

# Athletes and Rheumatic Diseases

## Hour 2: Axial Spondyloarthritis

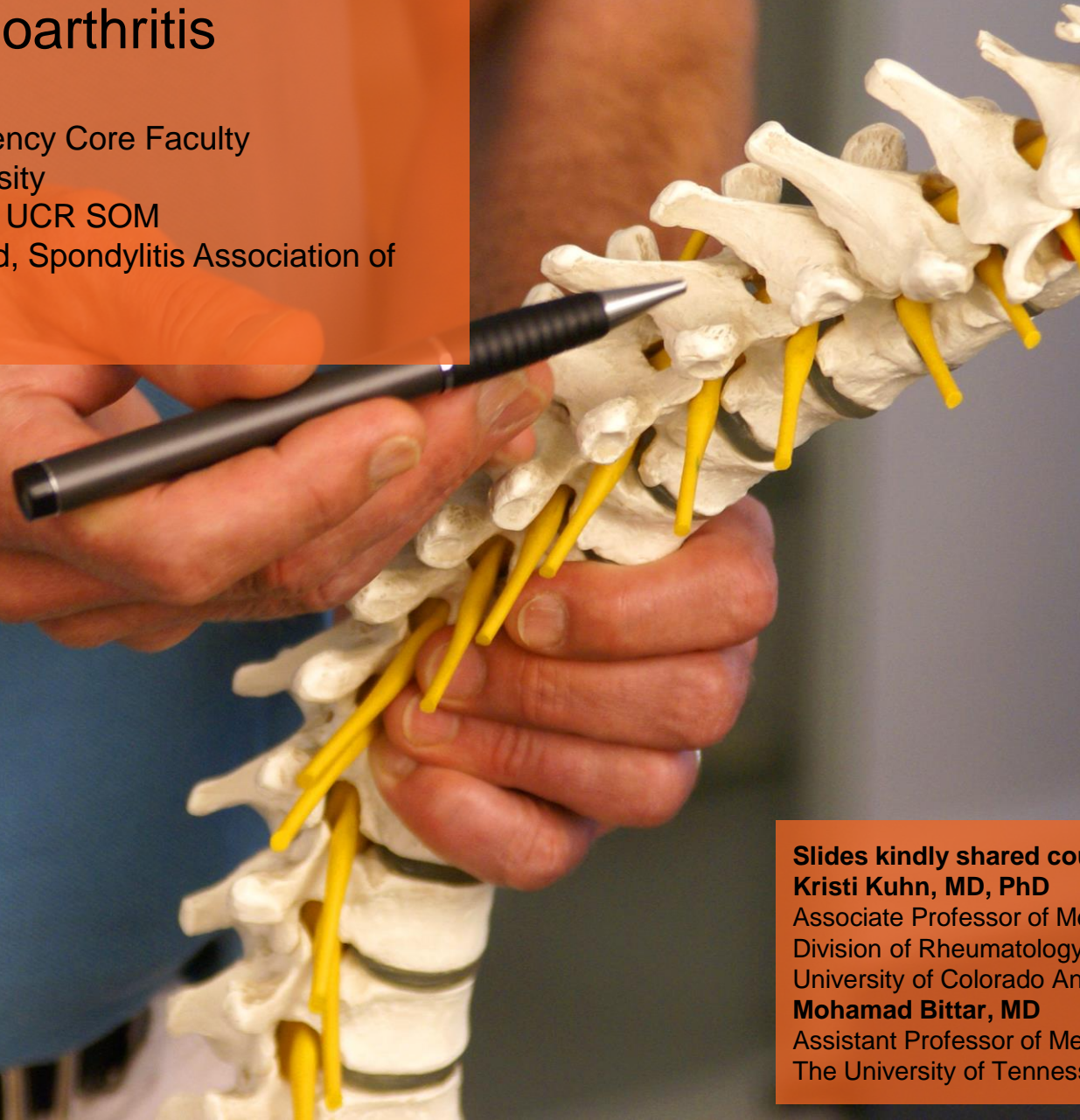
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Serving the Spondyloarthritis Community

**Slides kindly shared courtesy of SAA and colleagues:**

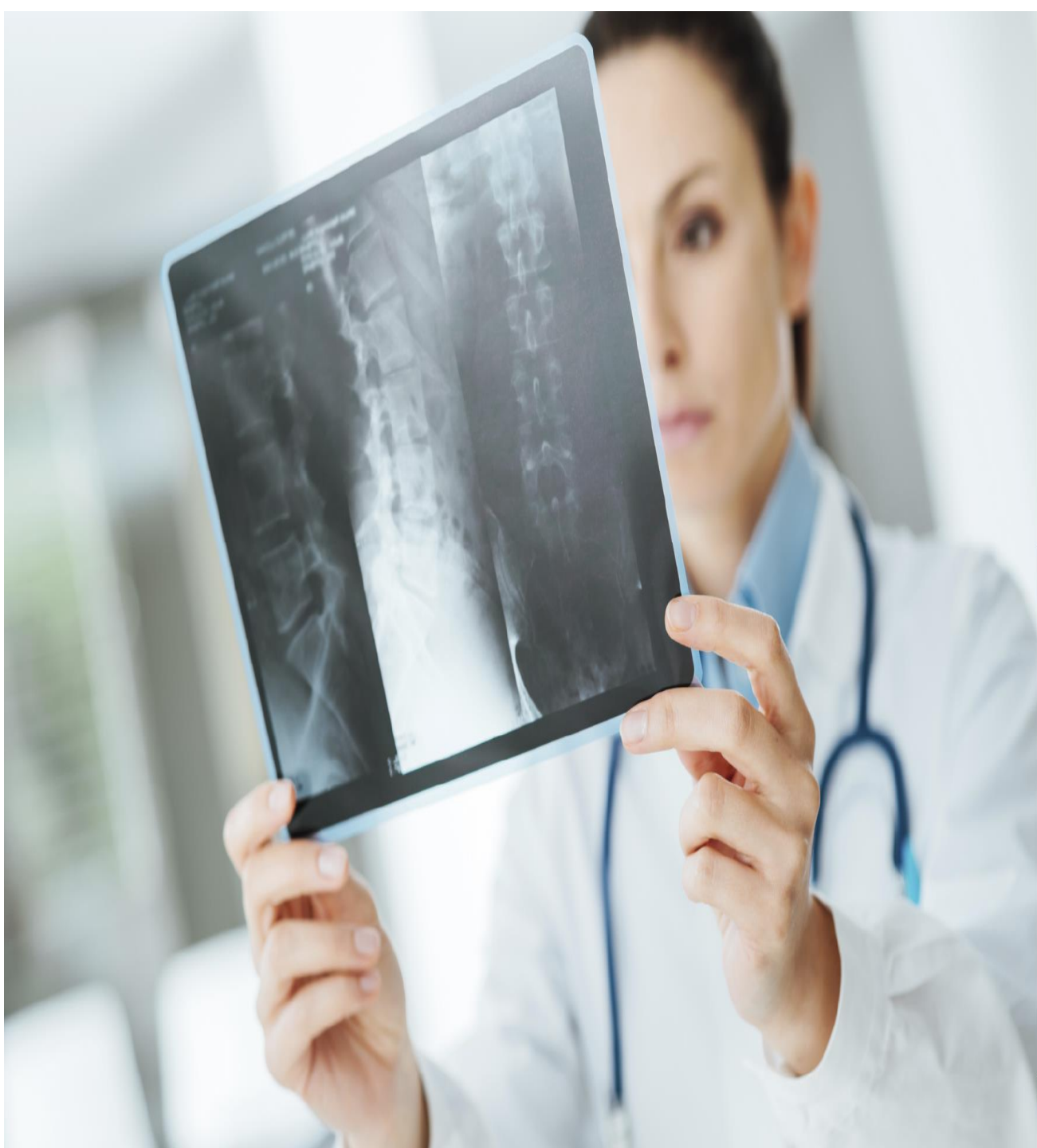
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Assistant Professor of Medicine  
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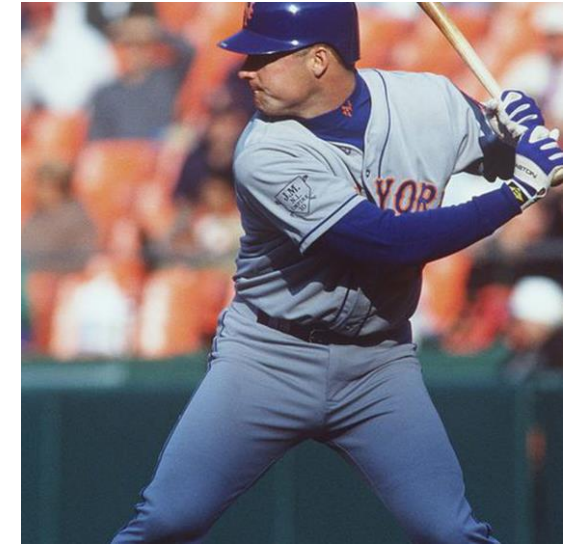


## Disclosures

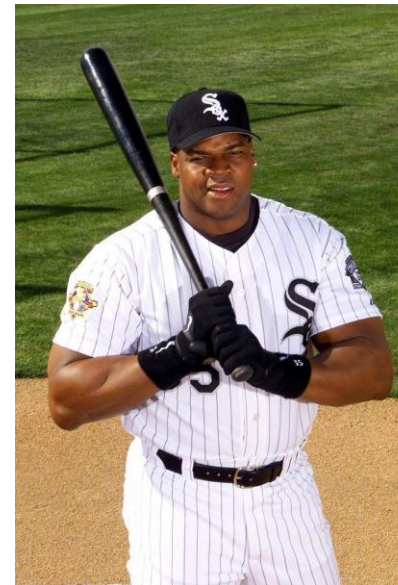
- Speaker:
  - Novartis
- Clinical Trials:
  - Roche/Genentech
  - Novartis
  - Amgen

# Case 1

- This 25 yo male professional baseball player started his MLB career in 1992 and holds the distinction for hitting the first home run in the opening season (1995) of Coors Field in Colorado. Several years later he developed chronic low back pain that required routine medications. He continued to play MLB but retired in 2001.



- Fred McGriff
- Frank Thomas
- Todd Helton
- John Kruk
- Rico Brogna

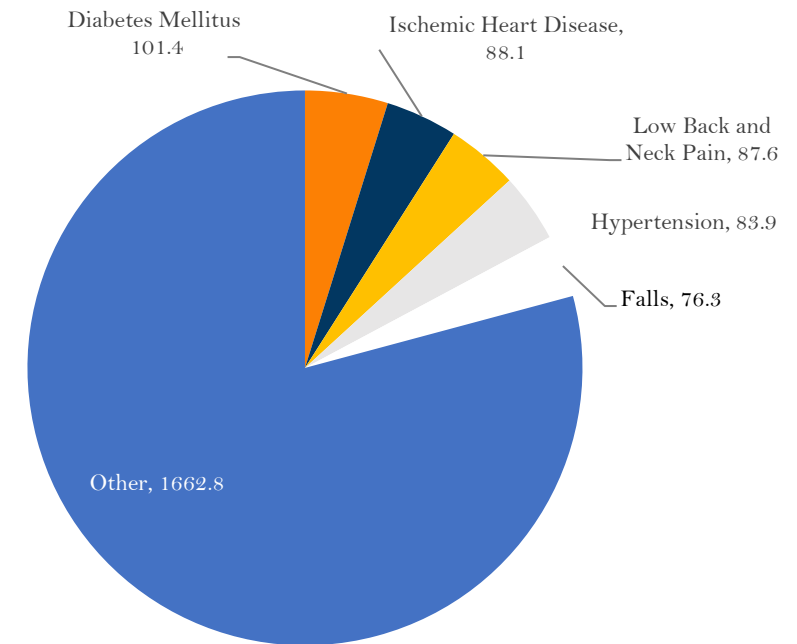




# Low Back Pain

- 26.4% of national survey respondents have experienced low back pain within the previous 3 months<sup>1</sup>
- Low back pain accounts for approximately 2% of visits to healthcare practitioners<sup>1</sup>

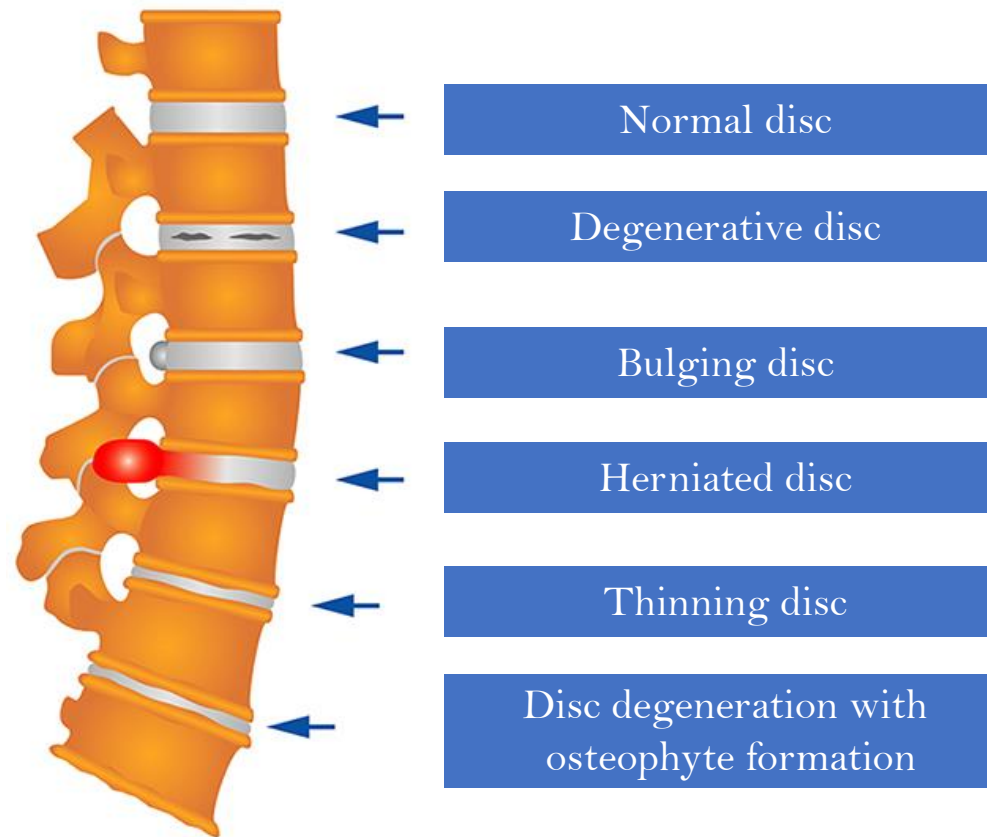
Personal Health Care Expenditures  
(Billions)<sup>2</sup>



Low back pain and neck pain account for the third highest US healthcare spending (1996-2013)<sup>2</sup>

# Common Causes of Back Pain<sup>1</sup>

- Lumbar strain
- Degeneration of spine
- Herniated disc
- Spinal stenosis
- Spondylolisthesis
- Osteoporotic compression fractures
- Spondylosis
- DISH
- Diffuse idiopathic skeletal hyperostosis



# Mechanical vs Inflammatory Back Pain

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## Mechanical back pain (MBP)

- Pain arising intrinsically from the spinal joints, intervertebral disks, or soft tissues<sup>1</sup>
- May be chronic but is usually acute and self-limiting<sup>2</sup>

## Inflammatory back pain (IBP)

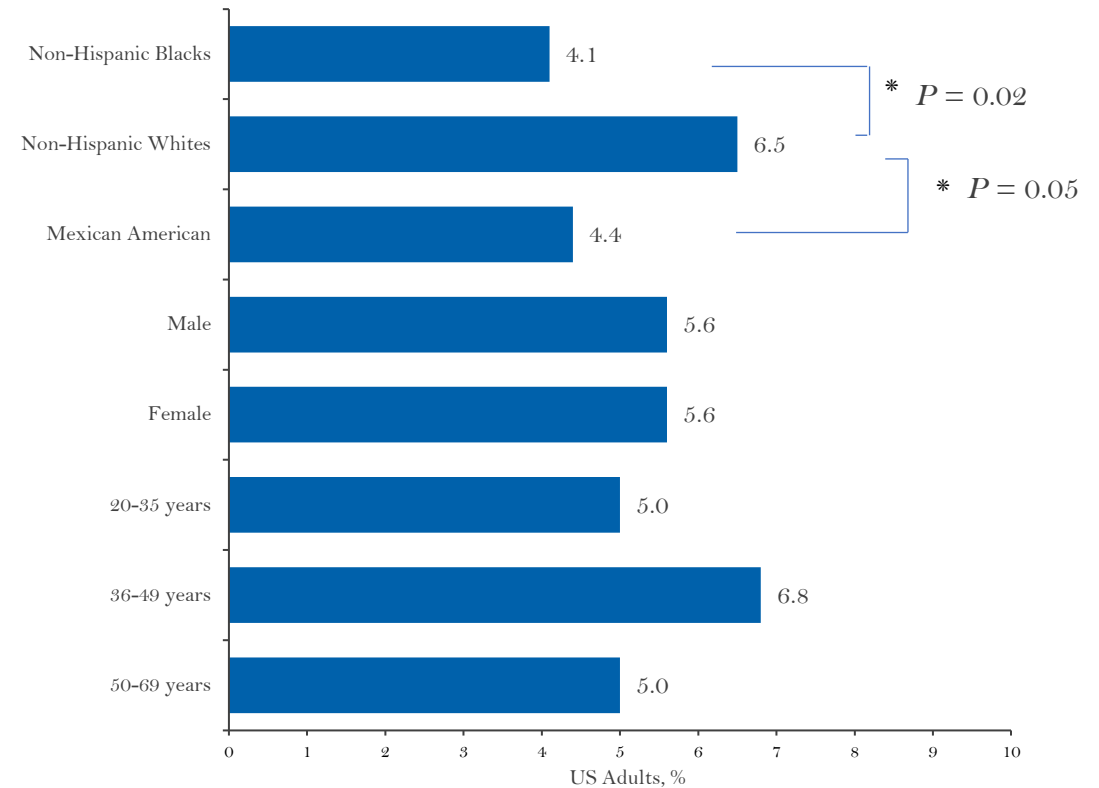
- Due to an underlying disease indicative of inflammation of the vertebrae, joints of the spine, and entheses<sup>2,3</sup>
- Age of onset is typically < 40 years; results in chronic back pain lasting > 3 months<sup>2</sup>

# Prevalence of Chronic and Inflammatory Back Pain<sup>1,2</sup>

Of 5103 US adults surveyed from 2009–2010, the NHANES study reported:<sup>1,2</sup>

- Point prevalence of **chronic low back pain** as **13.1%**
- Prevalence of **inflammatory back pain** as **5.6%** using **ESSG criteria**

IBP Criterion	ESSG
Spinal Pain Location	Neck/Dorsal/Back
Current Age	Any Age
Duration of Back Pain (3 Months)	√
“Insidious” Onset of Back Pain	√
Age-at-Onset Back Pain (years)	<45
Morning Stiffness > 30 Minutes	√
Pain Improves with Exercise or Activity	√



Prevalence of Inflammatory Back Pain Based on the ESSG Criteria (N = 274)<sup>2</sup>

\* Denotes significantly different

ESSG, European Spondyloarthritis Group; IBP, inflammatory back pain; NHANES, National Health and Nutrition Examination Survey.

1. Shmigel A, et al. *Arthritis Care Res.* 2016;68:1688-1694. 2. Weisman MH, et al. *Ann Rheum Dis.* 2013;72:369-373.



# Inflammatory Back Pain Criteria

## Calin et al

4/5 needed

- Age at onset <40 years
- Duration > 3 months
- Insidious onset
- Morning stiffness
- Improvement with exercise

Calin A, et al. JAMA  
1977;237:261;

## Rudwaleit et al

2/4 needed

- Alternating buttock pain
- Awakening at second half of the night because of pain
- AM stiffness > 30 mins
- Improvement with exercise, not with rest

Rudwaleit M, et al. Arthritis  
Rheum 2006;54:569-78;

## ASAS

4/5 needed

- Age at onset <40 years
- Insidious onset
- Improvement with exercise
- No improvement with rest
- Pain at night

Sieper J, et al. Ann Rheum Dis.  
2009, 68:784-788

# Distinguishing Inflammatory Back Pain: Questions based on rheumatologist-developed criteria<sup>1</sup>

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Do you find there is no improvement in your back pain when you rest?

Did your back pain start when you were < 40 years old?

Did your back pain develop gradually?

Do you suffer from back pain at night which improves upon rising?

Does your back pain improve with exercise?

**IBP requiring further investigation is usually indicated if the answer is “yes” to  $\geq 4$  of these parameters**

# Patient Case - Jim

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Chief complaint and reason for referral:  
“My back hurts”

Photo is for patient representation only. Case shared with permission from Dr. Steve Lee.

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# Patient Case History - Jim

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- 28 year old experiencing bilateral buttock and low back pain for the last four months
- Pain is dull and achy, but can also be sharp when coughing, sneezing, or while bending
- Pain radiates from the lower back to mid thigh
- Stiffness in the morning, which can last up to 4 hours
- Pain improves with hot showers and walking

# Patient Case - Jim: Rheumatology workup

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- No ankle pain
- Has an STD
- Eye redness
- Rashes
- Bloody diarrhea
- Labs
  - CBC and CMP are normal
  - ESR is elevated at 40mm/hr
- Ordered radiographs of L-spine and pelvis

Photo is for patient representation only. Case shared with permission from Dr. Steve Lee.

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CBC, complete blood count; CMP, comprehensive metabolic panel; ESR, erythrocyte sedimentation rate; L, lumbar; STD, sexually transmitted disease.

# Patient Case - Jim: Rheumatology workup

- L-spine and pelvic radiographs were “normal”
- Ordered MRI

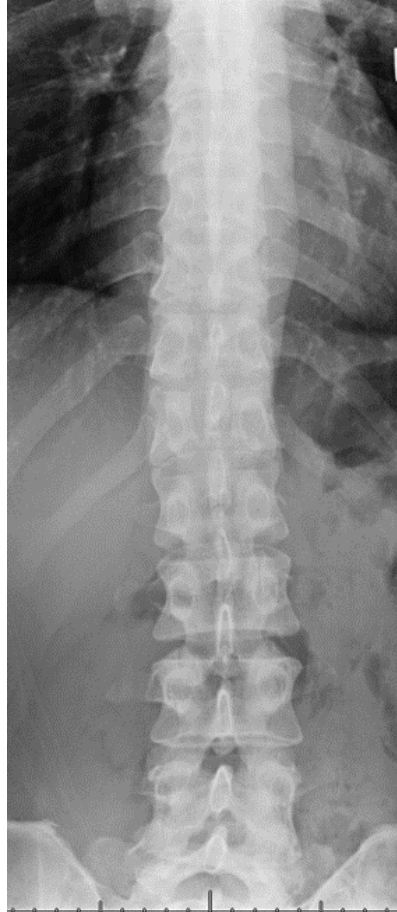
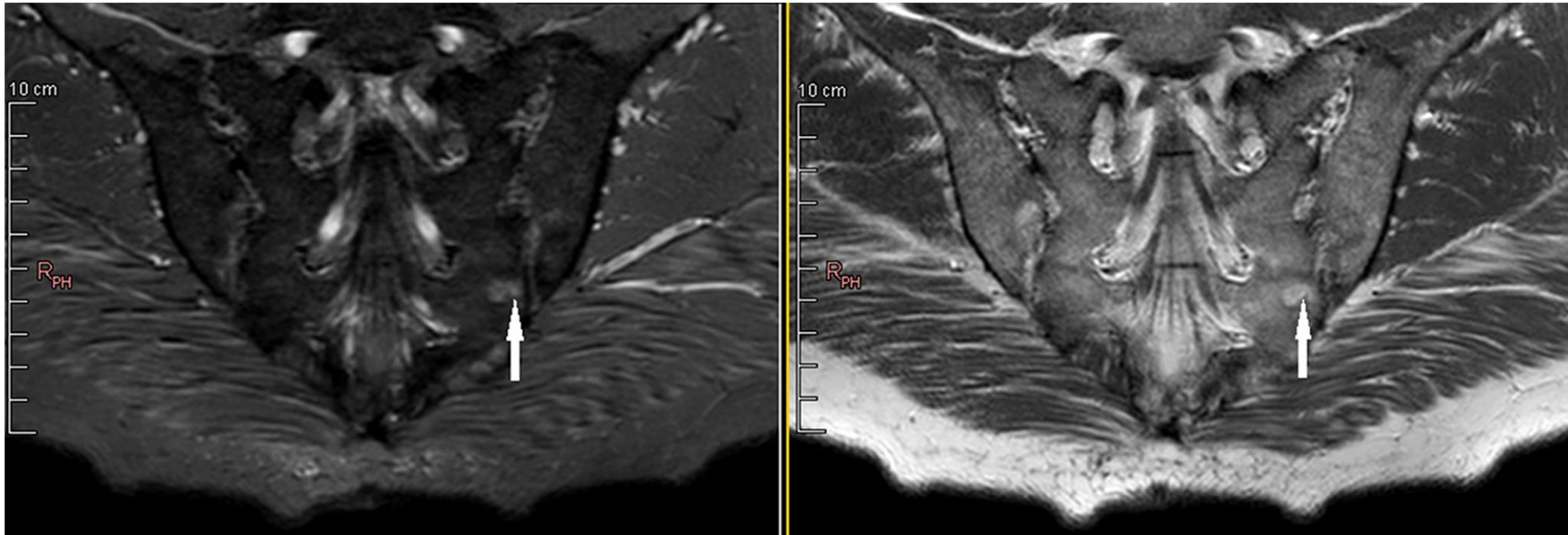


Photo is for patient representation only. Case shared with permission from Dr. Steve Lee.

L, lumbar; MRI, magnetic resonance imaging.

# Patient Case - Jim: Rheumatology workup

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With or without contrast, edema is observed on the MRI

Case shared with permission from Dr. Steve Lee.

MRI, magnetic resonance imaging.

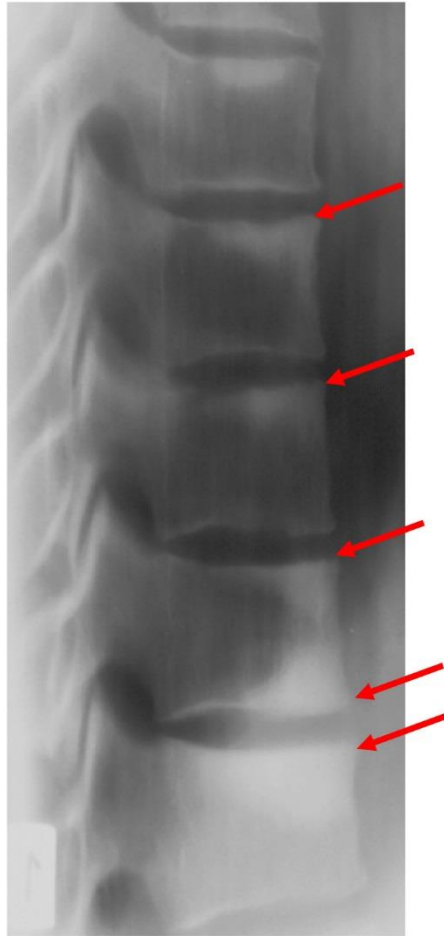
1. Kucybala I, et al. *Rheumatol Int.* 2018;38:1753-1762.

# What is axSpA?





# Evidence of Chronic Spinal Changes in Ankylosing Spondylitis



Sclerosis  
„shiny corners“



Syndesmophytes  
(and spondylophytes)



Bridging  
syndesmophytes

# Progression of Cervical Syndesmophytes 2-Year Intervals



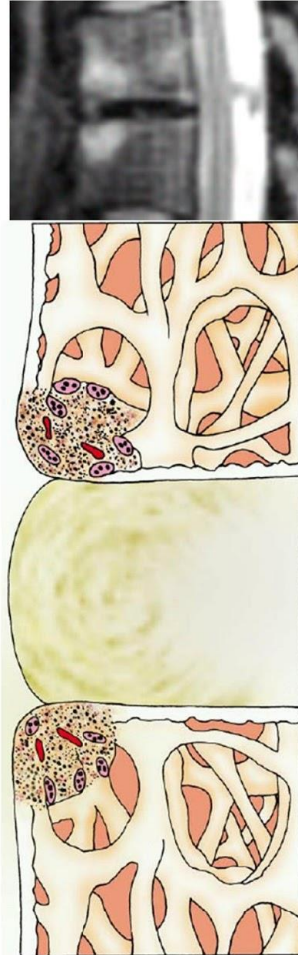
**AS, m, 30 y, disease duration 14 y**

ASAS handbook, Ann Rheum Dis 2009; 68 (Suppl II) (with permission)



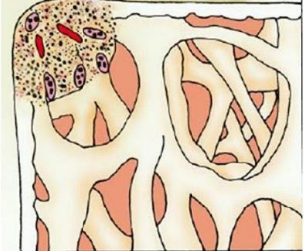
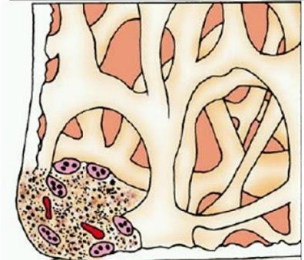
# Proposed Sequence of Structural Damage in Ankylosing Spondylitis

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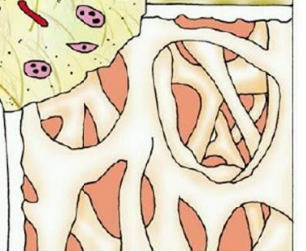
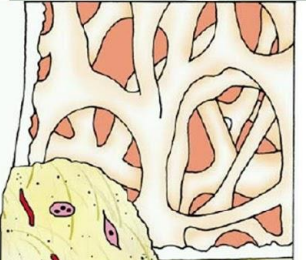
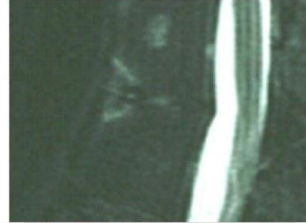


Inflammation

# Proposed Sequence of Structural Damage in Ankylosing Spondylitis

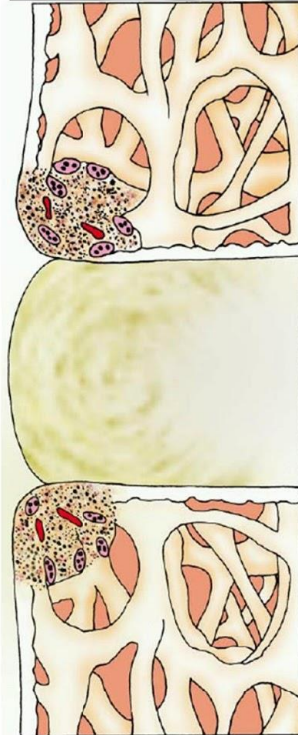


Inflammation

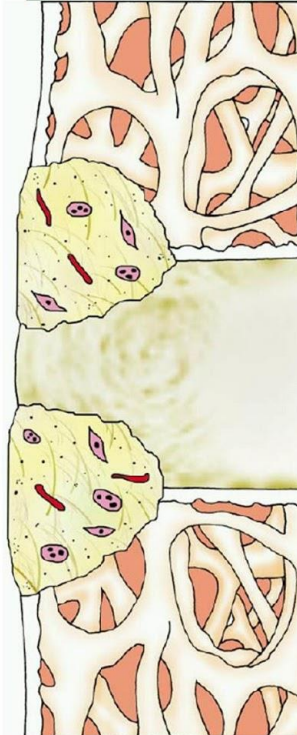
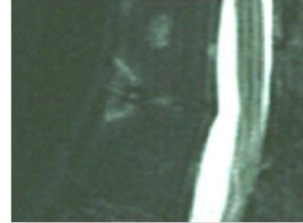


Erosive damage  
Repair

# Proposed Sequence of Structural Damage in Ankylosing Spondylitis



Inflammation

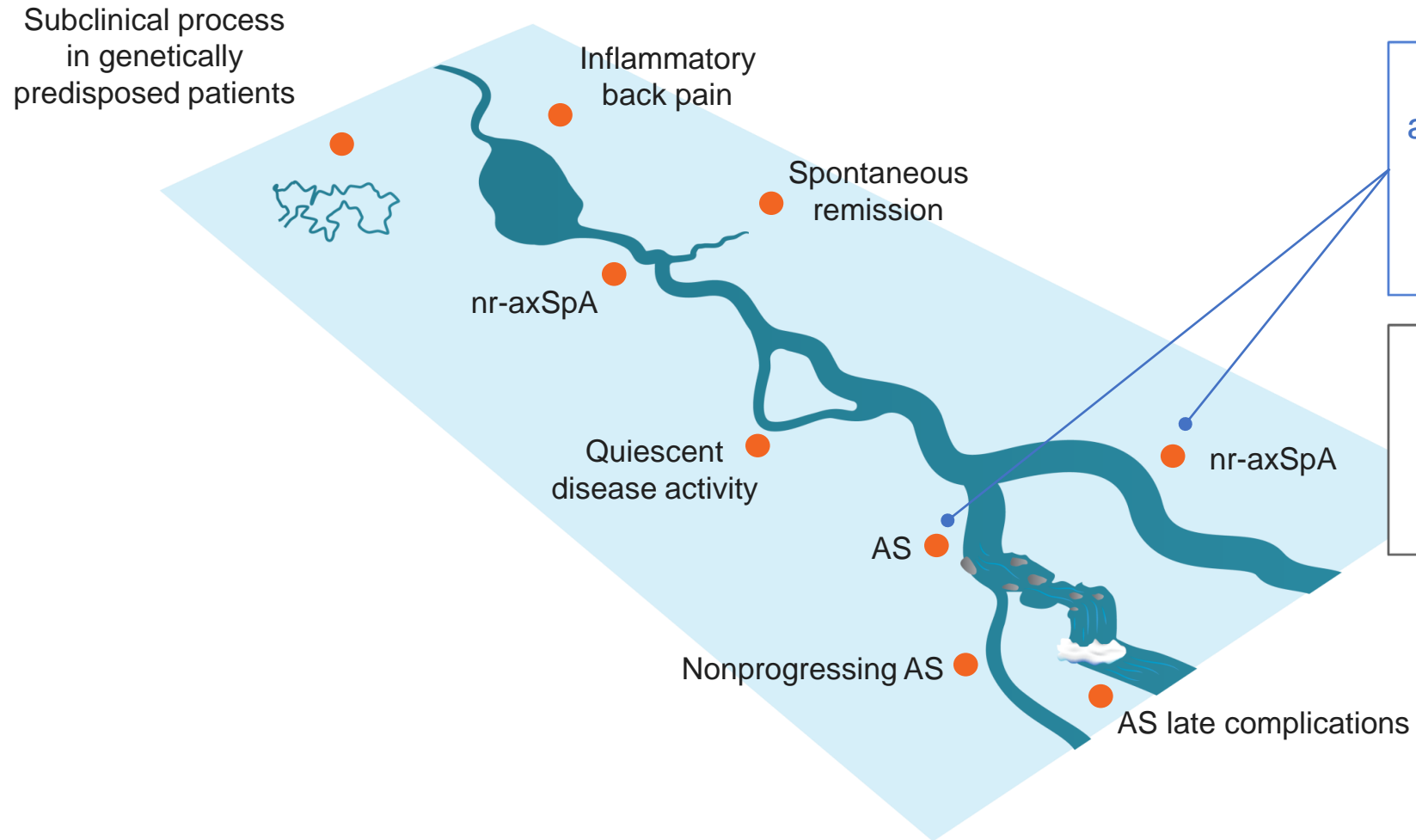


Erosive damage  
Repair



New bone formation

# The Natural History of axSpA Includes AS and nr-axSpA<sup>1,3</sup>



The terms AS and nr-axSpA are distinguished by the degree of “radiographic sacroiliitis” assessed by conventional radiography<sup>2</sup>

**These terms should only be used for classification of patients with axSpA and not as separate diagnoses<sup>2</sup>**

# Patient Case - Linda

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Chief complaint and reason for referral:  
“My neck is stiff and my toe is swollen”

Photo is for patient representation only. Case shared with permission from Dr. Steve Lee.

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# Patient Case History - Linda

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- 48 year old medical assistant diagnosed with fibromyalgia and depression
- Fifth toe on her right foot has been swollen for the past 3 weeks – getting worse despite mild improvement with NSAIDs
- Intermittent, mild-to-moderate low back pain for years
- Recently filed for medical leave as fatigue causes her to often miss work

Case shared with permission from Dr. Steve Lee.

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# Patient Case - Linda: Rheumatology workup

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- Moderate swelling of the fifth digit on the right foot
- Labs:
  - Normal CBC, ESR, uric acid and BUN/CRE
  - Elevated CRP at 25.0 mg/L
- Ordered radiograph of feet



Photo is for patient representation only. Case shared with permission from Dr. Steve Lee.

# Patient Case - Linda: Radiographic changes

- Radiograph of feet to examine changes in joint space
- What anomaly stands out on the radiograph?

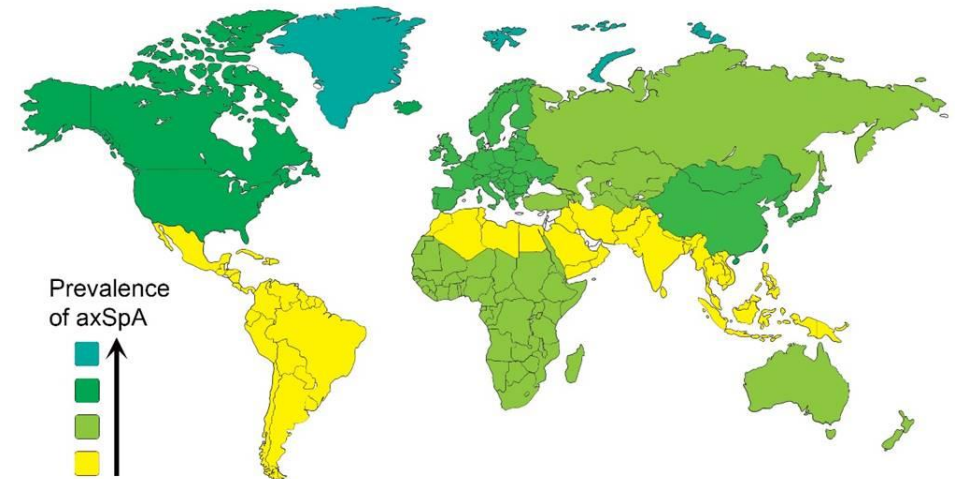


Case shared with permission from Dr. Steve Lee.

# What is axSpA?

Old Concept: AS, Young, Northern European, Males, full fusion of the spine

Now: Men=Women, heterogeneous, global disease, “non-radiographic”



**Just under 1% have axSpA worldwide**

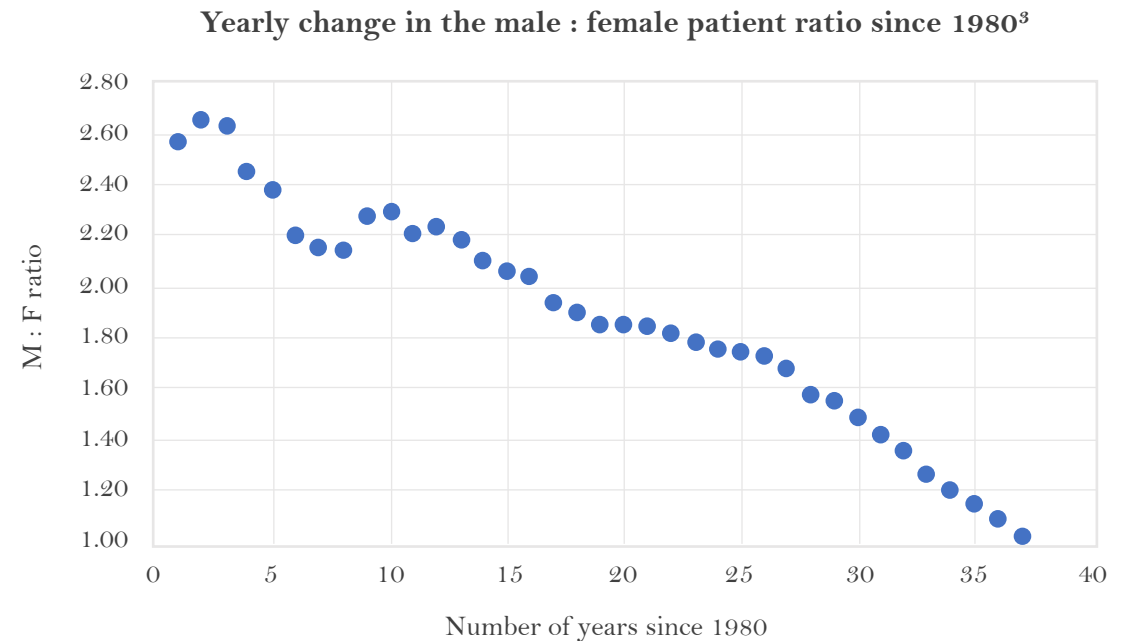
# Prevalence and Sex

## US prevalence<sup>1,2</sup>

- Dependent on criteria used to assess axSpA
- ASAS criteria: 0.7% of the population
- ESSG criteria: 1.4% of the population

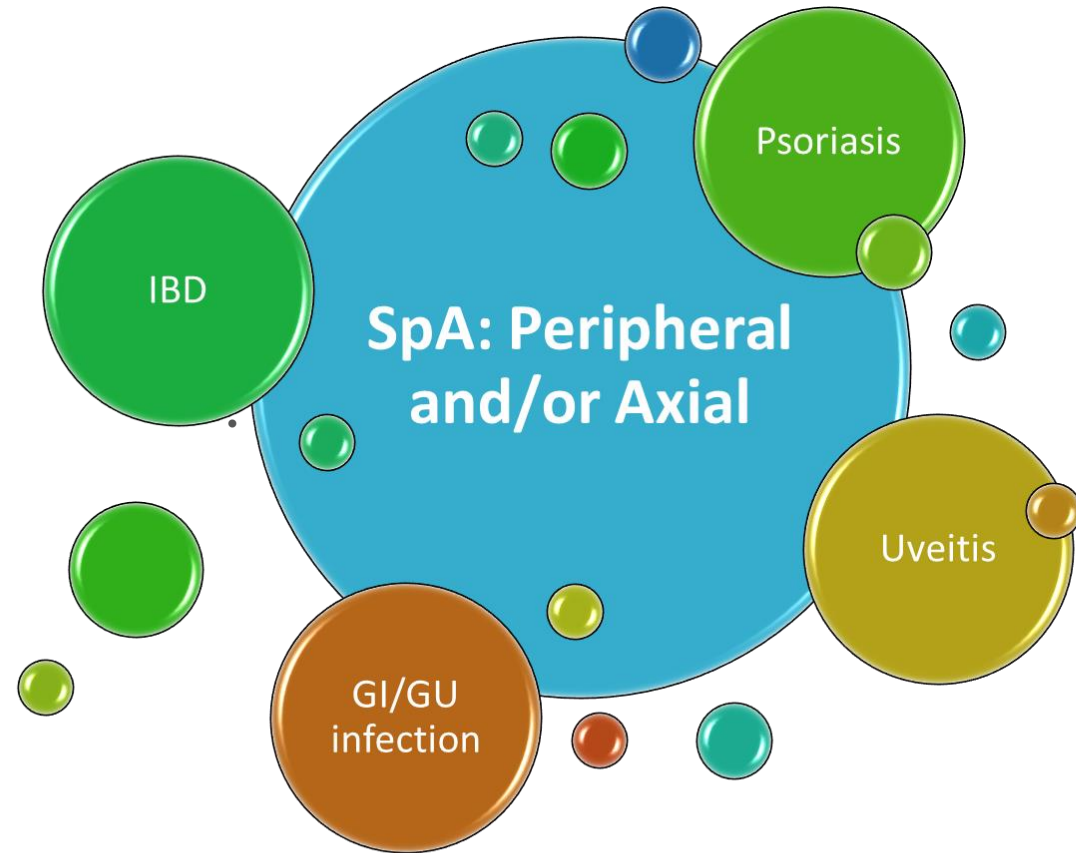
## Diagnosis rates in men and women<sup>3</sup>

- Data for Switzerland previously presented at EULAR indicated the decline in the M : F diagnosis ratio
- M : F ratio at 2.57 : 1 in 1980, down to 1.03 : 1 in 2016 within this population

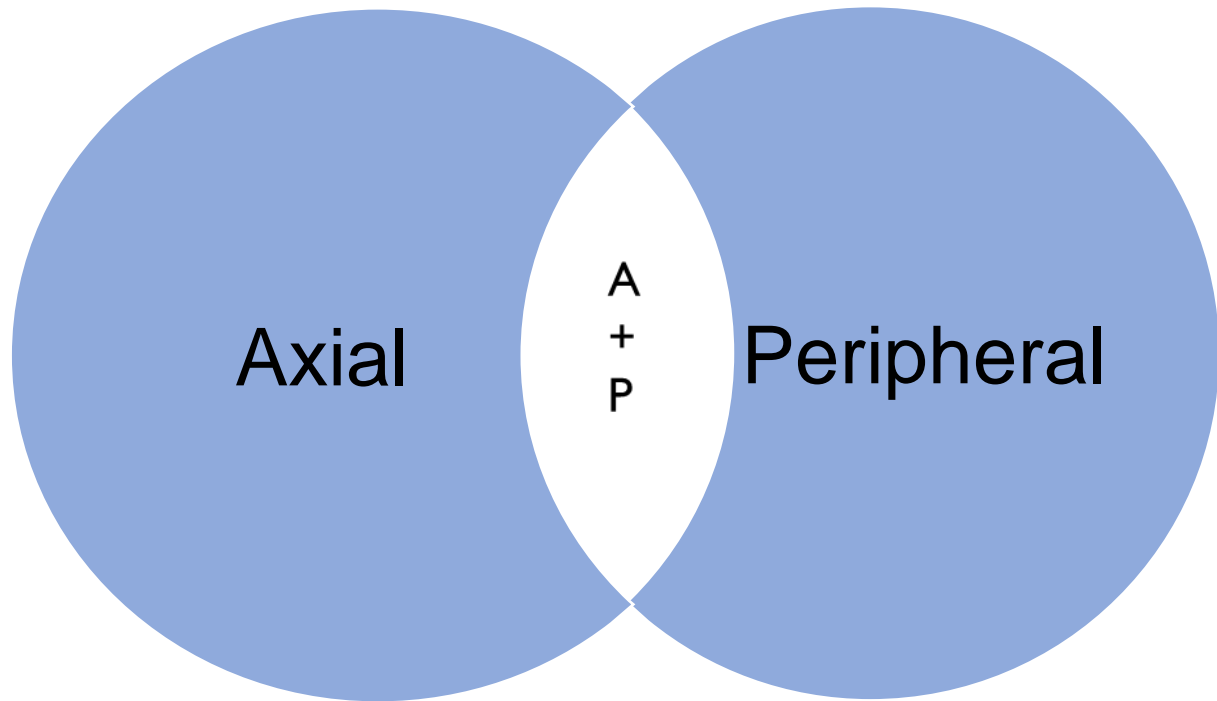


# AxSpA is Part of a Spectrum of Diseases Under the Umbrella of Spondyloarthritis

- May have overlapping features of multiple diseases in this family
- Shared genetic risks:
  - e.g. IL-23R, STAT3, NFkB1, IL2RA

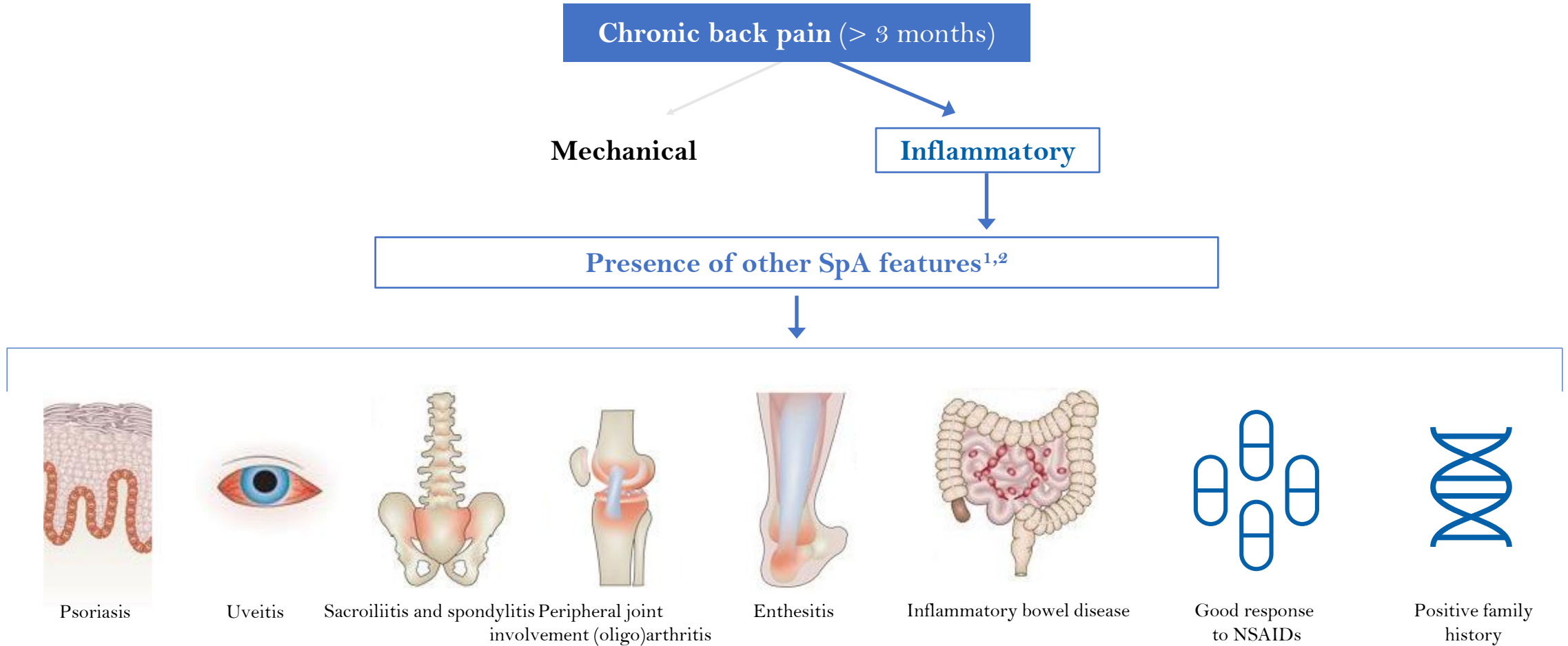


# Spondyloarthritis



- Ankylosing Spondylitis
- Non-radiographic axSpA
- Psoriatic arthritis
- Enteropathic arthritis
- Reactive arthritis
- Undifferentiated

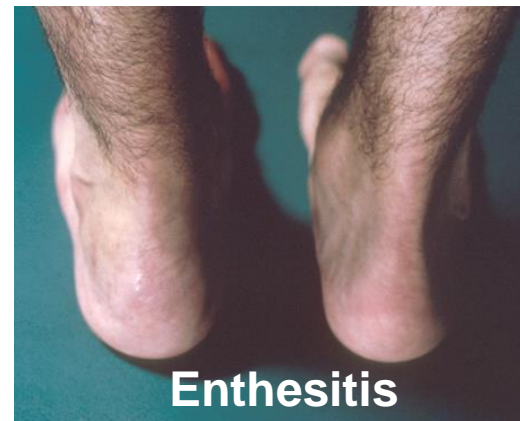
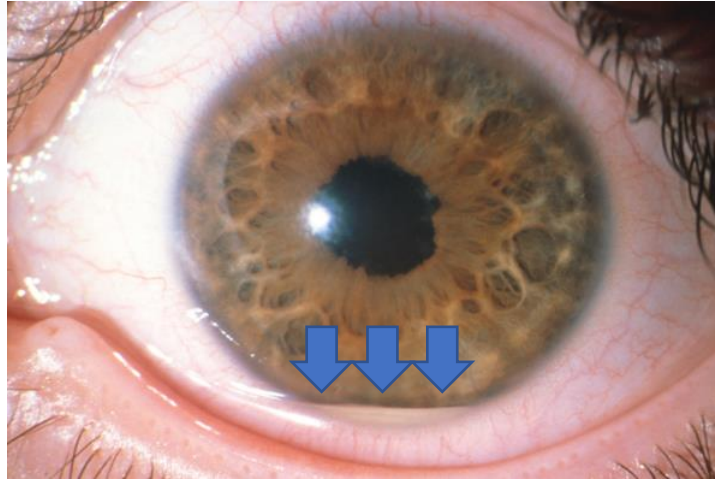
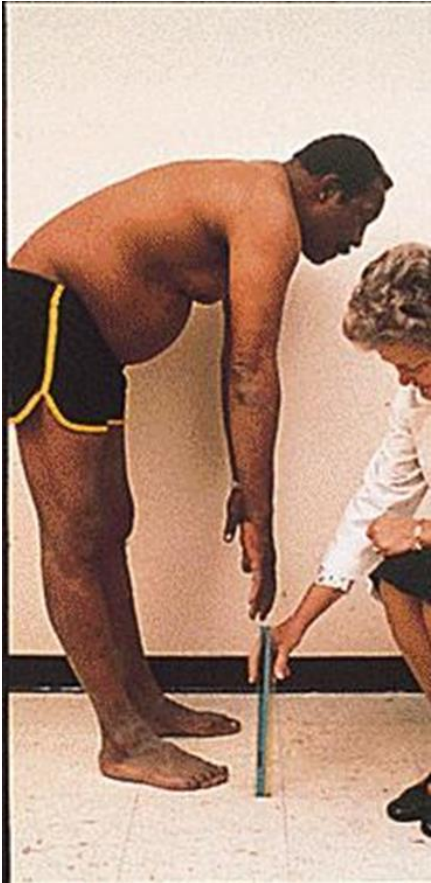
# Inflammatory Back Pain: Hallmark feature of axSpA



axSpA, axial spondyloarthritis; NSAIDs, nonsteroidal anti-inflammatory drugs; SpA, spondyloarthritis.

1. Rosenbaum JT, Rosenzweig HL. *Nat Rev Rheumatol.* 2012;8:249-250. 2. Rudwaleit M, et al. *Ann Rheum Dis.* 2009;68:777-783.

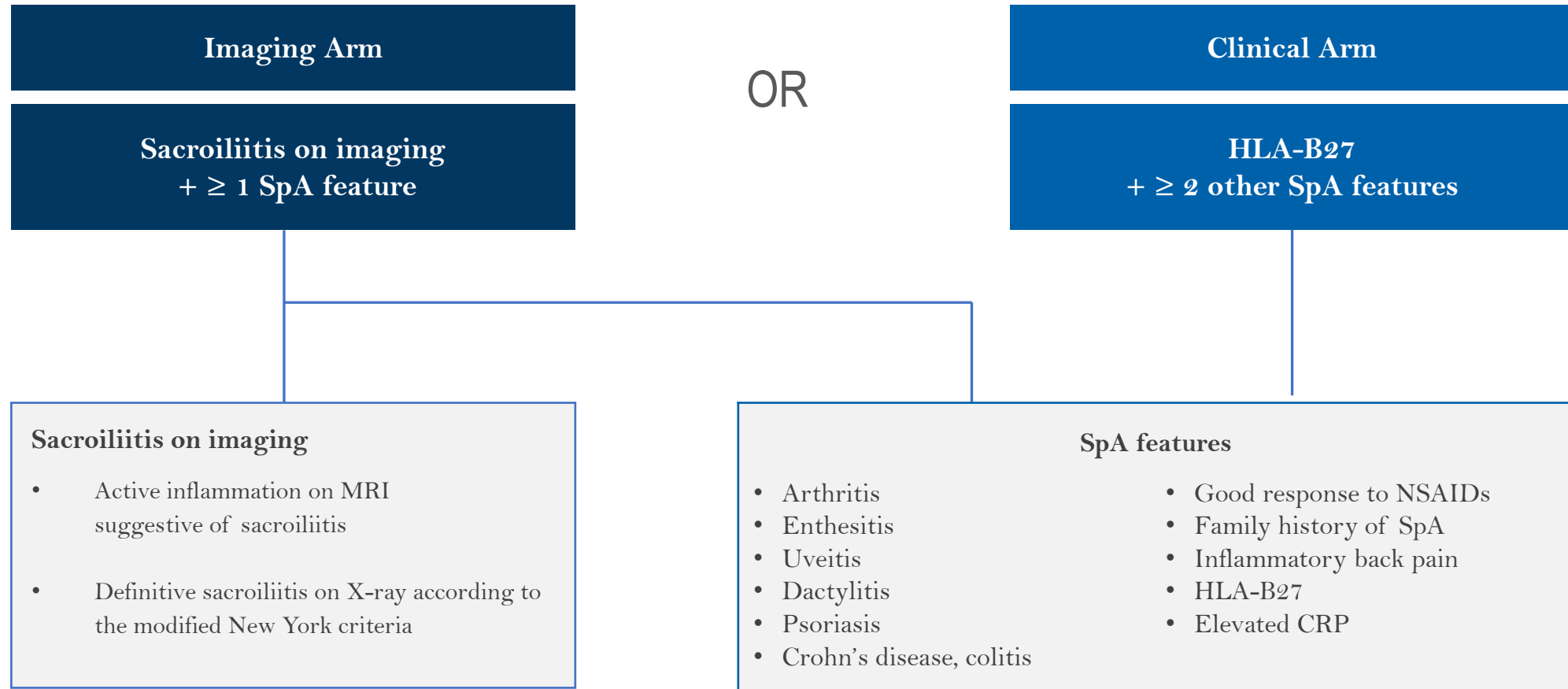
# Exam findings:





# ASAS Classification Criteria for axSpA<sup>1</sup>

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



ASAS, Assessment of SpondyloArthritis international Society; axSpA, axial spondyloarthritis; CRP, C-reactive protein; HLA-B27, human leukocyte antigen B27; MRI, magnetic resonance imaging; NSAIDs, nonsteroidal anti-inflammatory drugs; SpA, spondyloarthritis.

1. Rudwaleit M, et al. *Ann Rheum Dis*. 2009;68:777-783.

# The Role of HLA-B27 in Diagnosis...

- The prevalence of HLA-B27 within patient populations with SpA ranges 50-95%.
- SpA occurs in about 2% of the general population and in just over 10% of HLA-B27 positive individuals.
- **Despite a strong association with HLA-B27:**
  - ~80% of individuals with the gene don't get AS
  - ~20% of individuals with AS don't have the gene



# Treatment of axSpA

NSAIDs

- Continuous > on-demand
- No clear evidence for disease modification

TNFi

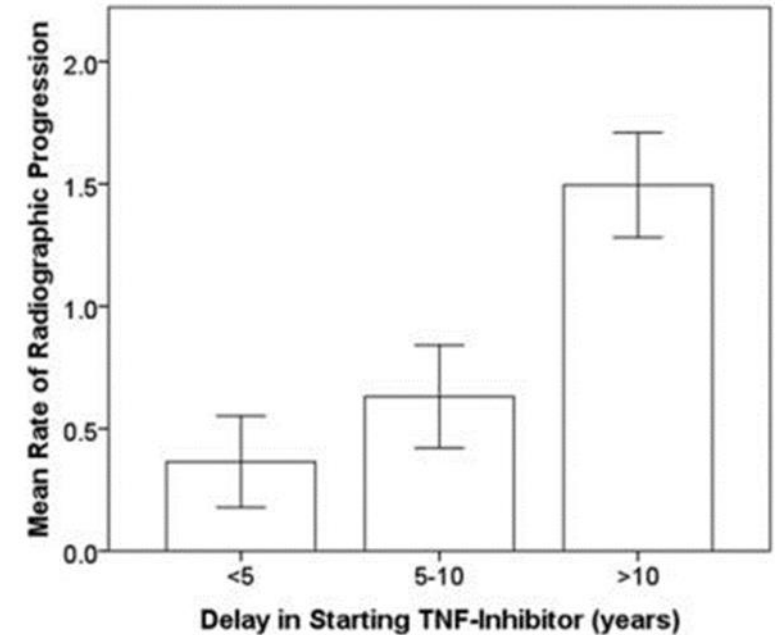
- Numerous trials with support for disease modifications

IL-17Ai

- Newest class; data limited with regards to disease modification
- Co-morbidities (IBD) may limit use

JAKi

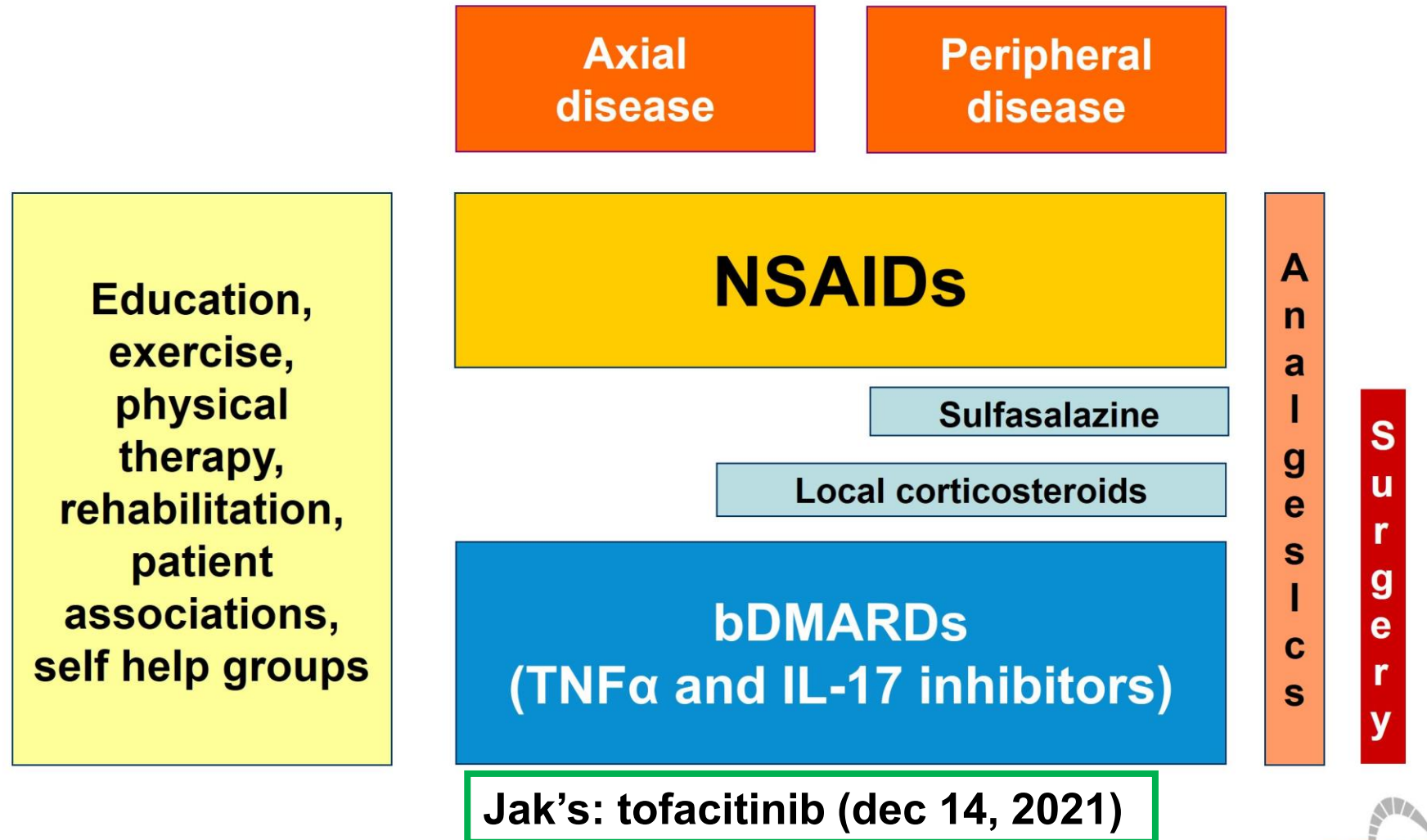
- Data in efficacy are early but promising



Haroon N et al. Arthritis & Rheumatology 2013.  
Ward MM et al. Arthritis & Rheumatology 2019

CRP and imaging may be helpful in monitoring response to therapy, not generally recommended.

# ASAS-EULAR Recommendations for the Management of Axial Spondyloarthritis



# Exercise!



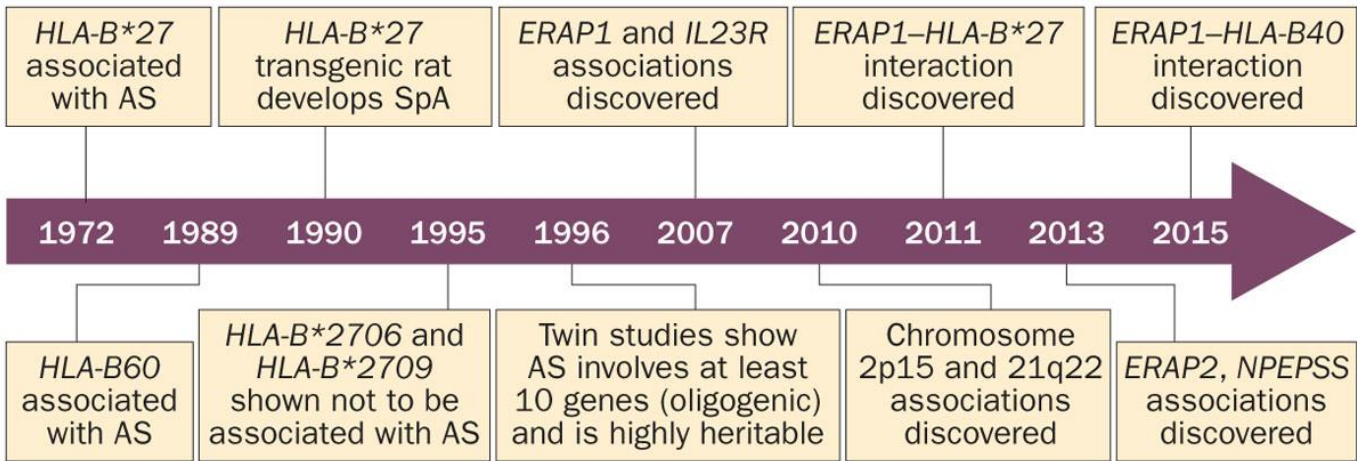
Physical function  
Mobility



Pain  
Patients' feelings of disease  
being active



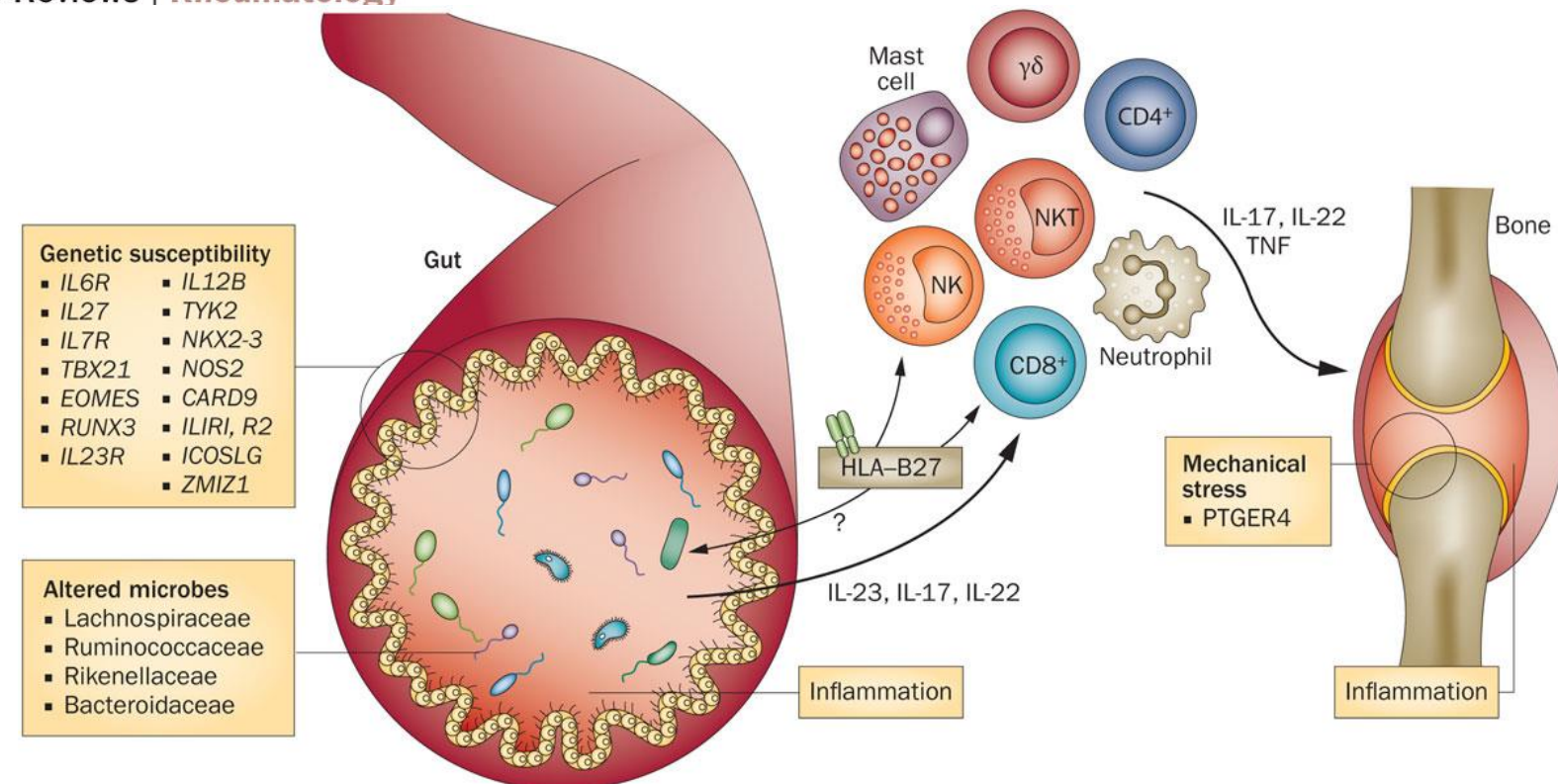
<https://spondylitis.org/about-spondylitis/treatment-information/exercise/>



# On the Horizon?

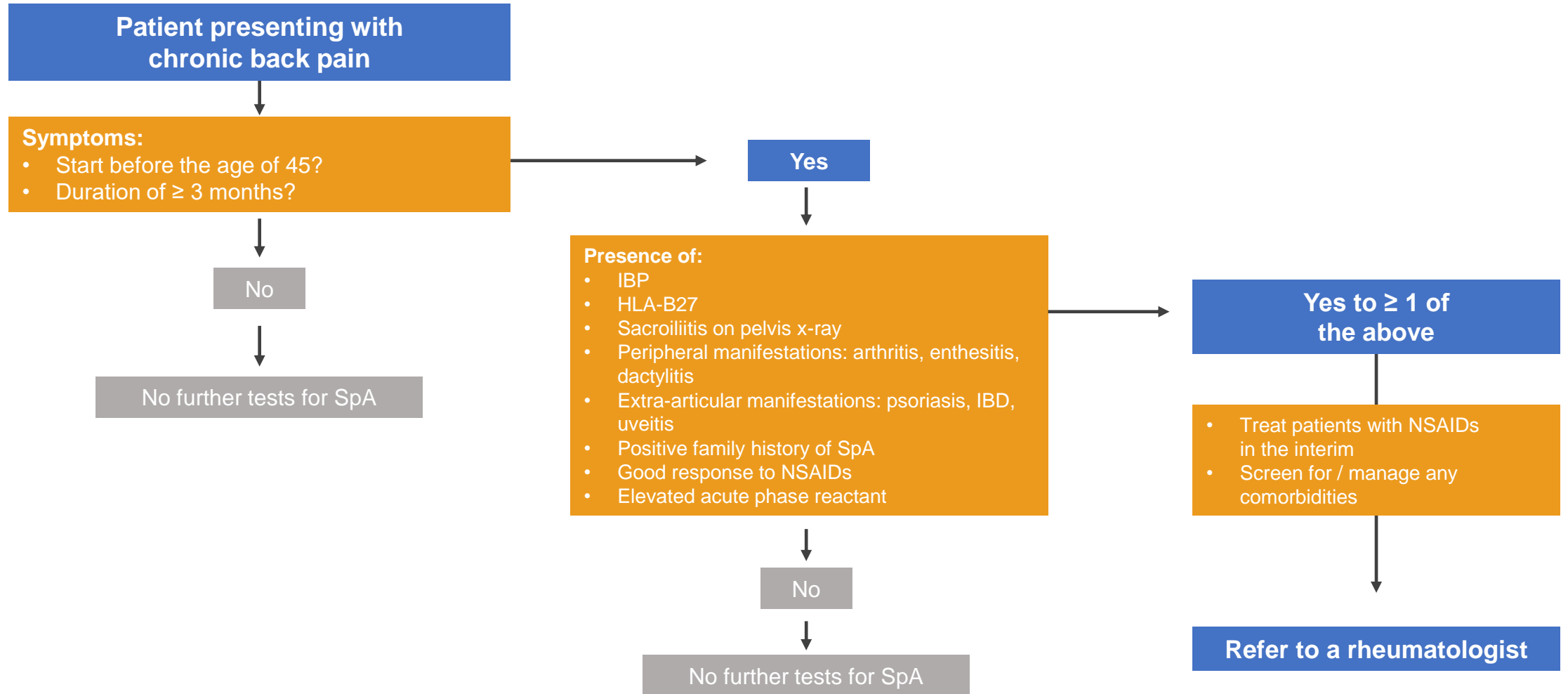
- Genetic risk scores
- Microbiome profiles
- Other blood factors

Nature Reviews | Rheumatology



Brown MA et al. Nature Reviews Rheumatology 2020

# Example Algorithm for Rheumatology Referral



# In Summary:

Patients presenting with features of axSpA should be referred to rheumatology

Decreasing the time to diagnosis could mean improved function and better management of patients with axSpA



Prevalence of axSpA may be greater than RA<sup>1-4</sup>



Features of axSpA include **axial, peripheral, and extra-articular** manifestations<sup>5</sup>



PCPs have an **important role in earlier** recognition of axSpA through **greater disease awareness**<sup>6</sup>

axSpA, axial spondyloarthritis; PCP, primary care physician; RA, rheumatoid arthritis.

1. Strand V et al. *Arthritis Care Res*. 2013;65(8):1299-1306. 2. Reveille JD et al. *Arthritis Care Res (Hoboken)*. 2012;64:905-910. 3. Curtis JR et al. *Perm J*. 2016;20(4):15-151.

4. Helmick CG et al. *Arthritis Rheum*. 2008;58(1):15-25. 5. Deodhar AA. *Am J Manag Care*. 2019;25(17):S319-S330. 6. Deodhar A et al. *Arthritis Rheumatol*. 2016;68(7):1669-1676.