Seronegative Spondyloarthropathies (SpA)

Objectives:

- Introduction
- SpA disease information
- Pathogenesis
- Clinical features

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Resources: 435 team + Davidson + kumar + Recall questions step up to medicine + Slides

- **Editing file**
- **Feedback**

- ## General Characteristic of SPA:

What is it?

These comprise a group of related inflammatory joint diseases, which show considerable overlap in their clinical features and a shared immunogenetic association with the HLA-B27 antigen[1], **They include:**

- Ankylosing spondylitis **(AS)**
- Psoriatic arthritis **(PsA)**
- Reactive arthritis (sexually acquired, Reiter's disease) **(ReA)**
- Enteropathic IBD related arthritis (Ulcerative colitis/Crohn's disease)
- Non-Radiographic Axial spondyloarthritis **(nr-axSpA)**
- Undifferentiated peripheral SpA

NEW YORK Criteria: MRI findings, Extra-articular features and HLA-B27.

Updated ASAS Concept of Spondyloarthritis (SpA):

Groups Diseases into 2 Broad Overlapping Categories:-

1-**Predominantly axial SpA**: (non-radiographic Axial spa) Ankylosing spondylitis.
2-**Predominantly peripheral SpA**: Psoriatic arthritis - Reactive arthritis - Enteropathic IBD related arthritis - Undifferentiated peripheral SpA.

- ## Back pain:
  - 80% of the population will experience back back pain during their lifetime.
  - More than 85% cannot attribute it to a specific disease or spinal abnormality.
  - Up to one third of patients report persistent back pain of at least moderate intensity 1 year after an acute episode.

Low Back pain caused by a specific disorder such as:

- Compression fracture
- Symptomatic herniated disc
- Spinal stenosis
- Ankylosing spondylitis (3%)
- Cancer
- Spinal infection

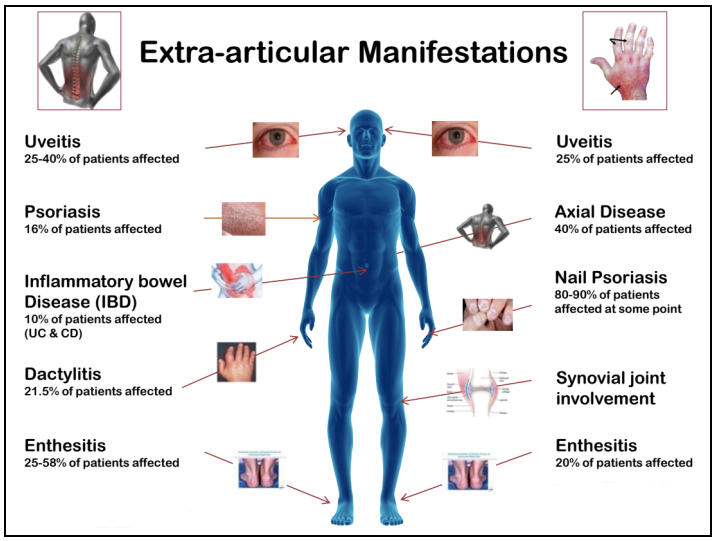
(Physician role is to recognize non-mechanical causes)

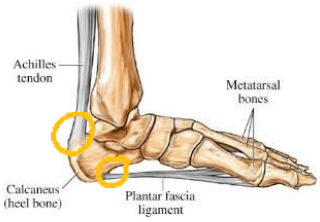
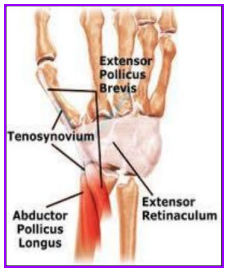
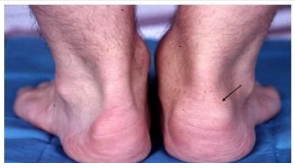
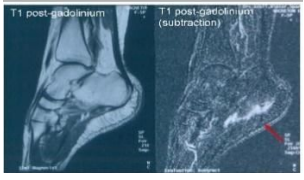
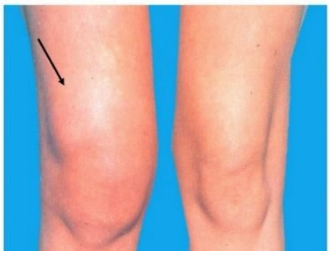
inflammation is bad but treatable. Inflammation with time is damaging.

[1] Human Leukocyte Antigen

Clinical features common to SPA:

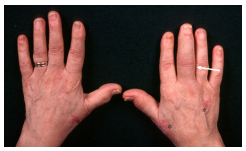
- Tendency for axial (spinal and sacroiliac) inflammation.
- Asymmetric Peripheral arthritis* (lower > upper limb)
- Absence of Rheumatoid factor and ACPA, hence 'seronegative'
- Inflammation of the enthesis* (See the Fig→)
- Strong association with HLA-B27, but its aetiological relevance is unclear.
- **Extra-articular features:**
  - eyes (Uveitis)
  - skin (Psoriasis, Erythema nodosum, Pyoderma gangrenosum, Keratoderma blenorrhagicum)
  - genitourinary tract



Enthesitis	Peripheral Arthritis
- Enthesitis is inflammation of Entheses. - Entheses are sites where tendons, ligaments, joint capsules, or fascia attach to bone. - Severe pain and tenderness Relatively specific to SpA. - <u>Most common Sites:</u> Achilles tendons, plantar fascia, lateral epicondyles and tenosynovitis enthesitis. Enthesitis most commonly affects the Achilles tendon (heel enthesitis)   Enthesitis (Insertion of Achilles Tendon at Calcaneus) Right Heel  Enthesitis of the Plantar Fascia by MRI 	- Predominantly involves the lower extremities. - Arthritis is frequently **ASYMMETRICAL** and often affects only one to three joints. - The severity ranges from mild to disabling. - The presence of **asymmetrical <u>oligoarthritis</u>** is very suggestive of SpA. But, it's absence would not be helpful in excluding this possibility. Acute Arthritis of the Right Knee in a Patient with Peripheral Spondyloarthritis 

Dactylitis: known as sausage toe or sausage finger. Found in:

- Psoriatic arthritis
- Occasionally reactive arthritis

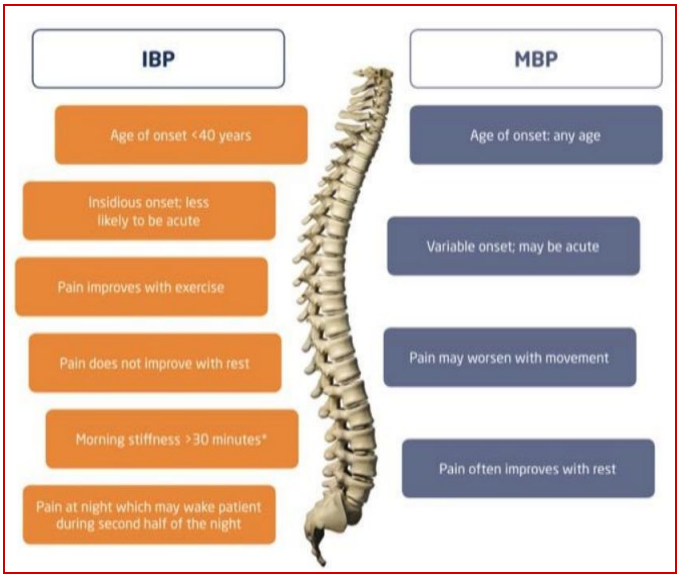


Unlike synovitis, in which swelling is confined to the joints, with dactylitis, the entire digit is swollen.

Dactylitis is not specific for SpA and may also be seen in: Tuberculosis, Syphilis, Sarcoidosis, Sickle cell disease, Tophaceous gout.

★ How To Differentiate Between Inflammatory Back Pain and Mechanical Back Pain? *important

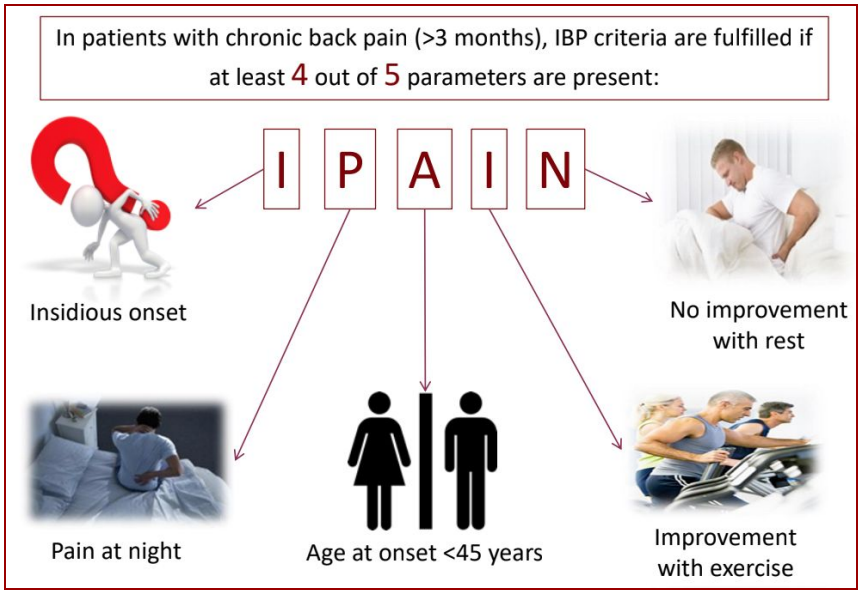
Differentiating between Inflammatory back pain (IBP) and Mechanical back pain (MBP) is important because IBP must be taken seriously.



- Inflammatory back pain is characterized by **6 features** "I PAIN +M" I'M PAIN:
  1. **I**nsidious (slow progression).
  2. **P**ain at night.
  3. **A**ge<45 (15-45).
  4. **I**mproved by exercise and movement.
  5. **N**ot improved with rest, it will make it worse.
  6. Early **M**orning stiffness of more than 30 minutes.

Inflammatory back pain present if at least 4 out of 5 parameters are fulfilled,

- Mechanical back pain gets worse with exercise.



Ankylosing Spondylitis (AS)

What is it?

- This is an inflammatory disorder of the spine, affecting mainly young adults.
- It is both more common and more severe in men than women. (3 times more common in male than female)
- AS most commonly affects the SI joint[2]. It also affects big joints like the knees and ankles.
- On average, It take 8 years from the onset of AS symptoms to reach a diagnosis. This is due to its response to NSAIDs and due to the high prevalence of back pain (around 80-90% of the population will experience back pain).

Aetiology:

- The cause of AS is not completely understood.
  - Theory > genetic mechanisms > major role in to AS.
  - Genome-wide studies have NOT revealed strong insights on the pathogenesis of new bone formation in AS
- Many genes are involved but the major gene product associated with AS and the other forms of SpA is **(HLA)-B27).**
- HLA-B27 is present in about 80 to 95% of patients with AS in most ethnic groups. (10% of AS pts Don't have the gene and about 10% of the general population have the gene).
- 6% of the general population have the gene. Fewer than 5% of HLA-B27 carriers in the general population develop disease.
- Familial predisposition: First, second, and third-degree relatives of patients with AS have markedly increased risks of developing the disease (relative risks of 94, 25, and 4, respectively).

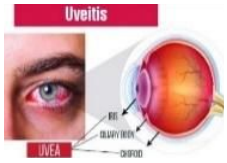
Clinical Features:

Cardinal features:
BACK PAIN, you can't have AS without having Back pain. The typical patient is: Young man (late teens, early 20s) who presents with low back pain and early morning stiffness with radiation to the buttocks or posterior thighs. Pain and stiffness improve with exercise but not with rest. There is a progressive loss of spinal movement.
Inspection of the spine reveals two characteristic abnormalities: • Loss of lumbar lordosis[3] and increased kyphosis. • Limitation of lumbar spine mobility. (Reduced spinal flexion is demonstrated by the Schober test)

Other features include:

- **Enthesitis:** Achilles tendinitis and plantar fasciitis التهاب اخمص القدم
- **Tenderness** around the pelvis and chest wall
- Transient **peripheral arthritis** of knees, hips, and shoulders (50%)
- **Reduction in chest expansion** (due to costovertebral joint involvement).

[2] Sacroiliac (SI) joint
[3] Loss of lumbar inward inversion

Non-articular features include:	
(Most commonly) Acute ANTERIOR uveitis	**Psoriasis**
1. Anterior 2. Most common extra-articular manifestation of AS 3. Acute onset. 4. Unilateral. 5. Spontaneous remission. 6. Does not correlate with disease severity 7. Recurrent & Related to HLA-B27. 	Present in up to approximately **10**% of patients with AS. (Psoriasis is associated with all forms of SpA)

Investigations:

1. **Best Initial Test** is an x-ray of the sacroiliac (SI) joint. In AS X-ray changes take 2 years to appear.
2. ESR and CRP are often raised. Levels are increased up to 70% in most AS Patients. With no relation with disease activity. Its absence doesn't exclude AS.
3. **The Most Accurate Test** is an MRI. MRI detects abnormalities years before the x-ray becomes abnormal. MRI shows **sacroiliitis**.
4. HLA-B27 testing is not usually performed. bc it's not a confirmatory diagnostic test since 8% of the general population is positive. The problem with HLA-B27 as a diagnostic test is that its positive in 90% of AS patients and is also positive in 10% of population.

Radiological changes in AS (SI scoring system) *Not required for you to study

- **Sacroiliitis Grade 0:** Normal.
- **Sacroiliitis Grade 1:** Suspicious changes. MRI should be performed

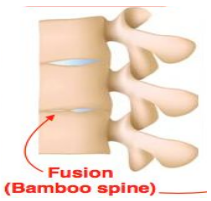
- **Sacroiliitis Grade 2:** Minimal abnormality - small localized areas with erosion or sclerosis, without alteration in the joint width. Narrowing, sclerosis and erosive changes.

The EARLIEST radiological appearances in the spine X ray are (**BLURRING**) of the upper or lower vertebral rims at the thoracolumbar junction (best seen on a lateral X-ray), caused by an enthesitis at the insertion of the intervertebral ligaments.

- **Sacroiliitis Grade 3:** Unequivocal abnormality - moderate or advanced sacroiliitis with one or more of: erosions, evidence of sclerosis, widening, narrowing or partial ankylosis. Partial effusion.

This heals with new bone formation resulting in bony spurs **(SYNDESMOPHYTES)** 'syndesmophytes is a bony growth originating inside a ligament'

- **Sacroiliitis Grade 4:** Severe abnormality - total ankylosis. Shows fusion.



In advanced disease: Progressive calcification of the interspinous ligaments and syndesmophytes eventually produce the (**BAMBOO SPINE**)

*When you see the Sacroiliac joints on X-ray, if One side is Grade 1 and the other is Grade 2 >That's not AS.

But, if both are Grade 2 >It's AS.

Management

- The key to effective management of AS is Early diagnosis and treatment, which is essential to prevent irreversible syndesmophyte formation and progressive calcification. With effective treatment most patients are able to lead a normal active life and remain at work.
- Morning exercises to maintain posture and spinal mobility.
- **Medications:**
    1) **FIRST LINE OF TREATMENT:** NSAIDs (taken at night are particularly effective in relieving night pain and morning stiffness)
    2) If NSAIDs failed, give → TNF-α-blockers (highly effective in active inflammatory disease and improve both spinal and peripheral joint inflammation)

- Treatment of AS: First line (whether Axial or peripheral) is NSAIDs. Steroids are not effective at all. If disease is Axial, second line is anti TNF. If disease is peripheral, second line is sulfasalazine/ local corticosteroids. If it fails Anti TNF is used.

Psoriatic Arthritis (PsA)

What is it? (7min Osmosis Psoriatic Arthritis Video)

- Arthritis occurs in 20% of patients with psoriasis, particularly in those with nail disease and may precede the skin disease. Psoriatic arthritis shares a lot of features with AS. What's special about it is that it affects the hands.
- Psoriasis is associated with all forms of SpA. (A scaly rash, most frequently occurring on the elbows, knees, and scalp)
- Psoriasis is present in up to approximately 10% of patients with AS.

Identifying PsA: Arthritis in the presence of psoriasis is the key to clinical diagnosis.

1. Psoriasis
2. Other manifestations such as (Peripheral arthritis, Spondylitis, tenosynovitis, enthesitis and dactylitis).

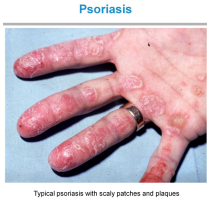
- Equal gender distribution, Peak years of onset typically between the ages of 20 and 40.
- Psoriatic plaque typically precede development of the arthritic component. The onset depends on subtype:
    1. Delayed after psoriasis onset: Asymmetrical & Spondylitis.
    2. Concurrent with psoriasis: Symmetrical.
- No correlation between the severity of psoriatic plaques and PsA has been identified.

Pathogenesis of PsA:

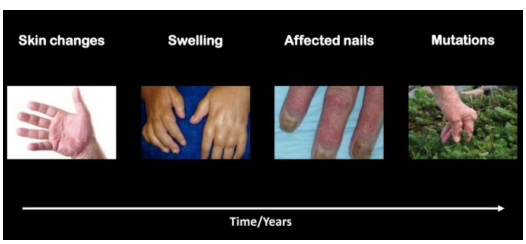
Synovial hyperplasia and cellular infiltration:
Pannus formation, cartilage erosion and prominent role for cytotoxic (CD8+) T cells.

Increased levels of TNFα found in joint:
Pro-inflammatory effect and stimulation of proteases.

Associated enthesitis present:



Typical psoriasis with scaly patches and plaques



Clinical Features: (Diagnosis is clinical and radiographic)

There are several types/patterns:

I. **Asymmetrical** involvement of the small joints of the hand, including the distal interphalangeal joints.
   - Most typical pattern of joint involvement in Psoriasis. Characterized by: Dactylitis[4] and Nail Dystrophy. Nail changes in psoriatic arthritis are onycholysis, ridging and pitting.
   - Typically involves one to three joints in the body - large or small - such as the knee, hip, or one or several fingers.

II. **Symmetrical** seronegative polyarthritis. (resembling Rheumatoid Arthritis)
Affects the same joints in multiple matching pairs of opposite sides of the body. It can be disabling, causing varying degrees of progressive, destructive disease and loss of function in 50% of people with this type of arthritis.

III. **Arthritis Mutilans.** Rare, severe form with destruction of the small bones in the hands and feet ('telescopic' fingers). Deforming, and destructive form of psoriatic arthritis that primarily affects the small joints in the fingers and toes closest to the nail. This leads to loss of function of the involved joints.

IV. **Sacroiliitis (Spondylitis).** (unilateral or bilateral)

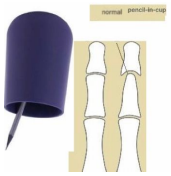
V. **Distal interphalangeal synovitis.** (DIP predominant psoriatic arthritis involves primarily the small joints in the fingers and toes closest to the nail. DIP psoriatic arthritis is sometimes confused with osteoarthritis, a chronic disease that causes the deterioration of joint cartilage and bone at the joints

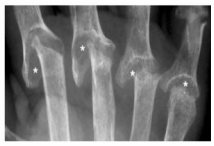
Both rheumatoid arthritis and psoriatic arthritis affect the hands. However, in psoriatic arthritis patients have psoriasis and Distal interphalangeal joint **(DIP) involvement**[5]. In contrast, DIP joint is spared in RA.

***Some features that are common in all PsA patterns:** Morning stiffness, nail disease and joint pain. Inflammatory neck pain and stiffness and Inflammatory back pain and stiffness.
***Morbidity associated with PsA:** Go back to the slides it you want. But, the data may not accurately reflect current morbidity trends following recent medical advances.

Investigations:

1. Best Initial Test is an **x-ray** of the joint showing a 'pencil in cup' deformity in the IPJs (bone erosions creates a pointed appearance and the articulating bone is concave).
   *'pencil in cup' deformity





2. Routine **blood tests** are unhelpful in the diagnosis. The ESR is often normal.

Treatments:

- This is with analgesia and NSAIDs.
- Local synovitis responds to intra-articular corticosteroid injections.
- In SEVERE cases, methotrexate or TNF-blocking drugs control both the arthritis and the skin lesions.

[4] Sausage digits
[5] DIP (distal Interphalangeal joint), we'll see the whole finger swollen, indicates a very bad prognosis.

Reactive Arthritis

General Characteristic:

- Reactive arthritis is a STERILE synovitis, which occurs secondary to: (Post GI or Urine infection)
  - **Gastrointestinal infection (**Post-dysenteric reactive arthritis): with Shigella, Salmonella, Yersinia, campylobacter, clostridium difficile or E.coli.
  - **Sexually acquired infection:** non-specific urethritis in the male or cervicitis in the female due to infection with Chlamydia trachomatis in urine or Ureaplasma urealyticum.

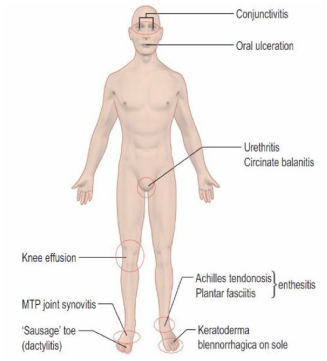
- Reactive arthritis is an immune reaction to an infection of the GIT or urinary tract. Since it is an immune reaction, antibiotics are not used. From the time of infection, the immune reaction takes 2 weeks (at least 10 days) to appear. (In books it says 14 days. however, it can be up to months)

Clinical Features:

Typical features:

- The typical case is a **young** man who presents with an acute arthritis shortly (within 2- 4 weeks) **after an enteric or sexually** acquired infection, which may have been mild or asymptomatic.

- The joints of the LOWER LIMBS are particularly affected in an ASYMMETRICAL pattern; the knees, ankles and feet are the most common sites.



igure 11.24 Clinical features of reactive arthritis.

At least one of the following is seen in all patients with this condition:
Asymmetric oligoarthritis (often affecting the lower extremities), Enthesitis, Dactylitis and Inflammatory back pain.

Additional features:

- **Classic triad of Reiter's syndrome:** (urethritis, Asymmetrical reactive arthritis and conjunctivitis). but most patients do not have the classic findings of Reiter's syndrome.
- **Enthesitis** (plantar fasciitis, Achilles tendonitis)
- Acute anterior uveitis
- Few patients develop sacroiliitis and spondylitis.

Skin lesions resembling psoriasis:

- **Keratoderma blennorrhagica:**
  Red plaques and pustules that resemble pustular psoriasis are found on the palms and soles of the feet.
- **Circinate balanitis**: causes superficial ulcers around the penile meatus)
- Nail dystrophy may also occur.

Investigations:

1) There is no specific test for reactive arthritis, THE DIAGNOSIS IS CLINICAL: If any patient has acute asymmetric arthritis that progresses sequentially from one joint to another → **Reactive arthritis** should be in the differential diagnosis.

2) Send synovial fluid for analysis (to rule out infection or crystals): → Aspirated synovial fluid is **sterile**, with a **high neutrophil count.**
3) The **ESR** is raised in the acute stage.

Laboratory Findings may include:
Evidence of the infection, elevated acute phase reactants and findings of inflammatory joint fluid in patients with arthritis.

Management:

- The acute joint inflammation responds well to **NSAIDs** and local **corticosteroid injections.**
- Any persisting infection is treated with antibiotics.
- Most patients have a single attack. Relapsing cases are treated with sulfasalazine or methotrexate and **TNF-blocking** drugs in severe cases.

- Antibiotic therapy should be used for treatment of active Chlamydia trachomatis infection, if present. In general, antibiotics are not indicated for uncomplicated enteric infections or for treatment of the arthritis itself.
  1. We give NSAIDs Initially. (patient didn't respond) ↓
  2. Intra-articular glucocorticoids. (patient didn't respond) ↓
  3. Low to moderate doses of systemic glucocorticoids. (prednisone, 20 mg daily, titrated to the lowest dose required to control symptoms)

- In patients who have not responded adequately to NSAIDs over at least four weeks and who require ongoing therapy with more than 7.5mg of prednisone or equivalent for more than three to six months we suggest a trial of a nonbiologic DMARD, rather than continuing moderate to high dose glucocorticoids without a DMARD.
  - We usually prescribe sulfasalazine (SSZ).
  - Methotrexate is an alternative to SSZ.

- The prognosis is good in the majority of patients, with spontaneous remission within 6 to 12 months of onset of arthritis. However, some patients have persistent but mild musculoskeletal symptoms, and others develop radiologic evidence of joint injury and evolve to a more chronic form of SpA.

Enteropathic Arthritis

What is it:

- Enteropathic arthritis is a large-joint mono- or ASYMMETRICAL oligoarthritis occurring in 10–15% of patients with **Ulcerative colitis or Crohn's disease.**
- It usually **parallels the activity of the inflammatory bowel disease** and consequently improves as bowel symptoms improve**.**

Treatment:

- The arthritis often remits with treatment of the bowel disease but DMARD and biological treatment is occasionally required**.**

- **Just Read this:**

ASAS Classification Criteria for Spondyloarthritis (SpA)

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

Sacroiliitis on imaging plus ≥1 SpA feature

OR

HLA-B27 plus ≥2 other SpA features

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

In patients with peripheral symptoms ONLY

Arthritis or enthesitis or dactylitis

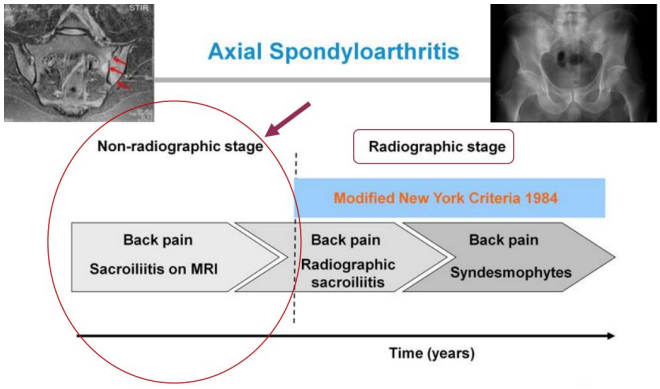
plus

≥1 SpA feature
- uveitis
- psoriasis
- Crohn's/colitis
- preceding infection
- HLA-B27
- sacroiliitis on imaging

OR

≥2 other SpA features
- arthritis
- enthesitis
- dactylitis
- IBP ever
- family history for SpA

Sensitivity: 79.5%, Specificity: 83.3%; n=975



Box 8 Signal characteristics of MRI sequences used for the imaging of spine and sacroiliac joints

Sequence	Spinal fluid (water content)	Intervertebral disc (water content)	Subcutaneous fat tissue	Active inflammatory lesions
T1-weighted	Hypointense[1]	Hypointense[1]	Hyperintense[1]	Hypointense[1]
T1-weighted post-gadolinium	Hypointense[2]	Hypointense[2]		Hyperintense
With fat saturation			Hypointense[2a]	
Without fat saturation (not recommended)			Hyperintense[2b]	
Short tau inversion recovery (STIR)	Hyperintense[3]	Hyperintense[3] (hypointense if disc is degenerative)	Hypointense[3]	Hyperintense

Modified New York Criteria for Ankylosing Spondylitis (1984)

1. Clinical criteria:

a.Low back pain and stiffness for more than 3 months which improves with exercise, but is not relieved by rest.

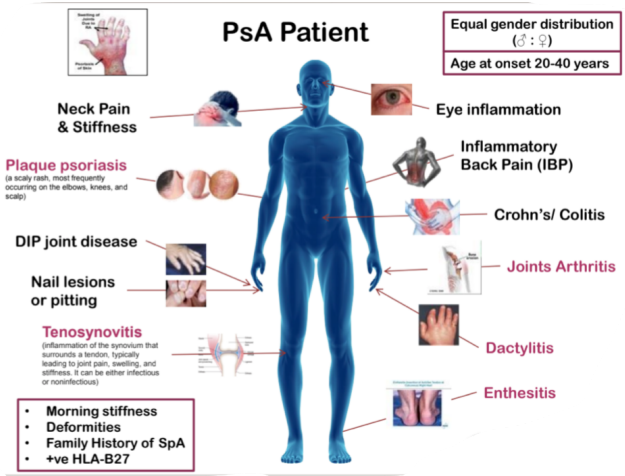
b.Limitation of motion of the lumbar spine in both the sagittal and frontal planes.

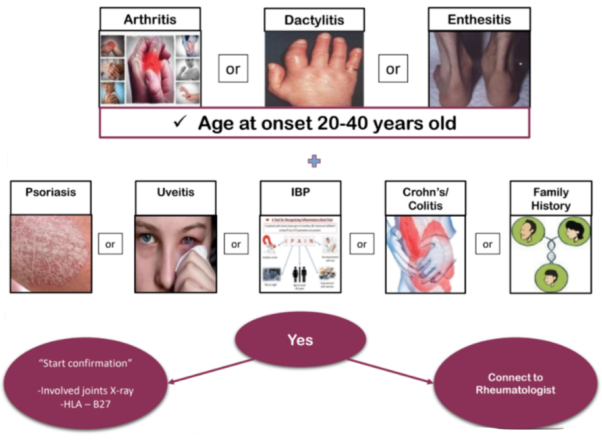
c.Limitation of chest expansion relative to normal values correlated for age and sex.

2. Radiological criterion:

Sacroiliitis grade ≥ 2 bilaterally or grade 3-4 unilaterally

Definite ankylosing spondylitis if the radiological criterion is associated with at least 1 clinical criterion.





Questions:

Q1: The most common extra-articular manifestation of Ankylosing Spondylitis?

A. Anterior Uveitis
B. Psoriasis
C. IBD
D. Aortic Regurgitation

Answer: A

Q2: Which of the following joints is affected the most in Ankylosing Spondylitis?

A. Knees
B. Ankles
C. SI joint
D. DIP joint

Answer: C

Q3: Which of the following is the minimum duration characteristic of Inflammatory back pain?

A. 10 minutes
B. 30 minutes
C. 1 hour
D. 4 hours

Answer: B

Q4: In Spondyloarthropathies, which of the following sites is affected the most with enthesitis?

A. Achilles tendons
B. Plantar fascia
C. Lateral epicondyles
D. Medial malleolus

Answer: A

Q5: What gene is responsible for SpA diseases?

A. HLA B27
B. HLA DR4
C. HLA DR3
D. HLA B24

Answer: A

Q6: It is said that Reiter's disease has been related to Chlamydia trachomatis infection. Is this correct?

A. True
B. False

Answer: A

Q7: Which of the following is a radiological sign of advanced Ankylosing Spondylitis?

A. Syndesmophytes
B. Blurring of the upper or lower vertebral rims at the thoracolumbar junction
C. Bamboo spine
D. None of the above

Answer: C

Summary

Disease	Psoriatic Arthritis	Reactive arthritis	Enteric Arthritis	Ankylosing spondylitis
S&S	Findings are: Dactylitis (Sausage digits) & Nail dystrophy Types: 1- Asymmetrical 2- Symmetrical 3- Arthritis Mutilans 4- Sacroiliitis	Typical case of a young man with an acute arthritis (within 2- 4 weeks) after an enteric or sexually acquired infection. Mainly affects joints of the LOWER LIMBS (knees, ankles and feet) & are in an ASYMMETRICAL pattern. Classic triad of Reiter's syndrome: (urethritis, Asymmetrical reactive arthritis and conjunctivitis). *But most patients do not have the classic findings of Reiter's syndrome.	Large joint mono- or Asymmetrical oligoarthritis occurring in patients with ulcerative colitis or Crohn's disease.	- Low back pain and early morning stiffness with radiation to the buttocks or posterior thighs. Pain and stiffness improve with exercise but not with rest. - Acute ANTERIOR uveitis (most common extra-articular manifestation of AS)
Dx	Best Initial Test is an X-ray of the joint showing a 'pencil in cup'.	- There is no specific test, THE DIAGNOSIS IS CLINICAL. - Send synovial fluid for analysis (to rule out infection or crystals) → Aspirated synovial fluid is sterile, with a high neutrophil count.	Best Initial Test is an X-ray.	Best Initial Test is an X-ray of the sacroiliac joint. The most Accurate Test is an MRI detects abnormalities years before the x-ray becomes abnormal shows sacroiliitis.
Rx	1st - NSAIDs injections 2nd - TNF-α-blockers *Methotrexate & Corticosteroid: helps with peripheral arthritis but not with axial disease.			
Inflammatory back pain is characterized by **6 features** "I'M PAIN": (**I**nsidious - Early **M**orning stiffness of more than 30 minutes - **P**ain at night - **A**ge<45 - **Improved** by exercise and movement - **Not** improved with rest, it will make it worse)				