Lecture 33

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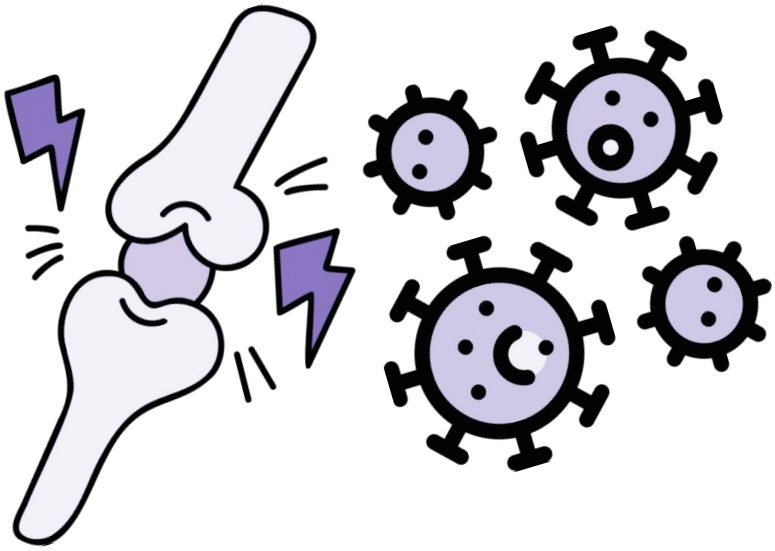


Reviewed By
Noura Alturki
Jehad Alorainy

# Seronegative Spondyloarthropathies (SpA)

## Objectives:

- ★ Understand the basic of Spondyloarthritis.
- ★ To differentiate between inflammatory and mechanical back pain.
- ★ To be able to take full detailed history and examination related to spondyloarthritis.
- ★ To understand the basic lab and genetics for SpA.
- ★ Basics therapy for spondyloarthritis.
- ★ To know the extra-articular features for SpA.

## Color index:

Original text Females slides Males slides
Doctor's notes Text book Important Golden notes Extra

EXAM Q

# Back pain

## ◄ Introduction

- 80% of the population will experience back pain during their lifetime.
- More than 85% cannot attribute it to a specific disease or spinal abnormality.
- Up to one third (1/3) of patients report persistent back pain of at least moderate intensity 1 year after an acute episode.
- **There are 2 types of back pain:**
  a) **Mechanical:** Symptomatic herniated disc, Spinal stenosis, Compression fracture.
  b) **Inflammatory: Ankylosing spondylitis (3%)**
  c) Others: Cancer, spinal infection

| Inflammatory back pain | Mechanical back pain |
|---|---|
| **<40y/o** | **any age** |
| **Insidious onset: Slowly progressive** | **Variable onset: can be acute** |
| **Pain improves with exercise** | **Pain may worsen with movement** |
| **Pain does not improve with rest** | **Pain often improves with rest** |
| **Significant early morning stiffness >30min** | **Onset often sudden and precipitated by lifting or bending** |

## ◄ Criteria for diagnosing IBP

★ **ASAS inflammatory back pain criteria by experts (chronic back pain; n=648): (IPAIN)**

1. **I**nsidious onset
2. **P**ain at night (with improvement upon getting up)
3. **A**ge at onset <40 years
4. **I**mprovement with exercise
5. **N**o improvement with rest

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

# Introduction

## What are Spondyloarthropathies (SpAs)?

- **Spondyloarthropathies (SpAs) aka <u>Seronegative</u> Spondyloarthropathies** comprise a **group of related inflammatory** musculoskeletal diseases that show overlap in their clinical features and have a shared **immunogenetic association** with **HLA-B27. They include:**

1. **Ankylosing spondylitis (AS)**
2. **Psoriatic arthritis (PsA)**
3. **Reactive arthritis (ReA)**
4. **Enteropathic spondyloarthritis (IBD + Arthritis)**
5. **Non-radiographic Axial spondyloarthritis (nr-axSpA)**
6. **Undifferentiated peripheral SpA**
7. **Juvenile SpA**

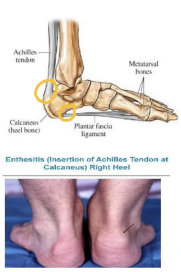
- In axial spondylitis and ankylosing spondylitis, the axial skeleton (i.e. the central core skeleton) is predominantly affected. **Based on this concept, SpAs can be classified into:**
  - **Predominantly axial SpA** (Spine or Chest or Hip Joints)**:** nr-axSpA and AS
  - **Predominantly peripheral SpA** (Fingers or Knees or Toes)**:** All SpAs except AS and nr-axSpA

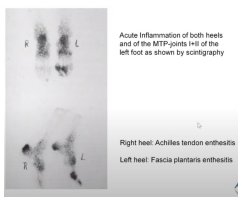
## Features common to SpAs

- In contrast to RA, in the SpAs there are frequent and notable **non-synovial musculoskeletal lesions** – mainly inflammatory in nature – of ligaments, tendons, periosteum and other bone lesions.

### Enthesitis

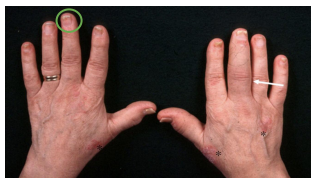
- Enthesitis= Inflammation at the site of a ligament or tendon insertion into bone.
- Causes severe pain and tenderness.
- Relatively specific to SpA
- **Most common sites: Achilles tendons (heel enthesitis, most common),** plantar fascia ligament into the calcaneus, lateral epicondyles, tenosynovitis enthesitis and gluteus medius insertion
- Can also happen in the chest (Costochondritis)




### Dactylitis

- Unlike synovitis, in which swelling is confined to the joints, with dactylitis, the **entire digit is swollen**.
- Known as **sausage toe**/digit/finger.
- **Usually seen in:**
  - **Psoriatic arthritis**
  - Occasionally reactive arthritis
- Dactylitis is **not specific for SpA** and may also be seen in: Tuberculosis, Syphilis, Sarcoidosis, Sickle cell disease, Tophaceous gout.



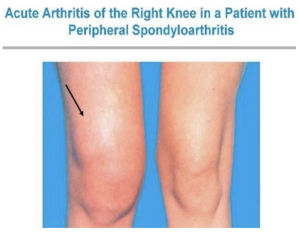
*Psoriasis plaque lesions
circle: Onycholysis

# Introduction cont.

## ◀ Features common to SpAs cont.

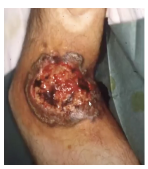
### Peripheral arthritis

- Predominantly involves the **lower extremities** (Hip, knee and ankle).
- Arthritis is frequently **ASYMMETRICAL inflammatory Mono/Oligoarthritis** (affects only one to three joints)
- The severity ranges from mild to disabling.
- **The presence of asymmetrical oligoarthritis is very suggestive of SpA**. But, it's absence would not be helpful in excluding this possibility.

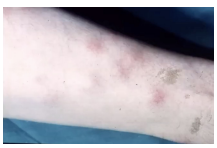



| Peripheral arthritis associated with IBD | |
|---|---|
| **Type 1 arthropathy** | **Type 2 arthropathy** |
| • Acute, pauciarticular<br>• The knee is the joint most commonly affected<br>• Early in the course of the bowel disease<br>• Self-limiting, nonerosive<br>• May occur prior to the onset of IBD → flares of the bowel disease | • Polyarticular disease<br>• (MCP) joints being particularly involved<br>• Episodes of exacerbations and remissions may continue for years<br>• Articular involvement rarely preceded the diagnosis of IBD<br>• Joint symptoms may occur prior to the onset of IBD symptoms, and this form of arthritis is often associated with flares of the bowel disease |

### Other features

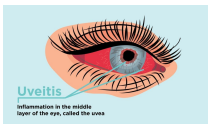


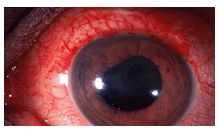
**Pyoderma Gangrenosum**

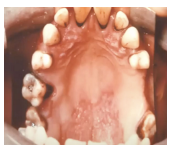


**Erythema nodosum**

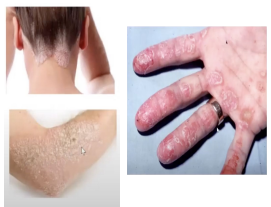
- History of inflammatory **back pain**
- Sacroiliitis and spinal osteitis
- Tendency for familial aggregation
- **Skin:** Psoriasis (associated with all forms of SpA), Erythema nodosum, Pyoderma gangrenosum and Keratoderma blenorrhagicum
- **Uveitis**
- Sterile urethritis and/or prostatitis
- Inflammatory bowel disease
- Aortic root lesions (aortic incompetence, conduction defects)



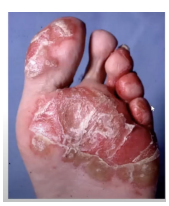





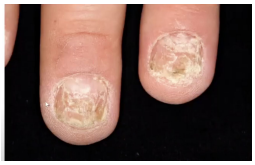
**Palatal erosion in reactive arthritis.** A sharply demarcated erosion of the hard palate is shown. This is among the more common of the oral manifestations of reactive arthritis



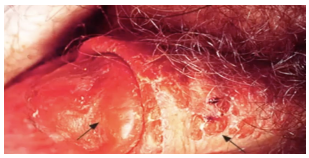
**Psoriasis.** Scaly patches and plaques



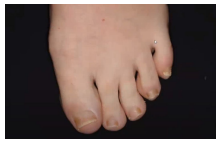
**Keratoderma Blenorrhagicum**



**Moderate to severe nail changes in patient with Psoriasis**



**Circinate balanitis** characterized by shallow ulcers on the glans penis and the shaft of the penis (arrows). The lesions are generally asymptomatic.



**Mild nail changes in a patient with psoriasis**

# 1- Ankylosing spondylitis (AS)

## ◀ What is ankylosing spondylitis?

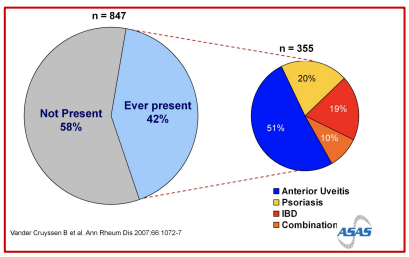
- This is an **inflammatory disorder of the spine**, affecting mainly young adults.
- Ankylosing spondylitis (AS) is defined by the **presence of sacroiliitis on X-ray** and other structural changes on spine X-rays, which may eventually progress to bony fusion of the spine. **What if the changes (sacroiliitis) were only seen on MRI?** then the term used is 'Non-radiographic **Axial** spondyloarthritis (nr-axSpA)' **NOT** ankylosing spondylitis.
- In general, MRI is much more sensitive than X-ray in detecting sacroiliitis. In X-ray, changes will not appear until the disease is advanced, while in MRI you can sometimes see the changes as early as a day after the symptoms develop..
- In the past, with the use of X-ray only, they used to say that AS is more common in males. But after MRI has been introduced this has changed:
  - Female gender generally >50% of non-radiographic axial SpA (detected by MRI or HLA-B27)
  - Male gender more common in AS study population
- AS can affect any part of the spine, but **most commonly affects the Sacroiliac (SI) joint.** It also affects big joints like the knees and ankles.

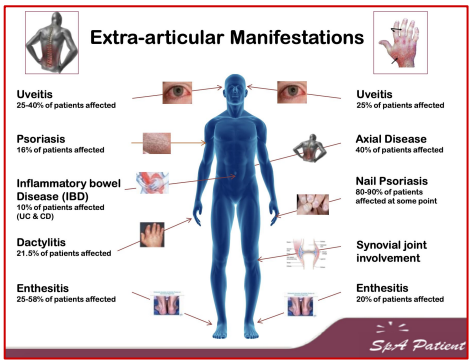
## ◀ Etiology

- The **cause of AS is not completely understood**, but there are theories that genetics is the major player in the pathogenesis of this disease.
- Genome-wide studies have **NOT** revealed strong insights on the pathogenesis of new bone formation on AS. (Genetic influences, Microbes effects, Biochemical stress)
- 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.
- **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).
- **Arthritogenic peptide hypothesis:** (They simply injected the gene into a rat and it developed SpA)
  - HLA-B27-transgenic rats.
  - Microinjection of fertilized 1-cell rat eggs with DNA fragments containing both HLA-B*2705
  - Spontaneously developed several SpA-like disease manifestations beginning at age 10 weeks
  - The most common persistent manifestation: Diarrhea, Arthritis of the hind limbs, dystrophy of the nails and hyperkeratosis of the tail.

## ◀ Clinical features

- AS typically evolves slowly, with fluctuating symptoms of spinal inflammation; ankylosis develops in many patients over a period of many years.[1]




### Typical presentation

**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,** hot shower and worsen with rest. There is a progressive **loss of spinal movement**

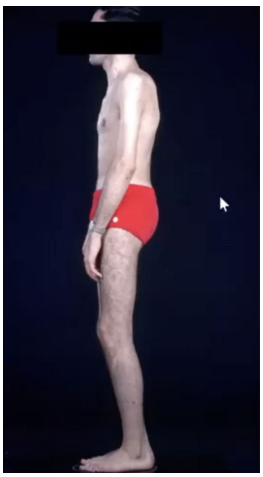
1- Even if severe ankylosis develops, functional limitation may not be marked, as long as the spine is fused in an erect posture. In AS, spinal fusion varies in its extent and in most cases does not cause a gross flexion deformity.

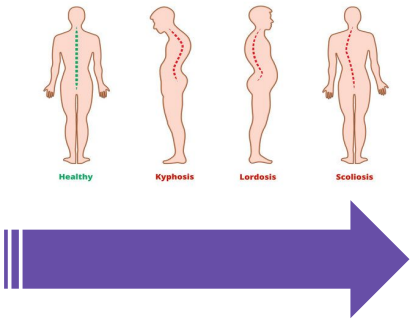
# 1- Ankylosing spondylitis (AS) cont.

## ◀ Clinical features cont.

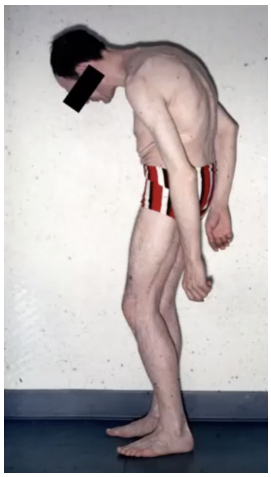
### Articular features

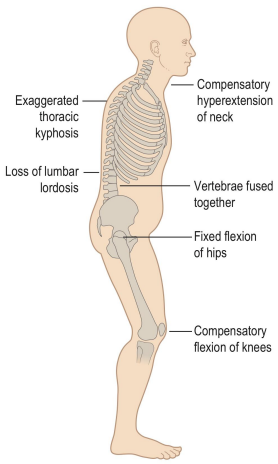
| Spine features | Other features |
|---|---|
| • **Loss** of lumbar **lordosis** (lumbar inward inversion) and increased **kyphosis** of the dorsal and cervical spine that may interfere with forward vision[1]<br>• **Limitation** of lumbar spine mobility. (Reduced spinal flexion is demonstrated by the **Schober test**[2]) | • **Enthesitis**: **Achilles tendonitis** and plantar fasciitis<br>• **Tenderness** around the pelvis and chest wall<br>• **Transient peripheral arthritis** of knees, hips, and shoulders (50%)<br>• **Reduction in chest expansion** (due to costovertebral joint involvement). |






That's why early diagnosis is essential, to prevent such damage. Final stage can only be corrected by surgery



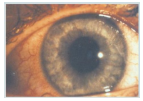



**AS patient with <u>disappearance of the lordosis</u> of the lumbar spine (Early stage)**

**Final stage of AS with severe kyphosis of thoracic and cervical spine.** Unable to look ahead while walking (patient cannot see the sun)

### Extra-articular features

| Acute <u>anterior</u> uveitis | Other features |
|---|---|
| ★ **Most common extra-articular manifestation** of AS.<br>• Occasionally precedes joint disease.<br>• It's **unilateral** with Acute onset<br>• Spontaneous remission<br>• Does **NOT** correlate with disease activity<br>• Recurrent<br>• Related to **HLA-B27.**<br>• Unlikely to cause vision changes (Usually presents with eye pain, redness) | • **Psoriasis** (present in up to 10% of pts with AS)<br>• Fatigue, anaemia<br>• **Prostatitis** (80% of men) and sterile urethritis<br>• Inflammatory bowel disease (up to 50% have IBD lesions)<br>• Osteoporosis<br>• Cardiovascular disease (aortic valve disease 20%)<br>• Amyloidosis (rare)<br>• Atypical upper lobe pulmonary fibrosis (very rare) |

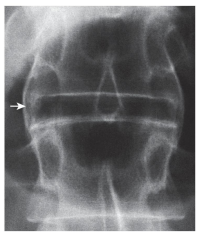


1- This may prove incapacitating, especially when associated with fixed flexion contractures of hips or knees.
2- Spinal stiffness can be measured by Schober's test; the skin over the midline of the spine is marked 5 cm below and 10 cm above the dimples of Venus and the increase in distance between those marks during flexion is recorded. An increase of <5 cm implies spinal stiffness.

# 1- Ankylosing spondylitis (AS) cont.

## ◀ Investigations

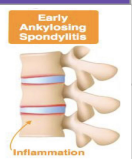
### X-ray (Best initial)

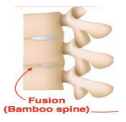


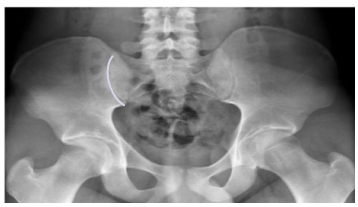
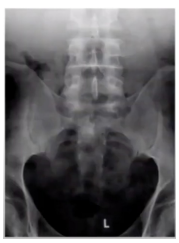
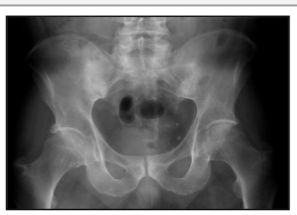
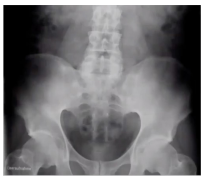
Fine **symmetrical** marginal **syndesmophytes** typical of ankylosing spondylitis (arrow)

- In AS, X-rays of the sacroiliac joint show **irregularity** and **loss of cortical margins**, **widening of the joint space** and subsequently **sclerosis**, joint space narrowing and **fusion**.
- Lateral thoracolumbar spine X-rays may show anterior 'squaring' of vertebrae due to erosion and sclerosis of the anterior corners and periostitis of the waist.[1]
- **Bridging syndesmophytes** may also be seen.
- **A syndesmophyte is bony growth originating inside a ligament**, commonly seen in the ligaments of the spine, specifically the ligaments in the intervertebral joints leading to fusion of vertebrae.
- In advanced disease, ossification of the anterior longitudinal ligament and facet joint fusion may also be visible.
- Calcification of the intervertebral ligaments and fusion of the spinal facet joints and syndesmophytes leads to what is often called a **'bamboo' spine**
- Erosive changes may be seen in the symphysis pubis, ischial tuberosities and peripheral joints.

| Grading of Radiographic Sacroiliitis (1966) | |
|---|---|
| **Grade 0** | **Normal** |
| **Grade 1** | **Suspicious changes** (MRI should be performed) |
| **Grade 2** | **Minimal abnormality:** Small localized areas with **erosion or sclerosis**, without alteration in the joint width |
| **Grade 3** | **Unequivocal abnormality:** Moderate or advanced sacroiliitis with one or more of: erosions, evidence of sclerosis, widening, narrowing, or partial ankylosis **"Partial Fusion"** |
| **Grade 4** | **Severe abnormality:** Total ankylosis **"Total Fusion"** |




| Grade 0 (Normal) | Grade 1,2 |
|---|---|
|  You can see the SI joint clearly |  Grade 2 right, Grade 1 left |
| **Grade 3** | **Grade 4** |
|  |  Bilateral, you will not be able to see the sacroiliac joint (Total fusion) |

1- 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.

# 1- Ankylosing spondylitis (AS) cont.

## ◀ Investigations cont.

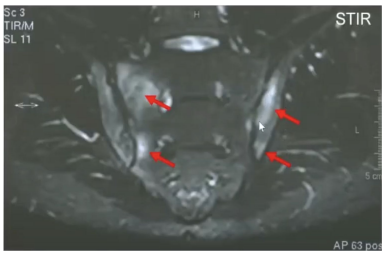
EXTRA

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

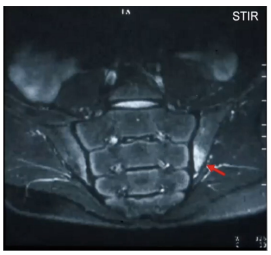
| Sequence | Spinal fluid (water content) | Intervertebral disc (water content) | Subcutaneous fat tissue | Active inflammatory lesions |
|---|---|---|---|---|
| T1-weighted | Hypointense[1] | Hypointense[1] | Hyperintense[1] | Hypointense[1] |
| T1-weighted post-gadolinium | Hypointense[2] | Hypointense[2] | | 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 |

### 2 MRI (Most accurate)

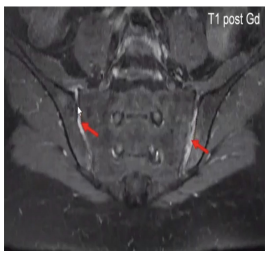
- MRI **with gadolinium** is more sensitive for detection of early sacroiliitis than X-rays and can also detect inflammatory changes in the lumbar spine, as well as persistent enthesitis.



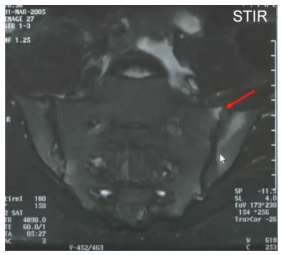

**Definition of positive MRI-SI joint:** Subchondral bone marrow edema Acute bilateral sacroiliitis




**Early (limited) sacroiliitis (Bone marrow edema).** Normal SI joint but there's inflammation surrounding it (red arrow)

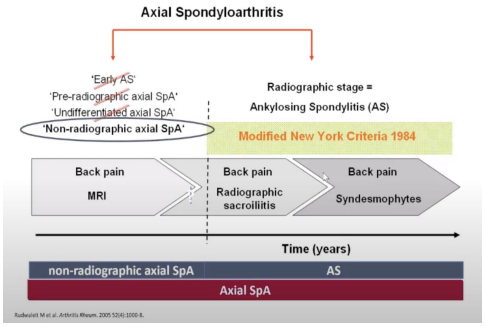



**Synovitis of sacroiliac joint**




**Bone marrow edema (BME)/Osteitis:** Bone marrow edema may be associated with structural changes such erosions

In the past , diagnosis was based on x-ray only which is not really sensitive and can't detect early changes in the disease leading to a lot of misdiagnosed cases. This has changed in the new criteria (2008), in which MRI and HLA-B27 testing has been introduced




### 3 Lab tests

- **Acute phase response (ESR & CRP):**
  - Increased in between 35-50% of patients with axial SpA.
  - Elevated levels of CRP are also a predictor of **radiographic progression** and for a good response to tumor necrosis factor(TNF)-blocker therapy.
  - If ESR or CRP is normal this doesn't exclude AS.
- **HLA-B27:**
  - Positive in 90% of AS patient. (also positive in 6% of general population)
  - 50-70% of patients with other forms of SpA
  - A positive HLA-B27 by itself is not diagnostic of SpA (criteria will be discussed next page)
- **Serology:**
  - Autoantibodies, such as RF, ACPA and ANA, are negative.

EXAM Q

# 1- Ankylosing spondylitis (AS) cont.

## ◀ ASAS criteria

**ASAS classification criteria for <u>axial</u> spondyloarthritis (SpA):**

- **This criteria only applies to:**
  Patients with **≥ 3 months back pain** and **age at onset <45 years**[1]

**Criteria**

**Sacroilitis on imaging*** **+** **≥ 1 SpA feature**

**Or**

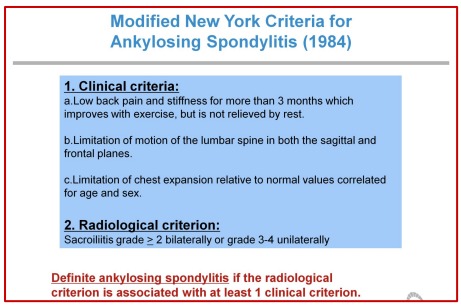
**+ve HLA-B27** **+** **≥ 2 <u>other</u> SpA features**

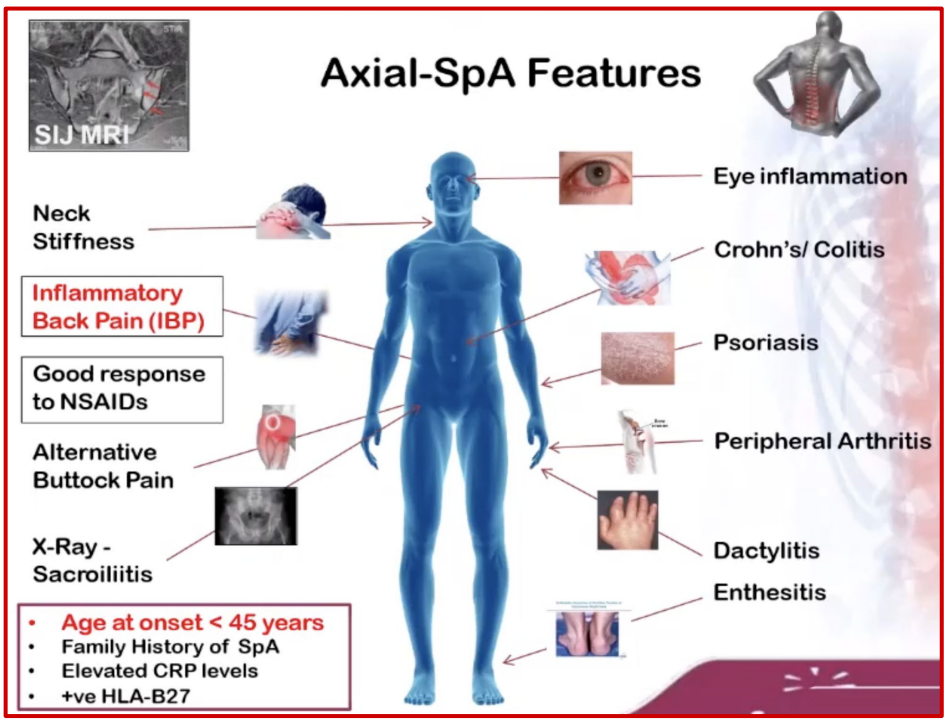
*** Sacroiliitis on imaging:**
- Active (acute) inflammation on **MRI** highly suggestive of sacroiliitis associated with SpA
- Definite radiographic (**x-ray**) sacroiliitis according to mod NY criteria (See the pic below)

**SpA features** SPINE-ACHE

1) Dactylitis (**S**ausage digit)
2) **P**soriasis
3) **P**ositive family history for SpA
4) **I**nflammatory back pain
5) Good response to **N**SAIDS
6) **E**nthesitis (heel)
7) **A**rthritis
8) **C**rohn's/colitis
9) **H**LA-B27
10) Uveitis (**E**ye)
11) **E**levated CRP

Q: Can we diagnose AS without imaging? Yes, by positive HLA-B27 + ≥ 2 other features




**If the pt has only peripheral symptoms, use this criteria:**

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

n=975

1- Because AS starts early, 16-45 y/o (But be careful, if a pt presents in his 50s this does not necessarily mean that he doesn't have the disease, you should ask him/her when did the symptoms start, this is a more accurate way, bc it might have started in his 30s but the pt presented to you in his 50s.)

# 1- Ankylosing spondylitis (AS) cont.

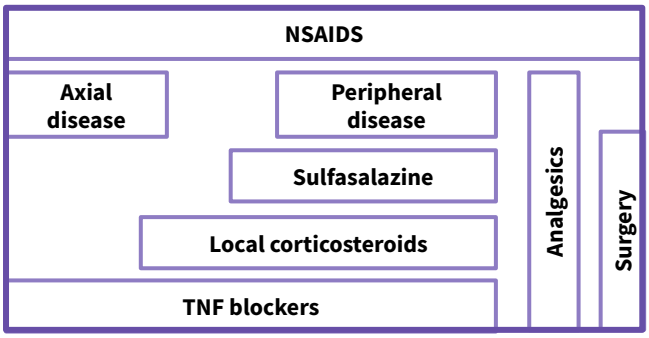
## ◀ Treatment

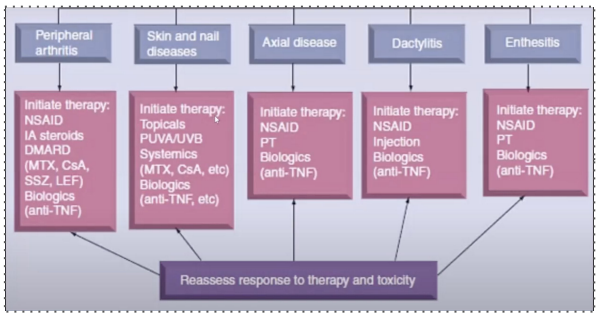
**Aims and outcomes of therapy in AS:**

- Decrease signs and symptoms (Disease activity, pain, morning stiffness, fatigue)
- Improve spinal mobility, activity, participation, productivity and quality of life
- Prevent osteoproliferative and osteodestructive changes in the axial skeleton and peripheral joints and entheses

**ASAS/EULAR Recommendations for the Management of Ankylosing Spondylitis:**

- Education, **Exercise**, Physical therapy, Rehabilitation, Patient association, Self help groups

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**Explanation:**

**First line:** NSAIDs (e.g. Diclofenac, Ibuprofen) to relieve symptoms

**Second line: (To prevent further damage)**

- **Axial (spine) AS:** Biologic therapy (Anti-TNF or IL-17 inhibitors)
- **Peripheral (e.g. knee) AS:** Sulfasalazine ± Local corticosteroids, didn't work? → Anti-TNF or IL-17 inhibitors

**Sulfasalazine & Local corticosteroids are NOT used for axial AS!**

**Anti-TNF can treat axial and peripheral arthritis**, it can also treat all the associated features e.g. uveitis, enthesitis and skin psoriasis

**Drug names**

**TNF-blockers:**

- Adalimumab (the best)
- Infliximab
- Etanercept
- Golimumab
- Certolizumab

**IL-17 inhibitors:**

- Secukinumab
- Ixekizumab

# 2- Psoriatic Arthritis (PsA)

## Definition

- Arthritis **associated with psoriasis**, which is a scaly rash, most frequently occurring on the elbows, knees, and scalp
- **Has 2 main identifying features:**
  1. Psoriasis
  2. Other manifestations such as: Peripheral arthritis, Spondylitis, tenosynovitis, enthesitis and **dactylitis**.

**Note:** Psoriatic plaques typically precede development of the arthritic component.

- 20-30% of psoriasis patients will develop psoriatic arthritis
- **Ankylosing spondylitis and PsA are very similar, there are two key features to differentiate between them:**
  - **a)** In ankylosing spondylitis: patient develops **back pain FIRST**, then it may progress to develop psoriasis. While in psoriasis arthritis the patient presents with **Psoriasis FIRST**, then slowly develops back pain
  - **b)** The arthritis in AS involves the large joints, mainly lower extremity. While in PsA the arthritis involves the joints of the **hands**, mainly small joints.

# 2- Psoriatic Arthritis (PsA) *cont.*



## ◀ Pathogenesis of PsA

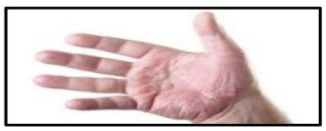
- PsA is a chronic progressive disease. Genetic factors have an important role in PsA and family studies have suggested that heritability may exceed 80%. Variants in the **HLA-B and HLA-C** genes are the strongest genetic risk factors.

**Increased levels of TNFα found in joint:**
- Pro-inflammatory effect
- Stimulation of proteases

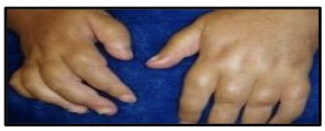
**Synovial hyperplasia and cellular infiltration:**
- **Pannus** formation
- Cartilage **erosion**
- Prominent role for cytotoxic **(CD8+) T cells**

**Associated enthesitis present.**

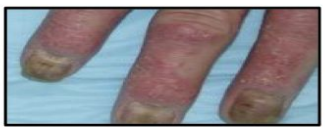
**Skin changes**



**Swelling**



**Affected nails**



**Mutations**

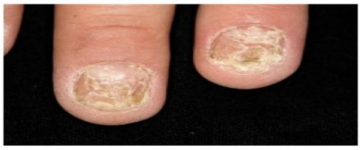
**Time/Years**

## ◀ Clinical features of PsA

- The presentation is with **pain** and **stiffness** affecting joints, tendons, spine and entheses. Joints are typically **not swollen**; however, several patterns of joint involvement are recognised (see next page).

| Clinical feature | Pt % |
|---|---|
| Actively inflamed joints | 97 |
| Plaque psoriasis | 94 |
| Nail lesions | 83 |
| DIP joint disease | 54 |
| Morning stiffness | 52 |
| Deformities: ≥1 / ≥5 | 43/16 |
| Skin and joints flaring simultaneously | 35 |
| Dactylitis | 33 |
| Inflammatory neck pain and stiffness | 23 |
| Inflammatory back pain and stiffness | 19 |
| ACR functional class III/IV | 11 |
| Sacroiliac stress pain | 10 |
| Iritis | 7 |

**Plaque psoriasis:** Scaly rash, most frequently occurring on the scalp, elbows and knees



Moderate to severe nail changes in patient with Psoriasis

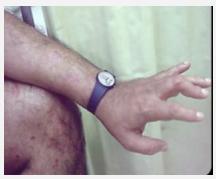
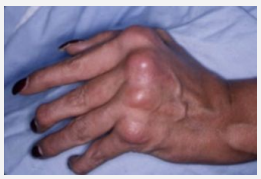
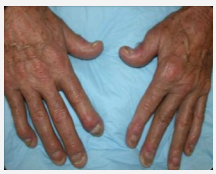
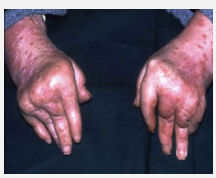
Fingernail **pitting**

# 2- Psoriatic Arthritis (PsA) *cont.*



## ◀ Patterns of joint involvement in PsA

- **Some features are common to nearly all patterns of PsA:**
  - **Morning stiffness**
  - **Nail disease** which are **onycholysis**, **ridging** and **pitting**.
  - **Joint pain**

| Pattern | Features | Rate |
|---|---|---|
| **Asymmetrical oligoarthritis**  | • Usually involves **small joints**, less frequently involves large joints<br>• It occurs most characteristically in the **hands and feet**, when synovitis of a finger or toe is coupled with tenosynovitis, enthesitis and inflammation of intervening tissue to give a **'sausage digit' or dactylitis**<br>• Normally **oligoarthritis (≤4 joints)**<br>• Asymmetric psoriatic arthritis does not affect matching pairs of joints on opposite sides of the body.<br>• Arthritis onset usually develop **after the psoriasis**. | **47%** |
| **Symmetrical polyarthritis**  | • Involves **small joints and large joints**<br>• Symmetric psoriatic arthritis affects the same joints -- usually in multiple matching pairs -- on opposite sides of the body.<br>• Symmetric psoriatic arthritis can be disabling, causing varying degrees of progressive, destructive disease and loss of function in 50% of people with this type of arthritis<br>• More common in women<br>• May be **RF positive** (clinically similar to RA)[1]<br>• Arthritis onset may develop **concurrently with psoriasis** | **25%** |
| **Psoriatic Spondylitis** | • **SIJ** and **vertebrae** affected **asymmetrically**<br>• More common in men<br>• This type presents with inflammatory back or neck pain and prominent stiffness symptoms<br>• May coexist with peripheral PsA<br>• Enthesitis prevalent. Coarse, asymmetrical non-marginal syndesmophytes.<br>• Arthritis onset usually develop **after the psoriasis** | **23%** |
| **DIP synovitis**  | • Restricted to **only DIP joints.**[2] Distal interphalangeal predominant psoriatic arthritis involves primarily the small joints in the fingers and toes closest to the nail. With nail dystrophy in the affected digit.<br>• DIP psoriatic arthritis is sometimes confused with osteoarthritis, a chronic disease that causes the deterioration of joint cartilage and bone at the joints.<br>• Associated with **dactylitis**<br>• Associated with **psoriatic nail disease** | |
| **Arthritis mutilans**  | • This is a **deforming destructive erosive arthritis** targeting the fingers and toes closest to the nails (**Joint lysis**)<br>• Prominent cartilage and bone destruction results in marked instability.<br>• The encasing skin appears invaginated and **'telescoped'** ('main en lorgnette') and the finger can be pulled back to its original length. | **5% (rare)** |

1- Nodules and other extra-articular features of RA are absent and arthritis is generally less extensive and more benign.
2- Both rheumatoid arthritis and psoriatic arthritis affect the hands. However, in psoriatic arthritis patients have psoriasis and Distal interphalangeal joint (DIP) involvement. In contrast, DIP joint is spared in RA.

# 2- Psoriatic Arthritis (PsA) *cont.*



## ◀ Investigations

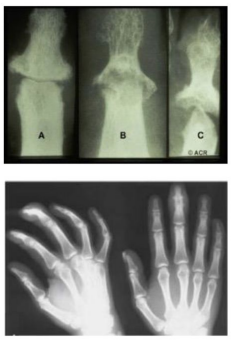
- **Arthritis in the presence of psoriasis is the key to clinical diagnosis.**
- **The onset of arthritis depends on the subtype:**
  - **Delayed** after psoriasis onset: Asymmetrical, Spondylitis.
  - **Concurrent** with psoriasis: Symmetrical.
- Diagnosis is clinical and radiographic.

### 1 Blood tests

- Autoantibodies are generally negative
- Acute phase reactants, such as ESR and CRP, are raised in only a proportion of patients with active disease but are often **normal**.

### 2 X-Ray (Best initial)

- Characteristic peripheral joint destruction progresses to cause a **"pencil in cup"** appearance
- Radiologically, psoriatic arthritis is erosive but the erosions are central in the joint, not juxta-articular.
- In spondylitis subtype, may also see sacroiliitis and changes in the spine.

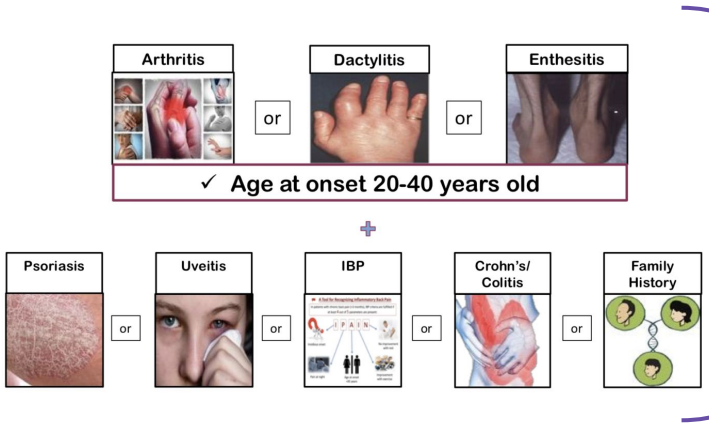




### 3 MRI and US

- MRI and ultrasound with power Doppler are increasingly employed to detect synovial inflammation and inflammation at the entheses.

## ◀ Diagnosis algorithm




**Start confirmation**
- Involved joints in X-ray
- HLA B27

**Present?**

**Connect to Rheumatologist**

# 2- Psoriatic Arthritis (PsA) *cont.*

## ◀ Treatment

**Same as AS, except that we start with methotrexate instead of sulfasalazine** (**Oral** corticosteroids may destabilize skin disease; they are best avoided. Local synovitis responds to intra-articular CS injections.)

- **First line:** NSAIDs
- **Second line:** Methotrexate (Only treats peripheral disease). If MTX fails, start them on sulfasalazine. if sulfasalazine fails then give biologic therapy.
- **Third line:** Biologic Therapy (TNF blockers/IL-17 Inhibitors) (If Axial, use biologic therapy as 2nd line instead of MTX and sulfasalazine)

# 3- Reactive arthritis (ReA)

### Definition

- **Reactive (spondylo)arthritis (ReA)** is a 'reaction' to a number of bacterial triggers with clinical features in keeping with all SpA conditions. It's simply **sterile synovitis**, which occurs **following an infection.**
- **Formerly called Reiter syndrome, classic triad: Conjunctivitis, Urethritis, Reactive Arthritis**

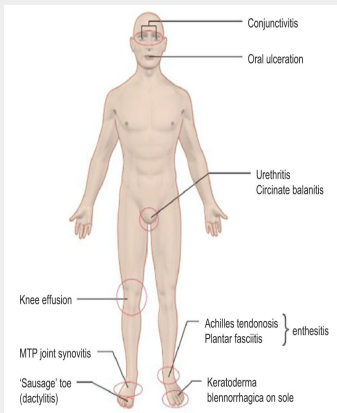
## ◀ Etiology

- **Preceding enteric infection (i.e. diarrhea)**
  - **Salmonella** of various serovars
  - **Shigella**, especially Shigella flexneri, but also dysenteriae and sonnei.
  - **Yersinia** including Yersinia enterocolitica 0:3 and 0:9 and Yersinia pseudotuberculosis
  - **Campylobacter** especially campylobacter jejuni
  - **Clostridium** difficile
- **Preceding genitourinary infection (i.e. urethritis)**
  - **Chlamydia** trachomatis

Note: The arthritis associated with rheumatic fever is also an example of a reactive arthritis that is not associated with HLA-B27.

## ◀ Clinical features

- The typical case is a young man who presents with an **acute arthritis shortly (within 4 weeks, it never occurs in the first 2 weeks) after an enteric or sexually acquired infection**.
- The onset is typically **acute**, with an inflammatory enthesitis, **oligoarthritis** and/or spinal inflammation.
- **Lower limb** joints and entheses (**Achilles insertional enthesitis**) are predominantly affected in an **asymmetrical pattern.**
- **Low back pain** and **stiffness** due to enthesitis and osteitis are common and 15–20% of patients develop sacroiliitis.
- **Circinate balanitis**, which starts as **vesicles** on the coronal margin of the **prepuce and glans penis**, later rupturing to form superficial erosions with minimal surrounding erythema, some coalescing to give a circular pattern
- **keratoderma blennorrhagica**, which begins as discrete waxy, **yellow–brown vesico-papules** with desquamating margins, occasionally coalescing to form large crusty plaques on the **palms** and **soles of the feet**
- **Nail dystrophy**



# 3- Reactive arthritis *cont.*



## ◀ Investigations

**The diagnosis is usually made clinically but joint aspiration may be required to exclude crystal arthritis and articular infection.**

1) **Joint aspirate: Aspirated synovial fluid is sterile, with a high neutrophil count.**
2) **ESR** and **CRP** are **raised**, urethritis may be confirmed in the **'two-glass test'** by demonstration of mucoid threads in the **first-void specimen that clear in the second**.
3) High vaginal swabs may reveal **Chlamydia on culture**.
4) **Except** for **post-Salmonella** arthritis, **stool cultures are usually negative** by the time the arthritis presents but serology may help confirm previous dysentery.
5) **Serology:** RF, ACPA and ANA are negative.
6) **Radiology:**
   a) In contrast to AS, radiographic sacroiliitis is often **asymmetrical** and sometimes **unilateral**, and **syndesmophytes** are predominantly **coarse and asymmetrical**, often extending beyond the contours of the annulus (**'non-marginal'**).
   b) Radiographic changes in the peripheral joints and spine are **identical to those seen in psoriasis.**

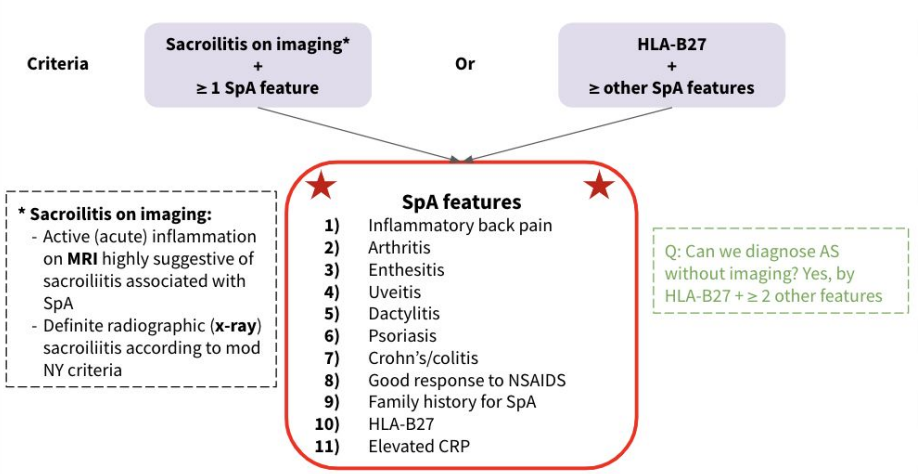
## ◀ Treatment

- **Acute ReA** → rest, NSAIDs and analgesics.
- **Monarticular synovitis** → Intra-articular glucocorticoids
- **Polyarticular disease** → Systemic glucocorticoids
- If **chlamydial urethritis** is diagnosed, it should be treated empirically with a short course of **doxycycline** or a single dose of **azithromycin**.
- **Relapsing cases, persistent marked symptoms**, **recurrent arthritis** or **severe keratoderma blennorrhagica**. → Treatment with DMARDs (usually sulfasalazine or methotrexate)
- **Anterior uveitis** is a medical emergency requiring topical, subconjunctival or systemic glucocorticoids.
- For **DMARD-recalcitrant cases**, anti-TNF therapy should be considered.

**Note:** There is no convincing evidence for the use of antibiotics unless a triggering infection is identified.

# Summary

## Ankylosing spondylitis

| | |
|---|---|
| **Definition** | Ankylosing spondylitis (AS) is defined by the presence of **sacroiliitis on X-ray** and other structural changes on spine X-rays, which may eventually progress to bony fusion of the spine. SI joint is the most common to be affected. |
| **Association** | HLA-B27 |
| **Typical presentation** | 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,** hot shower and worsen with rest. There is a progressive loss of spinal movement |
| **Other features** | • **Anterior uveitis**<br>• Loss of Lordosis<br>• Kyphosis |
| **Investigations** | **X-ray (Best initial)**<br>• Sacroiliac joint show irregularity and loss of cortical margins, widening of the joint space and subsequently sclerosis, joint space narrowing and **fusion**.<br>**MRI (most accurate)**<br>• More sensitive than x-ray |
| **Criteria** |  |
| **Treatment** | **First line:** NSAIDs (e.g. Diclofenac, Ibuprofen) to relieve symptoms<br>**Second line:**<br>- Axial AS: Biologic therapy (Anti-TNF or IL-17 inhibitors)<br>- Peripheral AS: Sulfasalazine, failed? → Local corticosteroids, failed? → Anti-TNF or IL-17 inhibitors<br>**NOTE:** Sulfasalazine & Local corticosteroids are NOT used for axial AS! Anti-TNF can also treat all the associated features e.g. uveitis, enthesitis, peripheral arthritis, skin psoriasis |

# Lecture Quiz

**Q1: A 23-year-old man presents to the rheumatology clinic with lower back and hip pain. These have been occurring every day for the past two months. Pain and stiffness are worse in the mornings. He also mentions that his right heel has been hurting. He is previously fit and well, but had occasions of lower back pain when he was a teenager. His symptoms have stopped him from playing tennis. Recent blood tests organized by his GP have shown a raised C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). What is the most appropriate treatment?**

A- NSAID and spinal exercises
B- NSAID and bed rest
C- Oral prednisolone
D- Methotrexate plus sulfasalazine
E- Bed rest

**Q2: A 20-year-old man presents to accident and emergency with sudden onset pain in the right eye, with associated blurred vision and discomfort when gazing at the lights. He has a history of back pain and has recently been diagnosed with ankylosing spondylosis. What is the most likely cause of his eye pain?**

A- Conjunctivitis
B- Retinal detachment
C- Anterior uveitis
D- Corneal ulceration
E- Acute glaucoma

**Q3: A 55-year-old man presents to his GP with a 2-week history of pain in his hands. The pain is particularly bad in his right hand. On examination, brown discoloration of the nails with onycholysis is noted and the distal interphalangeal joints are tender on palpation. What is the most likely diagnosis?**

A- Rheumatoid arthritis
B- Dermatomyositis
C- Reactive arthritis
D- Osteoarthritis
E- Psoriatic arthritis

**Q4: A 30-year-old man presents to his GP with a 1-week history of painful, swollen knees and a painful right heel. Further history reveals that he has been experiencing burning pains while urinating for the past 2 weeks and that his eyes have become red and itchy. What is the most likely diagnosis?**

A- Septic arthritis
B- Gout
C- Ankylosing spondylitis
D- Enteropathic arthritis
E- Reactive arthritis

**Q5: A 22-year-old man develops the insidious onset of low back pain improved with exercise and worsened by rest. There is no history of diarrhea, conjunctivitis, urethritis, rash, or nail changes. On examination, the patient has loss of mobility with respect to lumbar flexion and extension. He has a kyphotic posture. Which test or group of tests would be most supportive of your suspected diagnosis?**

A- MRI of the lumbosacral spine showing spinal compression fractures associated with bony destruction
B- An elevated sedimentation rate, a mild anemia on CBC, positive HLA-B27 in blood and sclerosis of the sacroiliac joints on plain films of the back.
C- A positive rheumatoid factor, anti-CCP, and an elevated C-reactive protein level
D- Lumbosacral x-rays showing vertebral joint space narrowing and osteophyte formation at various levels.
E- A colonoscopy with biopsy results consistent with Crohn disease.

Answers: Q1:A | Q2:C | Q3:E | Q4:E | Q5:B

Answers Explanation File!

# THANKS!!

## This lecture was done by:

Mashal AbaAlkhail

**Females co-leaders:**
Raghad AlKhashan
Amirah Aldakhilallah

**Males co-leaders:**
Mashal AbaAlkhail
Nawaf Albhijan

Send us your feedback:
We are all ears!