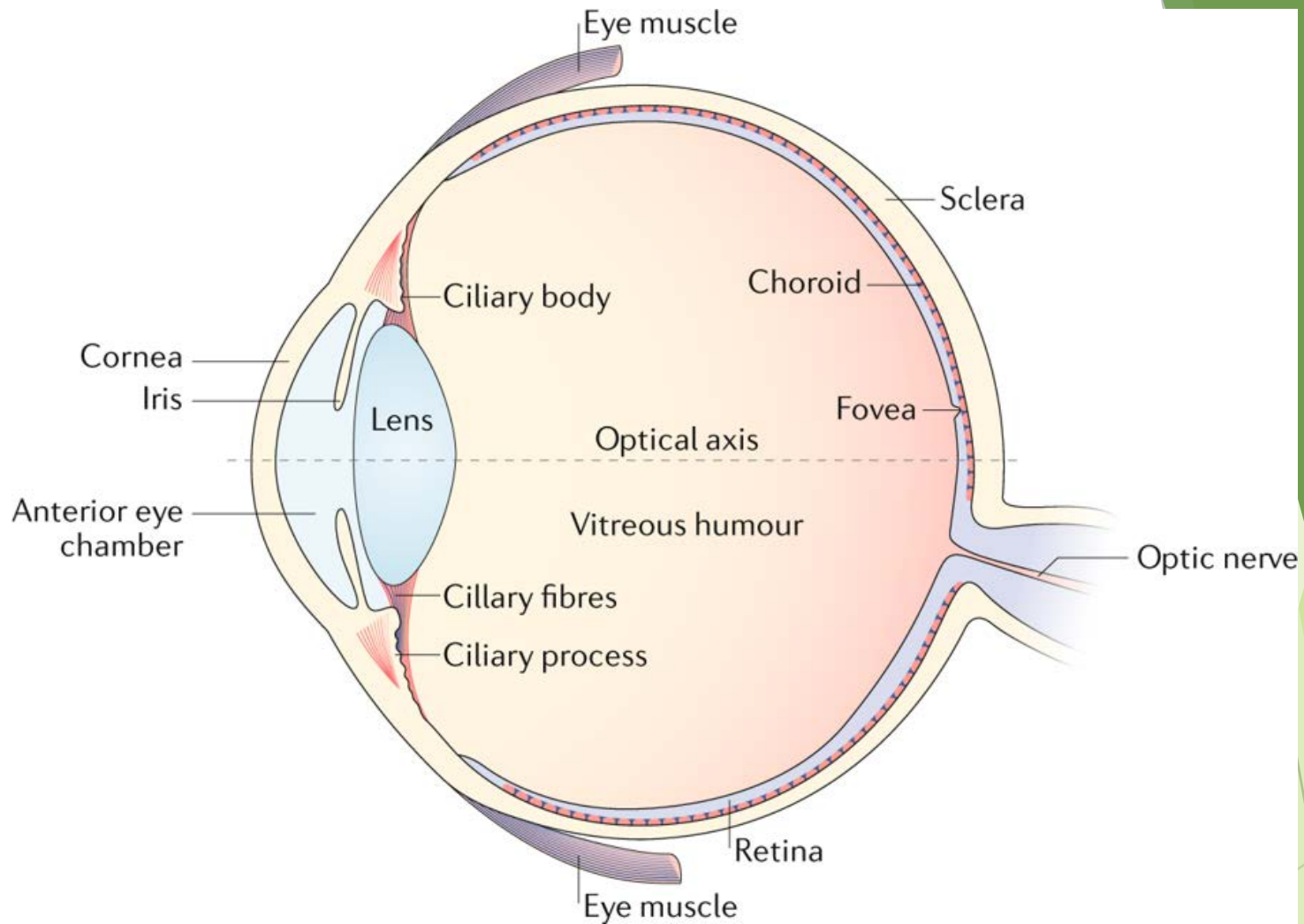


Dactylitis

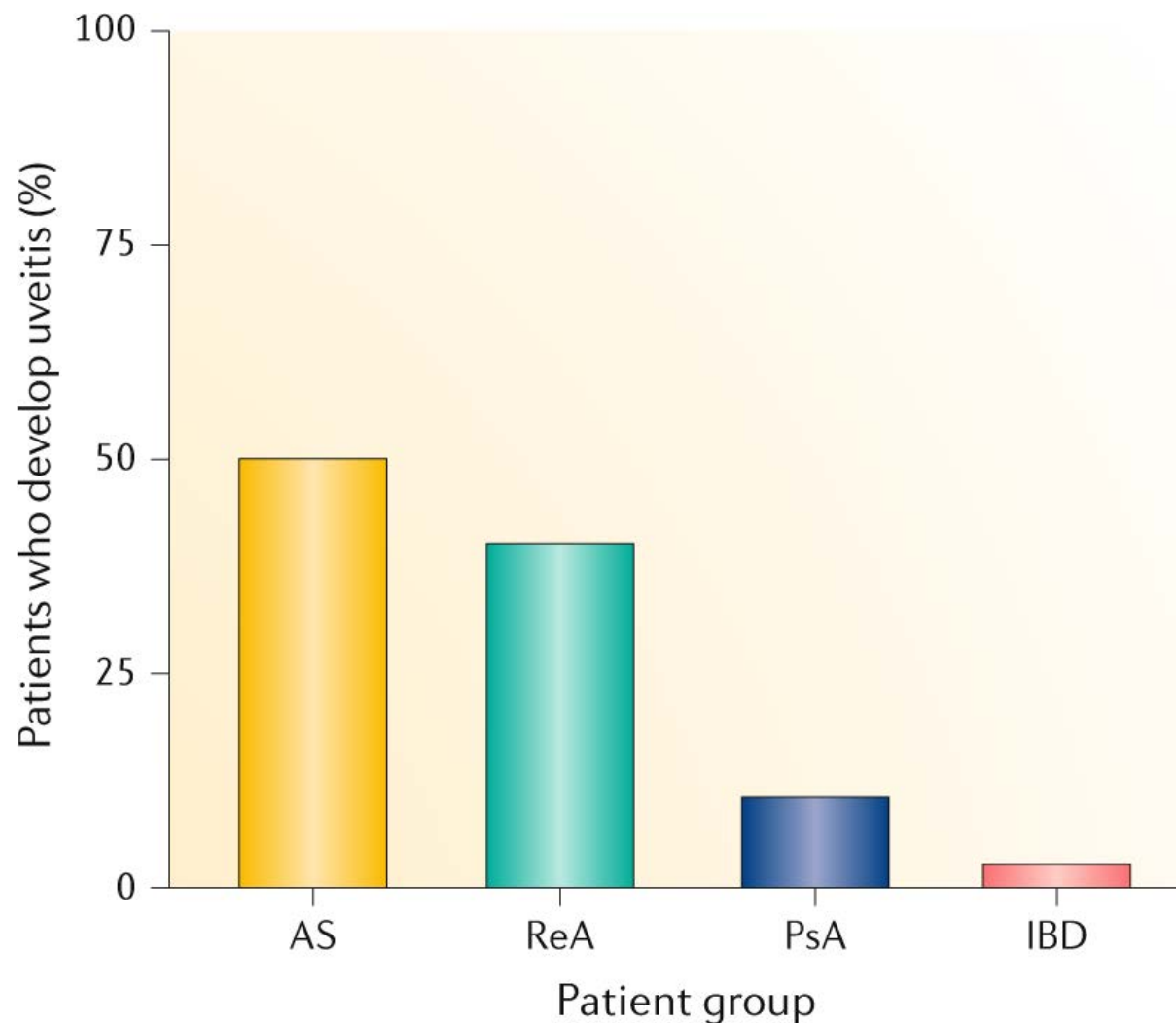
The anatomical relationship between the accessory pulleys A1–A5 and the flexor tendons (flexor digitorum profundus and flexor digitorum superficialis) seems to be important for **flexor tenosynovitis**, which is a common feature of **dactylitis**.

- a. **Dactylitis** of the right second toe.
- b. b | T1-weighted fat-suppressed post-contrast coronal high-resolution MRI of the same digit showing **widespread inflammatory changes in the digital soft tissues** and also bone edema (asterisks).
- c. Dynamic contrast-enhanced hand MRI from a patient with **dactylitis** of the middle digit showing that the initial contrast enhancement corresponds to the A1 pulley at the metacarpophalangeal joint (arrow).
- d. An axial image showing accumulation of contrast agent **adjacent to the flexor tendon** (arrowheads).





The **uveal tract** consists of the **iris, ciliary body and choroid** sandwiched between the outer layer (cornea and sclera) and inner layer (retina) of the eye.



Uveitis associated with different forms of spondyloarthritis. **Uveitis** associated with ankylosing spondylitis (AS) or reactive arthritis (ReA) is almost always **acute anterior** uveitis, whereas uveitis associated with psoriatic arthritis (PsA)²⁴ or inflammatory bowel disease (IBD) is more likely to be **chronic or posterior** to the lens of the eye.

HLA-B27



Human Leukocyte Antigen B*27 (subtypes B*2701-2724) is a class I surface antigen encoded by the B locus in the major histocompatibility complex (MHC) on chromosome 6 and presents microbial antigens to T-cells. HLA-B27 is strongly associated with a certain set of autoimmune diseases referred to as the “seronegative spondyloarthropathies.”

No definitive 'arthritogenic peptide' triggering an immune response in AS has been identified to date

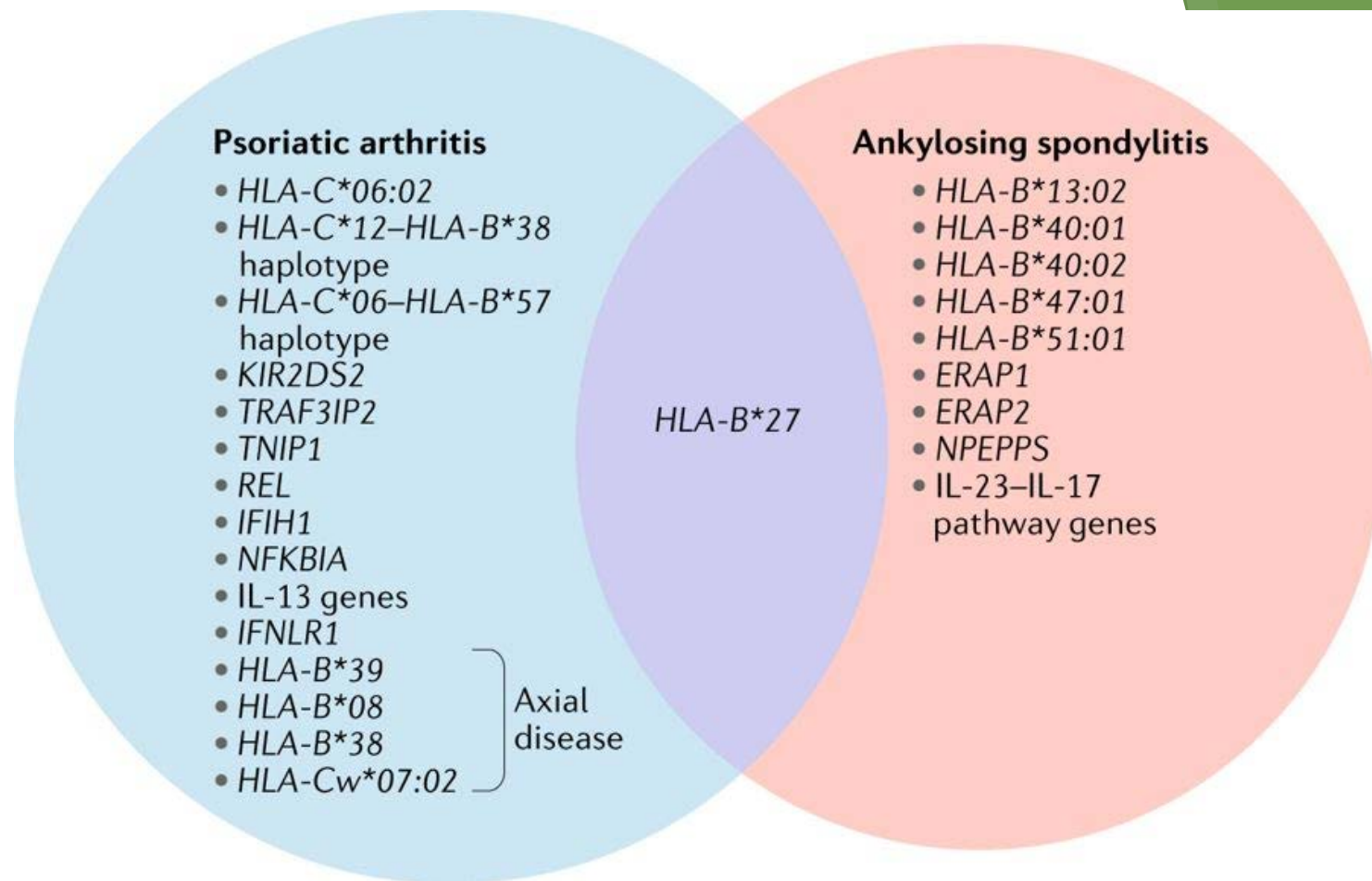
SpA and HLA-B27

Disease	Approximate Prevalence of HLA-B27 (%)
AS	90
Reactive arthritis (ReA)	40-80
Juvenile spondyloarthritis	70
Enteropathic spondyloarthritis	35-75
Psoriatic arthritis	40-50
Undifferentiated spondyloarthritis	70
Acute anterior uveitis	50
Aortic incompetence with heart block	80

Table 1**Association of *HLA-B* alleles with susceptibility to ankylosing spondylitis in European-descent subjects**

Round	<i>HLA-B</i> Allele	Odds Ratio (95% CI)	<i>P</i>-Value
1	27:05	62.41	$<10^{-321}$
2	27:02	43.41	1.07×10^{-122}
3	07:02	0.82	5.04×10^{-6}
4	57:01	0.75	5.13×10^{-4}
5	51:01	1.33	2.14×10^{-3}
6	47:01	2.35	2.25×10^{-3}
7	40:02	1.59	4.65×10^{-3}
8	13:02	1.43	4.29×10^{-3}
9	40:01	1.22	4.93×10^{-3}

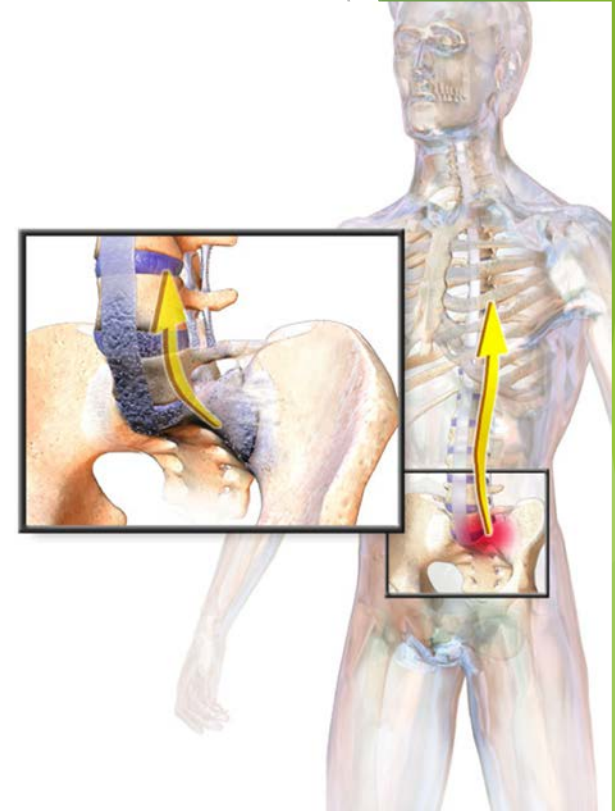
Findings are presented for consecutive conditional analyses, in which, for round 2 and onward, the test conditioned on the previous alleles.



Despite sharing several clinical features such as axial disease, enthesitis, peripheral arthritis and extra-articular manifestations, **psoriatic arthritis and ankylosing spondylitis show very little genetic overlap**. HLA-B*27 is the only genetic risk factor common to both diseases, and axial disease in psoriatic arthritis is actually more commonly associated with other HLA genes than with HLA-B*27.

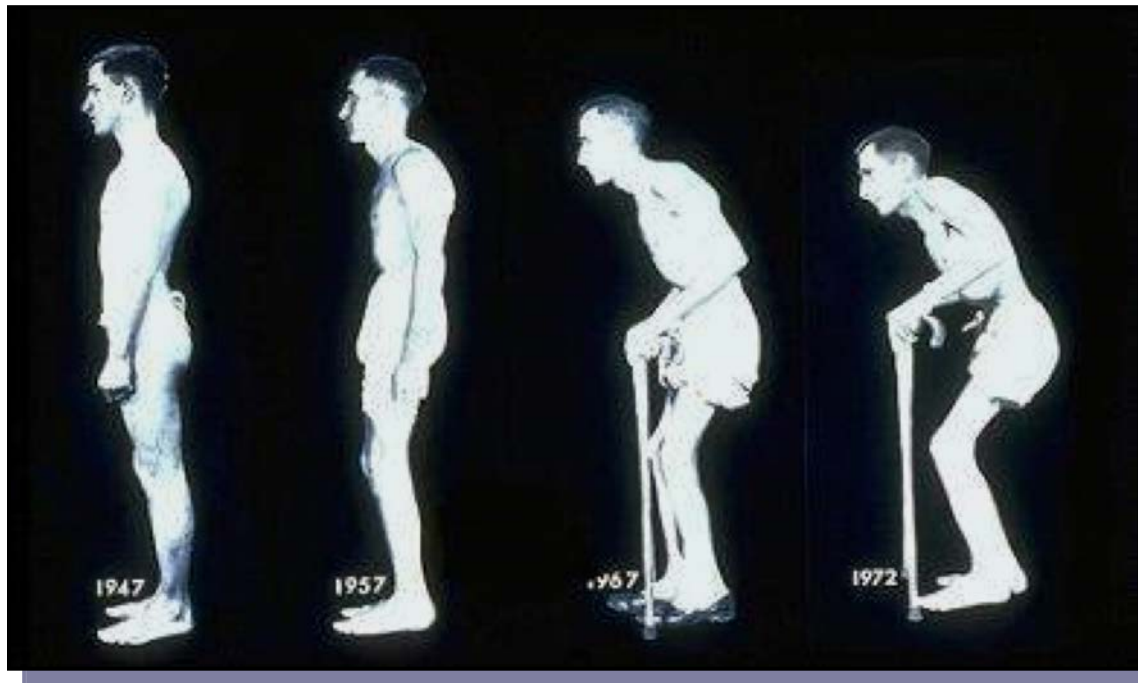
Ankylosing Spondylitis (AS)

- ▶ AS is a chronic, progressive immune-mediated inflammatory disorder that results in ankylosis of the vertebral column and sacroiliac joints¹
- ▶ The spine and sacroiliac joints are the common affected sites¹
 - ▶ Chronic spinal inflammation (spondylitis) can lead to fusion of vertebrae (ankylosis)¹-syndesmophytes



AS: A Debilitating Rheumatic Disease

Over time, joints in the spine can fuse together and cause a fixed, bent-forward posture



AS patients have an important impact on health care and non health-care resource utilization, resulting in a mean total cost (direct and productivity) of about \$6700 to \$9500/year/pt.¹

More than 30% of patients carry a heavy burden of disease and have a decreased QoL²

Kelley's Textbook of Rheumatology
8th ed. Saunders Elsevier;2009;p.1171

²Braun J & Sieper. J Rheumatology 2008;47:1738-40

AS: Clinical presentation

- **Inflammatory back pain**
 - Insidious, persistent (>3 months)
 - Nocturnal pain; worse with rest, better with exercise
 - Morning stiffness
- **Sacroiliitis**
 - Buttock pain
 - Lower anterior synovial portion of joint
- **Enthesitis**
 - Plantar fascia, Achilles tendon
 - Pelvis, tibial tubercles, sternal/chondrocostal junctions
- **Synovitis**
 - LE joints (hips), occasionally shoulders
 - Often oligoarticular, asymmetric
- **Systemic symptoms:** fatigue
- **Labs:** ESR, CRP

Ankylosing Spondylitis

“Bamboo Spine”

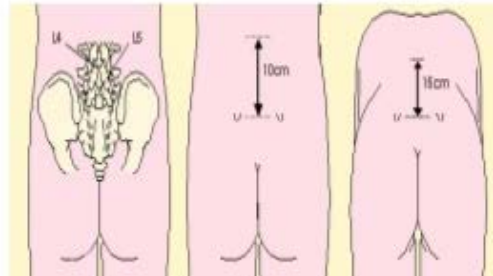
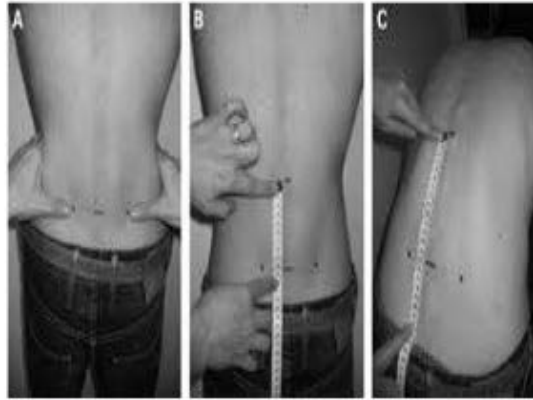
Repeated process of healing and bone formation leads to formation of syndesmophytes ‘bone bridges’



“Sacroiliitis”

Lumbar flexion (modified Schober)

- With the patient standing upright, place a mark at the lumbosacral junction (at the level of the dimples of Venus on both sides). Further marks are placed 5 cm below and 10 cm above. Measure the distraction of these two marks when the patient bends forward as far as possible, keeping the knees straight



The distance less than 5 cm is abnormal

modified

Chest expansion

- Measured as the difference between maximal inspiration and maximal forced expiration in the fourth intercostal space in males or just below the breasts in females. Normal chest expansion is ≥ 5 cm.



AS: Extra-articular Manifestations (EAM)

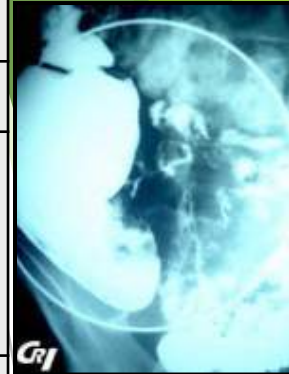


Anterior uveitis



Cardiac abnormalities

EAM	Prevalence in AS Patients (%)
Anterior uveitis	30-50
IBD	5-10
Subclinical inflammation of the gut	25-49
Cardiac abnormalities	
Conduction disturbances	1-33
Aortic insufficiency "Bamboo Spine"	1-10
Psoriasis	10-20
Renal abnormalities	10-35
Lung abnormalities	40-88
Airways disease	82
Interstitial abnormalities	47-65
Emphysema	9-35
Bone abnormalities	
Osteoporosis	11-18
Osteopenia	39-59 "Bamboo Spine"



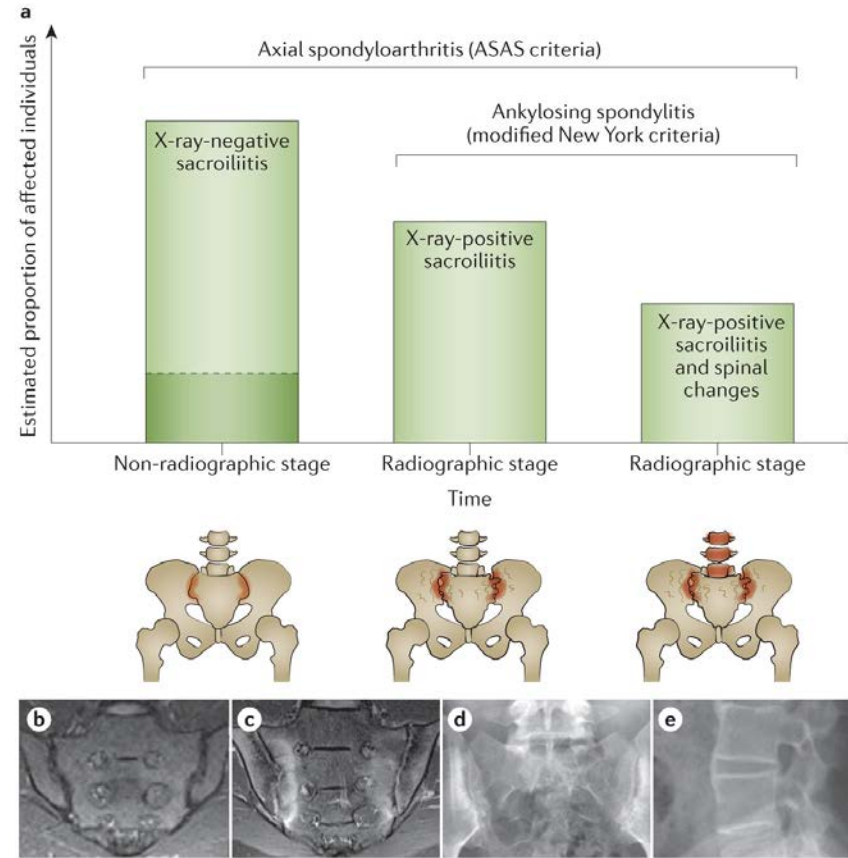
Terminal ileitis

Table 1. Demographic features, clinical and laboratory characteristics, disease activity and functional status of ankylosing spondylitis patients according to the gender

Parameter	AS patients (n=40) Mean ± SD or n (%)		P value
	Male (n=21)	Female (n=19)	
Age (years)	35.4 ± 9.3	33.1 ± 7.4	0.39
Age at onset (years)	29.4 ± 6.9	28.5 ± 6.8	0.7
Back MS (minutes)	112.9 ± 44.4	72.4 ± 52.4	0.01
IBP duration (years)	5.6 ± 7.8	4.2 ± 7.2	0.56
Bilateral sacroiliitis	18 (85.7)	13 (68.4)	0.02
Peripheral arthritis	9 (42.9)	4 (21.1)	0.15
Uveitis	1 (4.8)	0 (0)	0.33
Schöber's test (cm)	4.5 ± 0.8	4.9 ± 0.7	0.046
Finger-to-floor (cm)	40.7 ± 9.2	27.9 ± 9.7	<0.001
Chin-to-chest (mm)	0.06 ± 0.14	0.02 ± 0.07	0.24
Occiput-to-wall (mm)	0.22 ± 0.34	0.03 ± 0.11	0.02
Chest expansion (cm)	4.2 ± 1.1	4.8 ± 0.51	0.06
ESR (mm/1 st hr)	42.3 ± 30.8	25.2 ± 25.9	0.06
CRP (mg/dl)	41.04 ± 39.6	10.1 ± 14.7	0.003
RF positivity	0 (0)	3 (15.8)	-
HLA-B27 positivity	18 (85.7)	9 (47.4)	-
BASDAI	5.7 ± 1.9	6.5 ± 1.4	0.16
BASFI	5.8 ± 1.4	6.7 ± 1.1	0.04

MS: morning stiffness, IBP: inflammatory back pain, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, RF: rheumatoid factor, HLA-B27: human leucocyte antigen, BASDAI: Bath ankylosing spondylitis disease activity index, BASFI: Bath ankylosing spondylitis functional index. Bold values are significant at p<0.05.

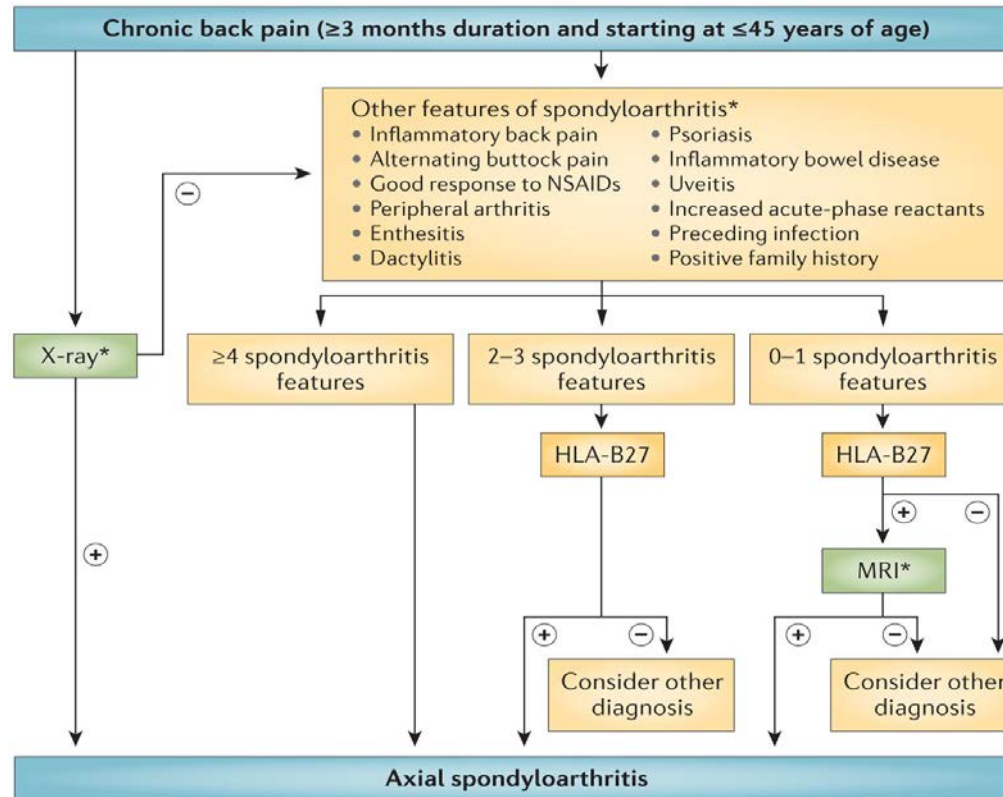
Spectrum of axial spondyloarthritis



Nature Reviews | Disease Primers

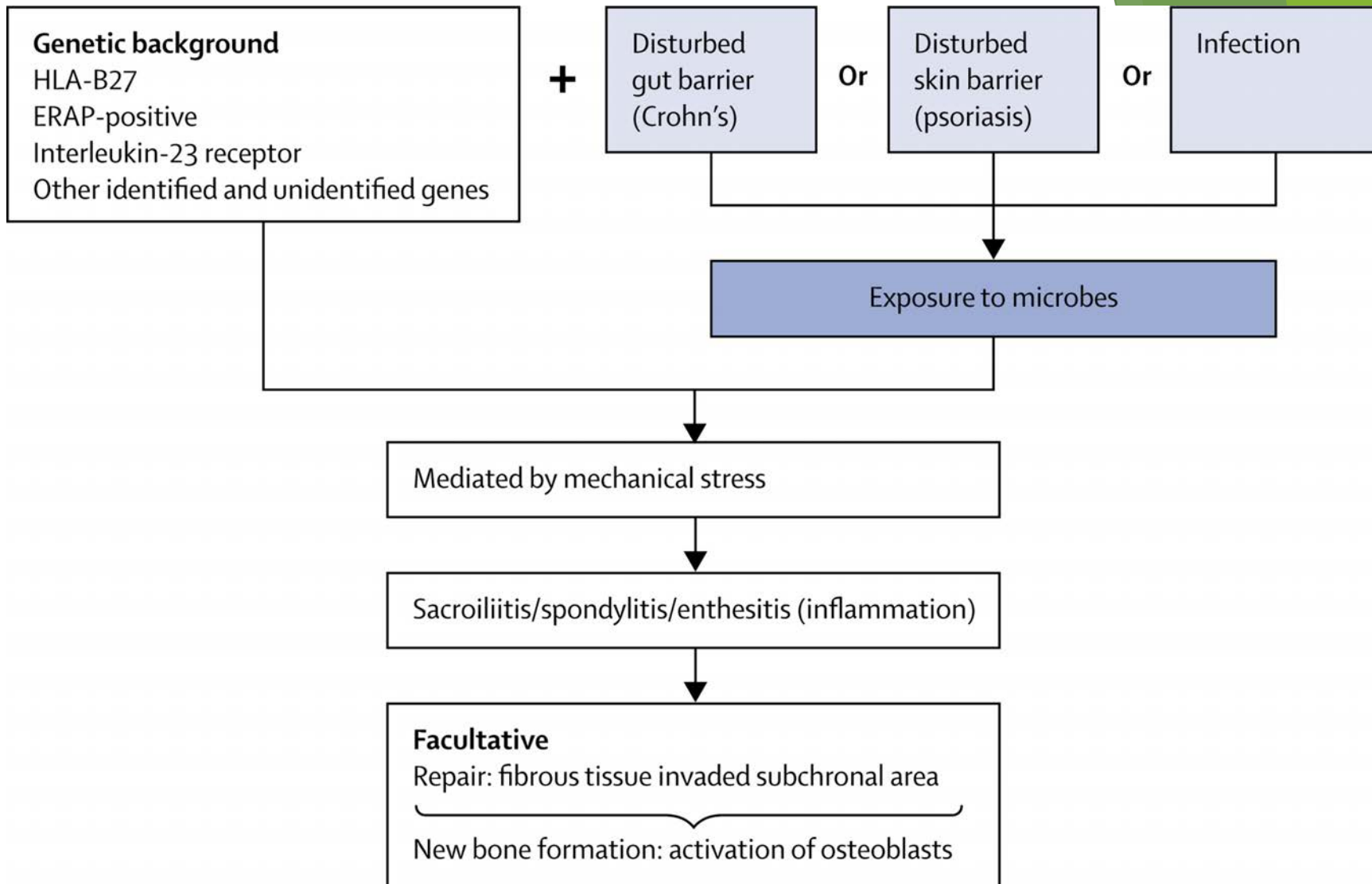
The spectrum of axial spondyloarthritis, normally starts with inflammation in the sacroiliac joints (non-radiographic stage; part a). **Structural damage that is visible on X-ray scans (radiographic stage) develops later but not in all patients.** Abnormalities in the spine also develop later and only in some patients. Some patients with non-radiographic disease show no abnormalities on MRI of the sacroiliac joints (part b). However, in **most patients, inflammation of the sacroiliac joints is detectable by MRI before structural changes occur** (part c). Structural changes that are visible on X-ray scans include sclerosis, erosion and new bone formation (part d). Syndesmophytes of the spine (bone growth between vertebrae) are characteristic of spinal involvement in axial spondyloarthritis.

Diagnostic approach



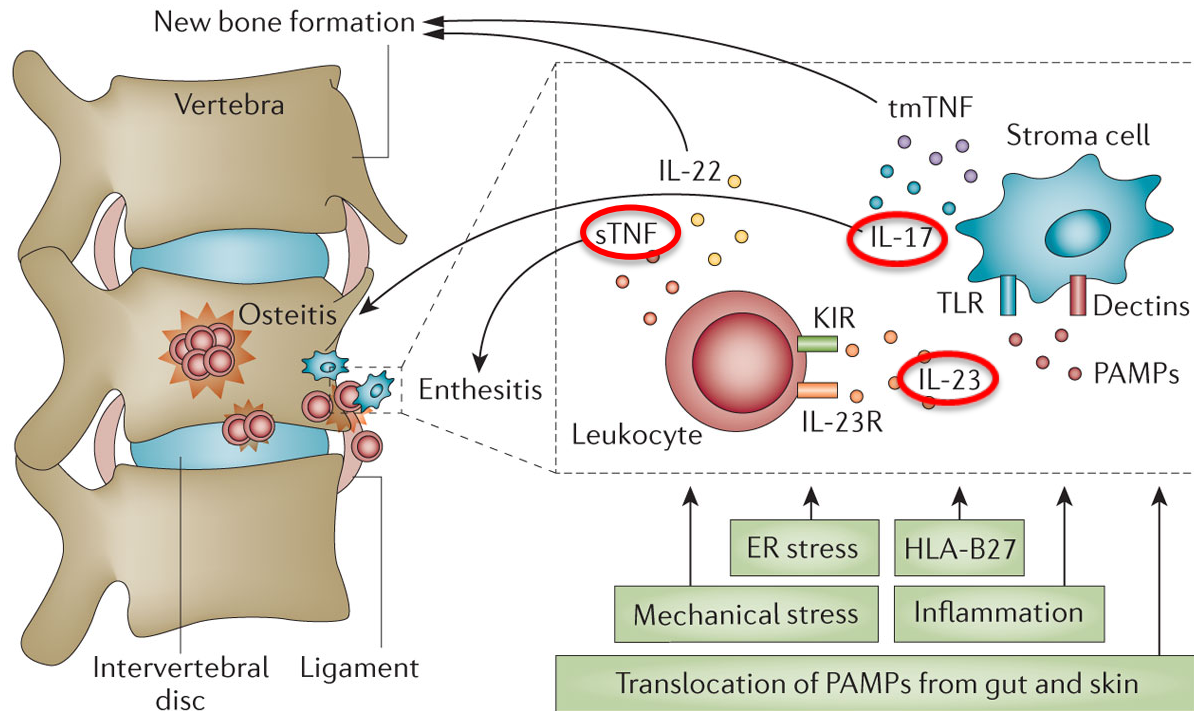
Nature Reviews | **Disease Primers**

For patients with **chronic back pain (for ≥3 months) starting at ≤45 years of age**, the following diagnostic approach is proposed. X-rays are used to detect radiographic changes of the sacroiliac joints. Patients **without radiographic disease** are further evaluated based on the presence of several features that are indicative of axial spondyloarthritis and, if needed, for the presence of **HLA-B27 and MRI changes of the sacroiliac joints**. Note that axial spondyloarthritis in the absence of both a positive imaging result and a positive HLA-B27 test is rather rare. Other causes of signs and symptoms (*) should always be excluded.



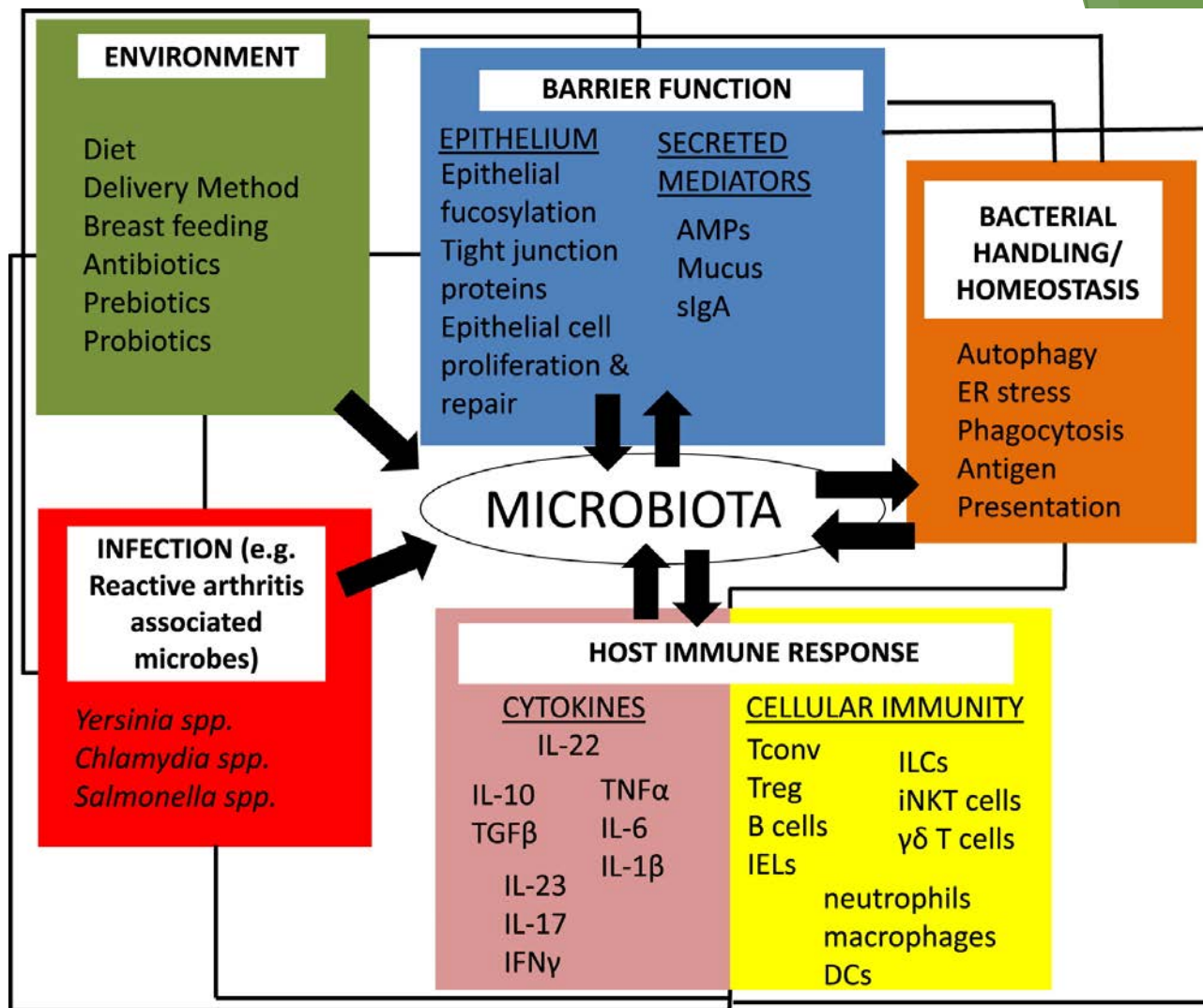
Pathogenesis of axial spondyloarthritis

The pathophysiology of axial spondyloarthritis



Nature Reviews | **Disease Primers**

The interaction of **genetic factors**, in particular **HLA-B27**, with various stresses including **mechanical stress, endoplasmic reticulum stress and microbial stress** at body surfaces lead to the production of **pro-inflammatory cytokines** including **IL-23, sTNF, and IL-17** which are proposed to be strong **inflammatory drivers** leading to new bone formation and ultimately ankylosis of the axial joints.



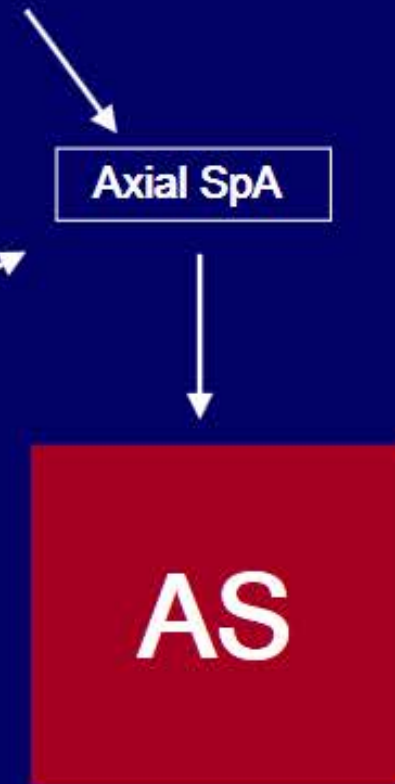
Multiple pathways implicated in IBD and SpA pathogenesis impact the host–**microbiota** relationship. Approximately **one-half** of SpA patients exhibit signs of **microscopic gut inflammation**.

Spondyloarthritis - main manifestations

1. Axial involvement/spinal inflammation
2. Peripheral arthritis
3. Peripheral enthesitis

SpA subtypes





1. Ankylosing spondylitis (AS)
2. Undifferentiated SpA
3. Psoriatic SpA
4. Reactive SpA
5. SpA associated with chronic inflammatory bowel diseases





REACTIVE ARTHRITIS/REITERS SYNDROME



- Reactive arthritis refers to acute ***non-purulent arthritis*** complicated by an infection elsewhere in the body.
 - Syndrome was described by Hans Reiter in 1916.
 - A clinical triad of ***urethritis, arthritis*** and ***conjunctivitis*** occurring some weeks after *dysentery* or *genitourinary infection*.
- 
- 
- 
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Epidemiology

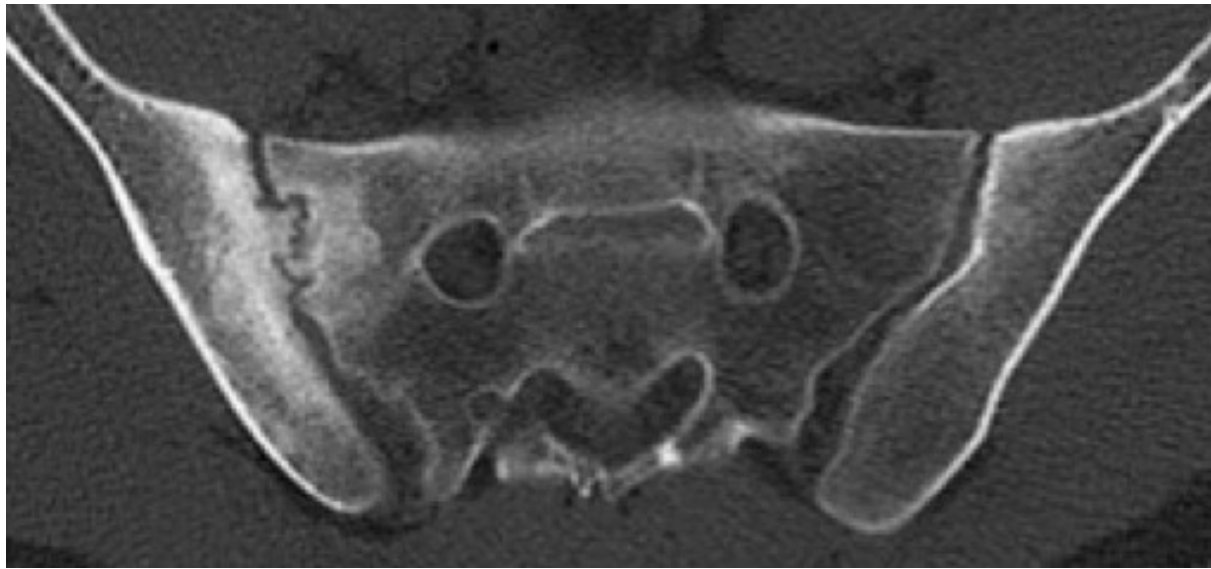
- age - is 18–40 years
- gender ratio in ReA following enteric infection is nearly 1:1, whereas venereally acquired ReA occurs mainly in men
- 60–85% of patients were found to be B27-positive - its presence contributes to the chronicity of the disease.

Triggering infections

- Reactive arthritis is an arthritis induced by one of the following bacteria:
 - Urogenital:
 - Chlamydia trachomatis
 - Enteric:
 - Shigella (*S. flexneri* has most often)
 - Salmonella
 - Yersinia
 - Campylobacter
- At least presumptive evidence for a related antecedent infection is a must

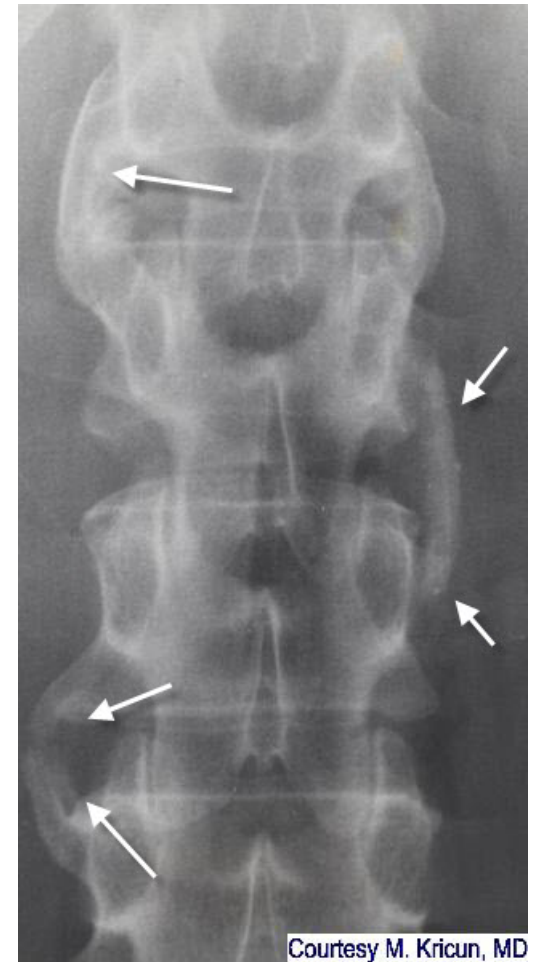
Reactive arthritis

- ~50% post *Chlamydia*, *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*
- Characteristically an asymmetric lower extremity oligoarthritis
- Enthesitis common (Achilles tendonitis, plantar fasciitis), sausage digit
- Sacroiliitis in 50%, but rare progression to ankylosing spondylitis



Unilateral sacroiliitis

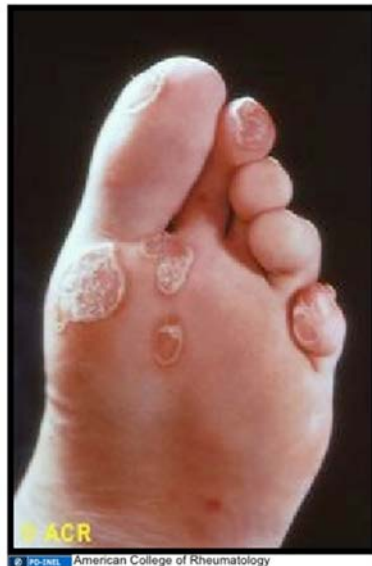
**Nonmarginal
syndesmophytes**



Courtesy M. Kricun, MD

Reactive arthritis: Extraarticular manifestations

- Keratoderma blenorrhagicum
- Circinate balanitis
- Urethritis, cervicitis, salpingitis
- Oral ulcers
- Acute anterior uveitis



Predominant manifestation

Axial manifestations:
Back pain and stiffness

Peripheral manifestations:
arthritis, enthesitis, dactylitis

First-line therapy

NSAIDs

Non-pharmacological treatment: education, exercise, physical therapy, rehabilitation, patient associations, self help groups

Local steroids

DMARDs sulfasalazine, methotrexate

Second-line therapy

TNF α blocker or IL-17 blocker

Additional therapy and therapy in special clinical situations

Analgesics

Surgery

Recommendations for the **treatment of axial spondyloarthritis**

Based on ASAS/EULAR⁸⁹ and ACR/AAS/SPARTAN,⁹⁰ including the current approval status for the interleukin-17 blocker secukinumab. Secukinumab—an interleukin-17-antagonist—is currently approved only for ankylosing spondylitis. NSAIDs=non-steroidal anti-inflammatory drugs. DMARDs=disease modifying antirheumatic drugs. TNF=tumour necrosis factor.

Table 2 | Efficacy of biologics and other novel drugs in axial SpA and other chronic inflammatory diseases

Target	Therapeutic agent	Efficacy				
		Axial SpA*	PsA	Psoriasis	Crohn's disease	RA
TNF	Adalimumab (monoclonal antibody to TNF)	+	+	+	+	+
	Certolizumab pegol (monoclonal antibody to TNF)	+	+	+	+	+
	Etanercept (fusion protein against TNF)	+	+	+	-	+
	Golimumab (monoclonal antibody to TNF)	+	+	+	+	+
	Infliximab (monoclonal antibody to TNF)	+	+	+	+	+
IL-1	Anakinra (IL-1 receptor antagonist)	-?	+?	?	?	+
B cells	Rituximab (monoclonal antibody to CD20)	+?	+?	?	-	+
T cells	Abatacept (inhibitor of T-cell co-stimulation)	-?	+	+?	-	+
IL-6	Tocilizumab (monoclonal antibody to IL-6 receptor)	-	?	?	?	+
	Sarilumab (monoclonal antibody to IL-6 receptor)	-	?	?	?	+
IL-17	Secukinumab (monoclonal antibody to IL-17)	+	+	+	-	-
	Ixekizumab (monoclonal antibody to IL-17)	?	?	+	?	+?
	Brodalumab (monoclonal antibody to IL-17 receptor)	?	+	+	?	-
IL-12 and IL-23	Ustekinumab (monoclonal antibody to IL-12 and IL-23)	+?	+	+	+	-
	Guselkumab (monoclonal antibody to IL-23)	?	?	+	?	-
	Tildrakizumab (monoclonal antibody to IL-23)	?	?	+	?	?
	BI 655066 (monoclonal antibody to IL-23)	?	?	+	?	?
PDE4	Apremilast (PDE4 inhibitor, small molecule)	-?	+	+	?	-
JAK	Tofacitinib (JAK1 and JAK3 inhibitor, small molecule)	+	?	+	-	+

Efficacy of biologics and other novel drugs in axial SpA and other chronic inflammatory diseases

Sieper, J. & Poddubnyy, D. (2016) *Nat. Rev. Rheumatol.*

Spondyloarthritis, Psoriasis and PsA

Psoriasis (Pso)

- Psoriasis affects 2% of population
- 7% to 42% of patients with Pso will develop arthritis³

Psoriatic Arthritis

- A chronic and inflammatory arthritis in association with skin psoriasis⁴
- Usually rheumatoid factor (RF) negative and ACPA negative⁵
 - Distinct from RA
- Psoriatic Arthritis is classified as one of the subtypes of spondyloarthropathies
 - Characterized by synovitis, enthesitis, dactylitis, spondylitis, skin and nail psoriasis⁴

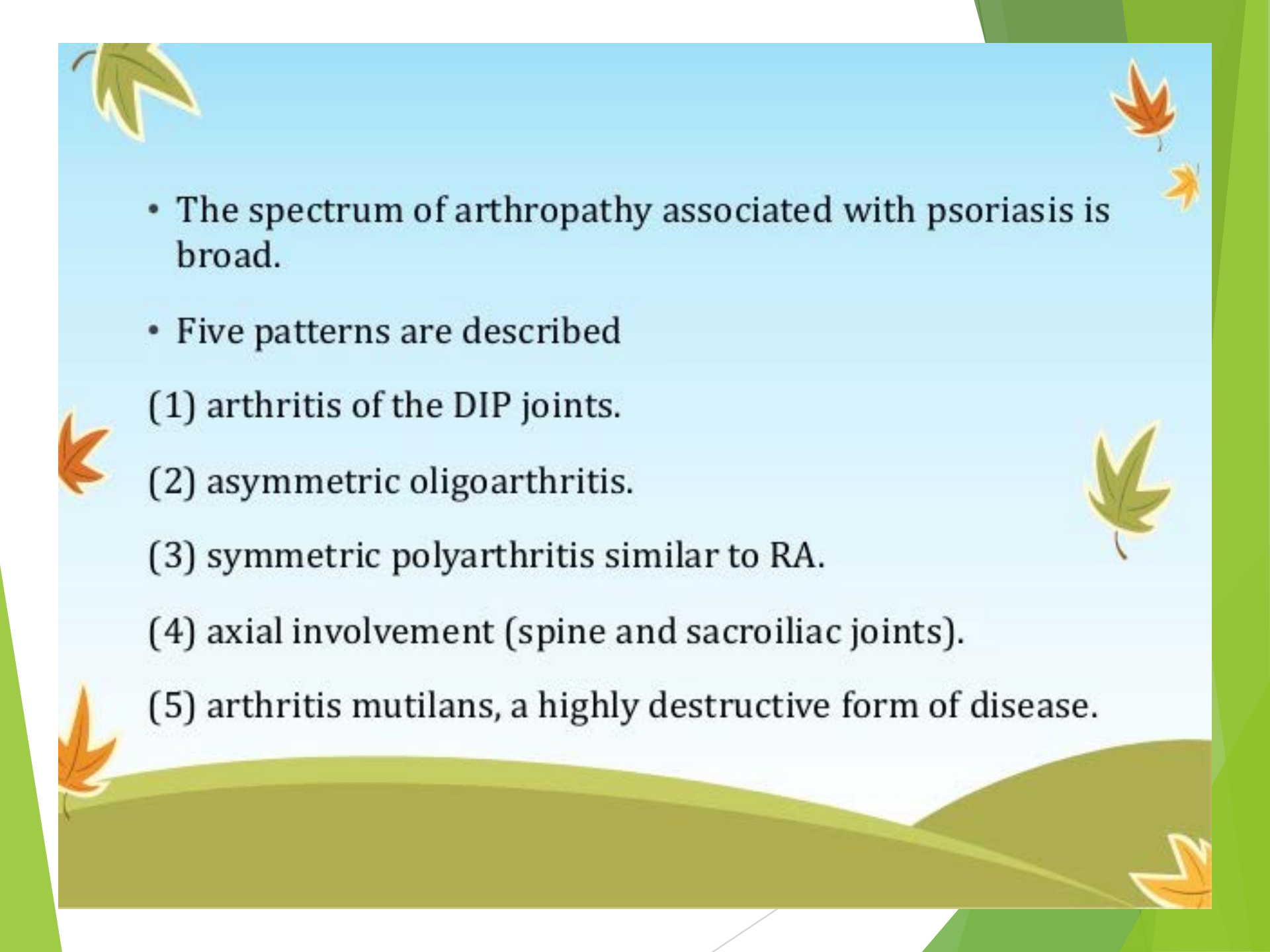


¹Rudwaleit M et al. Ann Rheum Dis 2004;63:535-543; ²Braun J et al. Scand J Rheumatol 2005;34:178-90;

³Fitzgerald "Psoriatic Arthritis" in Kelley's Textbook of Rheumatology, 2009;

⁴Mease et al. Ann Rheum Dis 2011;70(Suppl 1):i77-i84. doi:10.1136/ard.2010.140582;

⁵Pasquetti et al. Rheumatology 2009;48:315-325

- 
- The spectrum of arthropathy associated with psoriasis is broad.
 - Five patterns are described
 - (1) arthritis of the DIP joints.
 - (2) asymmetric oligoarthritis.
 - (3) symmetric polyarthritis similar to RA.
 - (4) axial involvement (spine and sacroiliac joints).
 - (5) arthritis mutilans, a highly destructive form of disease.



Pauci-articular psoriatic arthritis

- Nail changes-Pitting of the fingers or toes occur in 90% of patients with PsA.

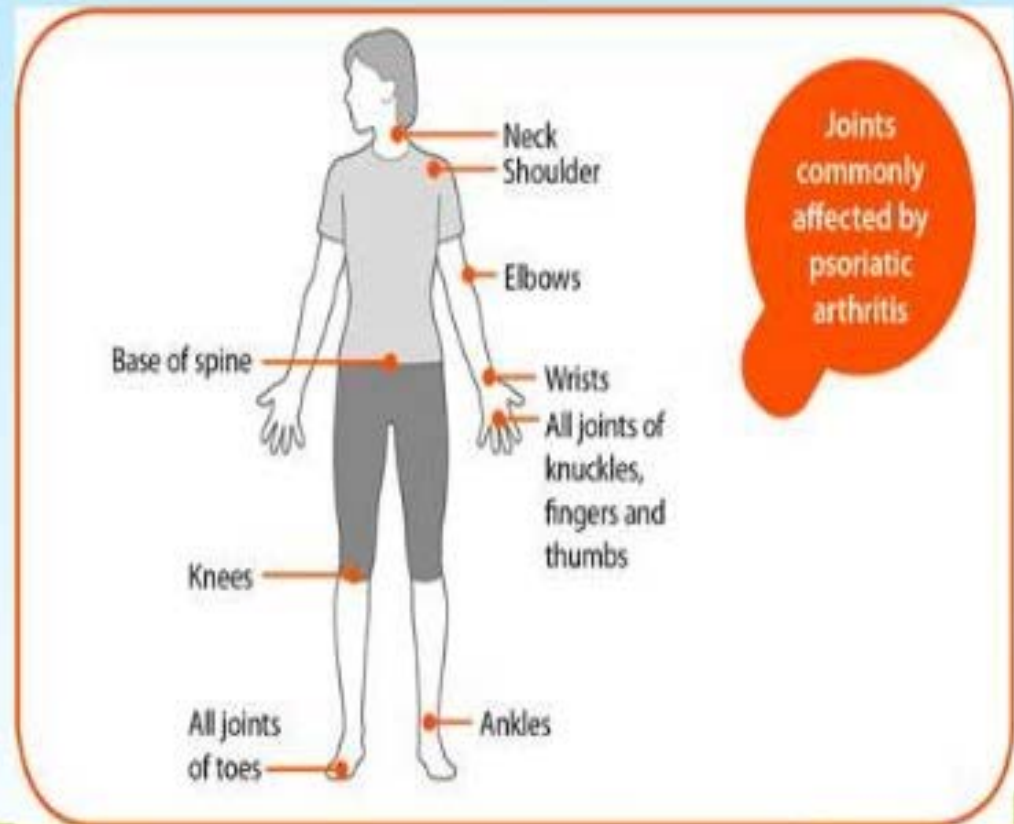
Figure 2. A: Pitting of the fingernail. B: Onycholysis with an erythematous border.



Image courtesy of International Journal of Clinical Reviews
<http://www.remedicajournals.com/International-Journal-of-Clinical-Reviews/BrowseIssues/November-2010/Article-Nail-Psoriasis-topical-and-systemic-therapies>

Clinical Features

- In 60–70% of cases, psoriasis precedes joint disease.
- In 15–20% of cases, the two manifestations appear within 1 year of each other.
- In about 15–20% of cases, the arthritis precedes the onset of psoriasis.



- Widespread shortening of digits (“Telescoping”).
- Eye involvement, either conjunctivitis or uveitis, is reported in 7–33% of PsA patients.

Psoriatic Arthritis: Arthritis Mutilans—Telescoping

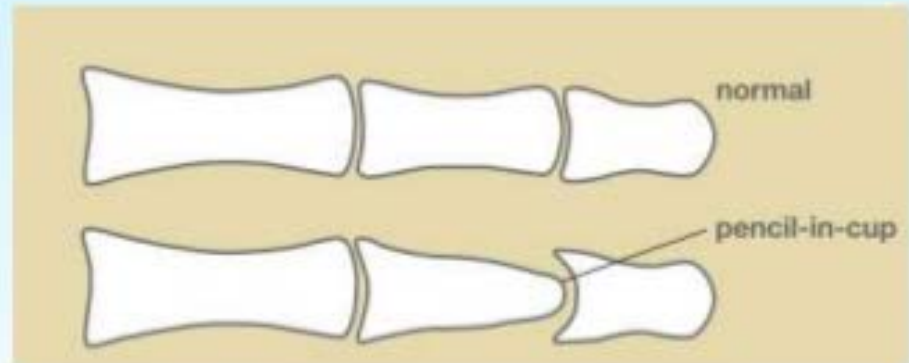


- Marginal proliferative erosions.
- Small-joint ankylosis.
- Osteolysis of phalangeal and metacarpal bone, with *telescoping* of digits.
- Periostitis and proliferative new bone at sites of enthesitis.



Radiographic Findings

- Characteristics of peripheral PsA include DIP involvement, including the classic "*pencil-in-cup*" deformity.

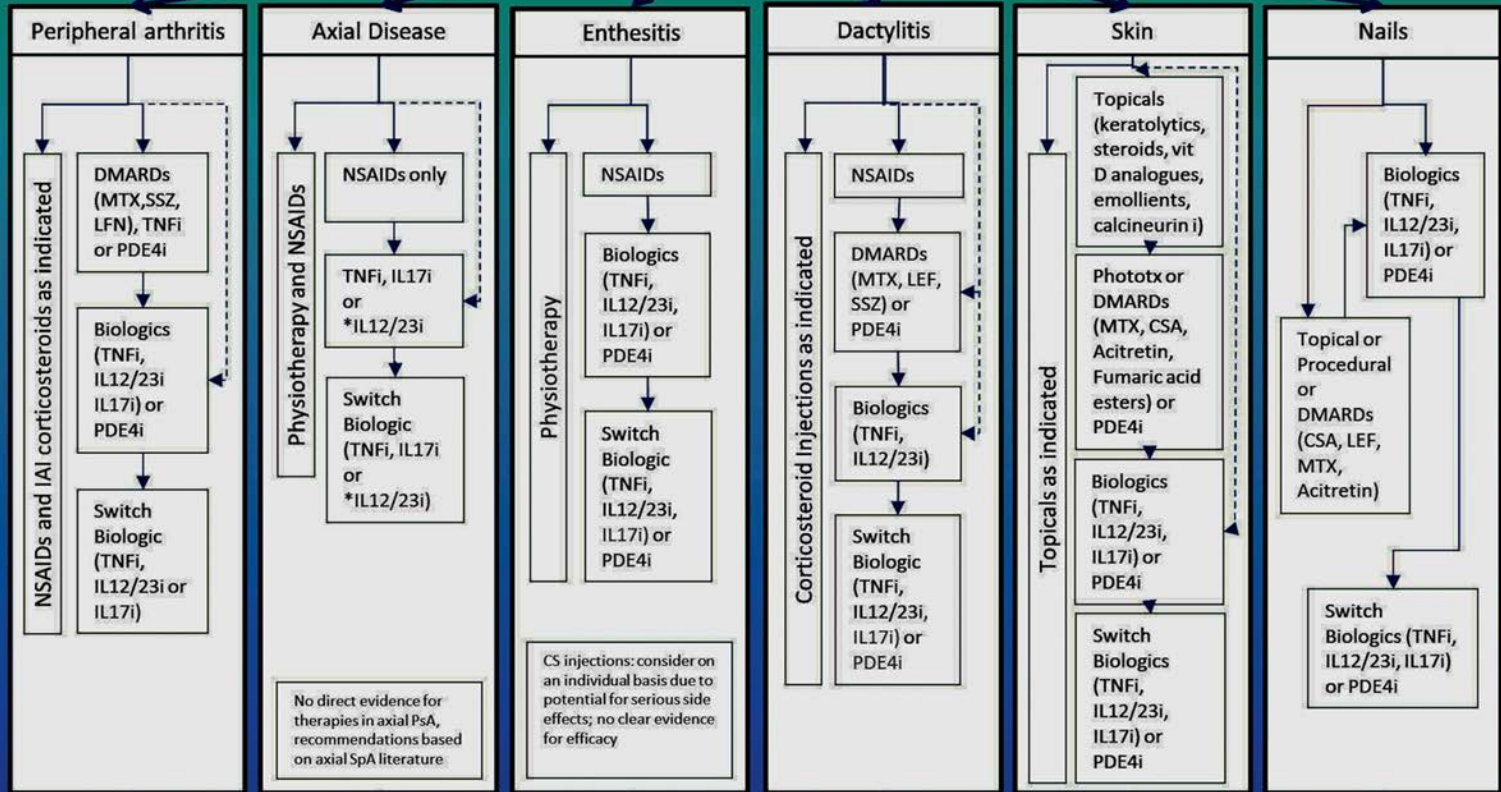


- Characteristics of axial PsA include *asymmetric sacroiliitis*; compared with idiopathic AS, less apophyseal joint arthritis, fewer and less symmetric and coarse syndesmophytes.



Which domains are involved?

Assess activity, impact and prognostic factors



Consider previous therapy, patient choice, other disease involvement and comorbidities. Choice of therapy should address as many domains as possible

Treat, periodically re-evaluate and modify therapy as required

GRAPPA Treatment Schema for PsA

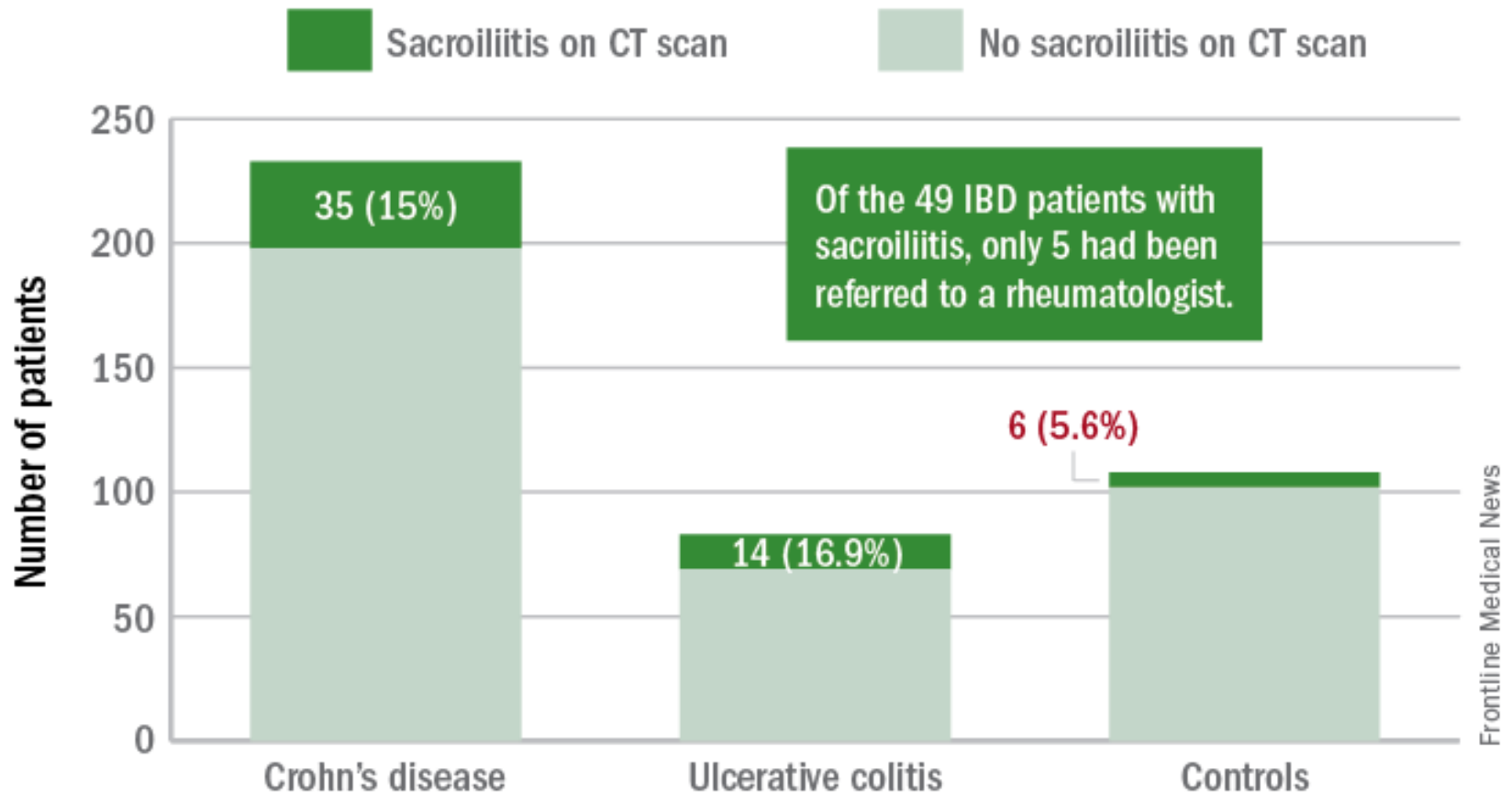
Enteropathic spondyloarthritis

- Inflammatory bowel disease: Ulcerative colitis and Crohn's disease
- Develop arthritis in 10-20%
 - Peripheral: 15%
 - Pauciarticular, asymmetric, favors lower extremities, large joints, - HLA B27
 - Nonerosive
 - Often correlated with bowel disease
 - Colectomy in UC->arthritis remission
 - Axial: like AS: 10%
 - Activity does NOT parallel bowel disease



HLA B2 + in 60%

Sacroiliitis prevalence in patients with inflammatory bowel disease

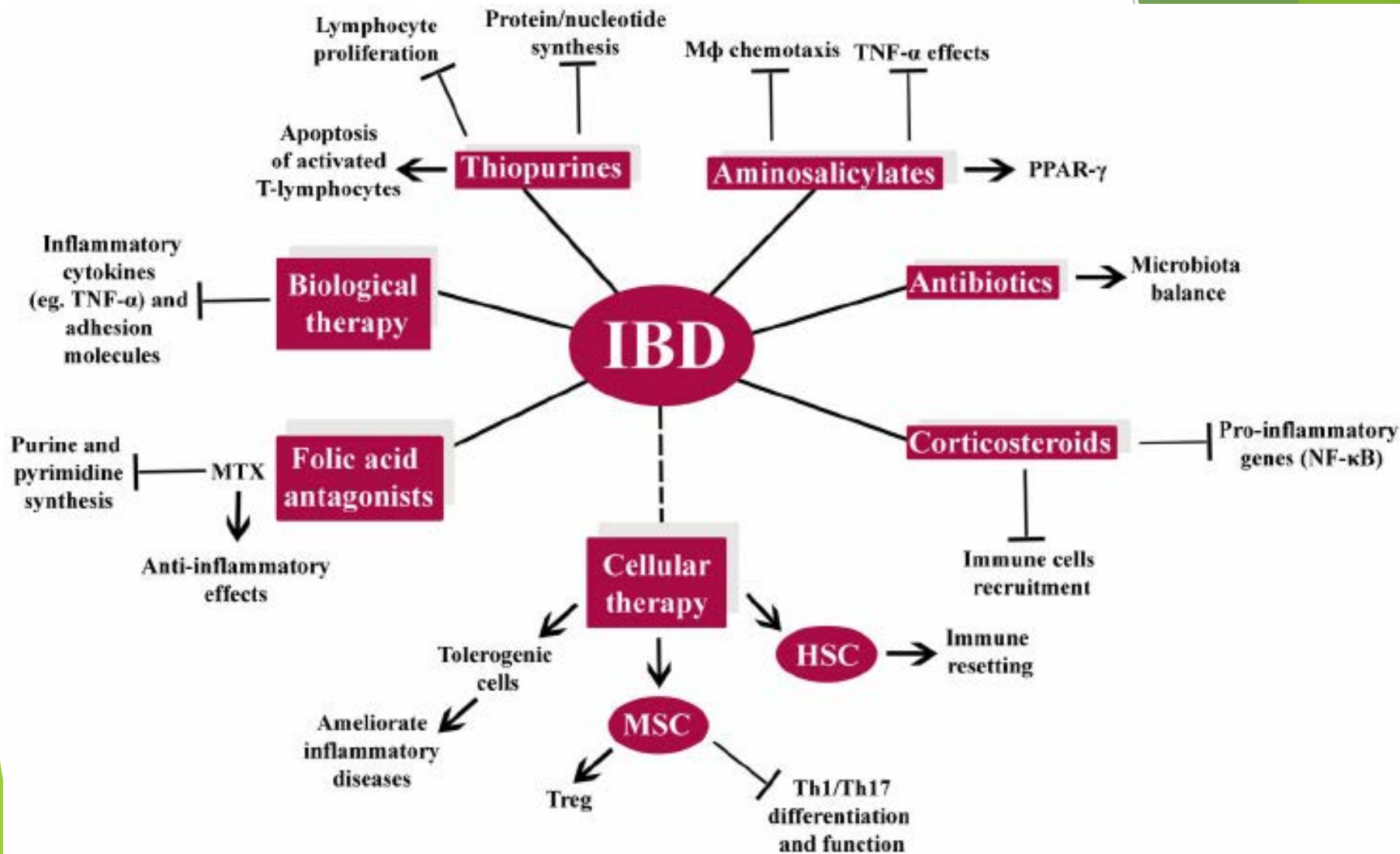


Note: IBD patients were recruited from an IBD clinic, controls from a urology clinic.

Source: Arthritis Care Res. 2017 .

Enteropathic spondyloarthritis

- Extraarticular manifestations:
 - Skin: erythema nodosum, pyoderma gangrenosum
 - Uveitis, oral ulcers
- Treatment:
 - Minimize NSAID use
 - SSZ: common treatment for IBD
 - TNF blockers:
 - Infliximab, adalimumab treat bowel disease also
 - Etanercept: doesn't work for bowel



Spondyloarthropathies

Enthesopathies

