Medicine TEAM 437

MED437 KING SAUD UNIVERSITY

Spondyloarthritis (SpA) diseases

Objectives :

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

Done by :

Team leader: Al Hanouf Al Jaloud

Team Members:

Abdullelah Al Saeed — Munira Al Hadlg

Rahaf Al Thunayan — Saleh Mahjoub

Revised by: Aseel Badukhon & Yazeed Aldossari

Resources :

Doctors slides + notes: dr. Mohammed Bedaiwi

Step up to medicine

Kumar & Clark's clinical medicine

Disclaimer!!!!:

Slides that were skipped by the doctor have not been mentioned in the teamwork. Revisit Doctors slides for the whole content.

Important Notes Before Studying:

- All Spondyloarthropathies overlap and Share similar characteristics but differ in their main presentation.
- These common characteristic are:
  - -ALL are seronegative
  - -ALL have some association (especially AS!) with HLA-B27 Gene.
  - -ALL might develop (Enthesitis, Dactylitis, Uveitis)
  - - First line treatment is always NSAIDs
- Know how to differentiate between Mechanical vs Inflammatory back pain.
- Know how to differentiate between Axial vs peripheral SpAs.
- Differentiate between **Ankylosing spondylitis** vs **Psoriatic arthritis** vs **Reactive arthritis** presentation and management.

Spondyloarthritis (SpA) diseases:

Group of diseases characterised as being seronegative.

Predominantly Axial

- **Ankylosing spondylitis (AS)**
- Non-radiographic axial spondyloarthritis (nr-axSpA) (same as AS but without X ray changes yet)

Predominantly Peripheral

- Psoriatic Arthritis (PsA)
- **Reactive Arthritis (ReA)**
- IBD related arthritis (ulcerative colitis/ Crohn's disease)
- Undifferentiated Peripheral SpA

Updated ASAS Concept of Spondyloarthritis (SpA) into Two Broad Overlapping Categories

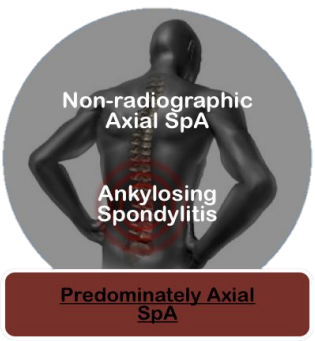
All these Diseases overlap and Share similar characteristics but differ in their main presentation.

1-The Axial SpA:
- Spine or Chest or Hip Joints

(Ankylosing spondylitis (AS)/Non-radiographic axial spondyloarthritis (nr-axSpA))

2- The Peripheral SpA:
- Fingers or Knees or Toes

Psoriatic Arthritis (PsA) / IBD related arthritis (ulcerative colitis/ Crohn's disease) / Reactive Arthritis (ReA) / Undifferentiated Peripheral SpA



Back Pain

- 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.

Back pain is a very common and vague symptom that's why SpA Dx is commonly missed "underdiagnosed disease"

Low Back Pain is caused by a specific disorder:

Back pain pain and Kyphosis

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

Physician role is to recognize non-mechanical cause

Inflammation is bad but treatable. And with time it can cause damage.

Comparison of inflammatory back pain (IBP) and chronic mechanical back pain (MBP) Important*****

IBP	MBP
Age of onset: <40 years (15-45)	Ex: Disc / Muscle strain ...etc
Insidious onset: **less likely to be acute**	Age of onset: any age
Pain improves with exercise Ptn keeps moving in waiting room and cant sit	Variable onset: may be acute
Pain does not improve with rest	Usually following trauma
Morning stiffness >30 minutes	Pain may worsen with movement
Pain at night (especially in buttuck + alternating) which may wake patient during second half of the night	Pain often improves with rest

Spondyloarthropathy Patients will have symptoms of IBP not MBP!

Inflammatory back pain:

Chronic back pain (>3 months) IBP criteria are fulfilled if at least 4 out of 5 parameters are present:

IPAIN:

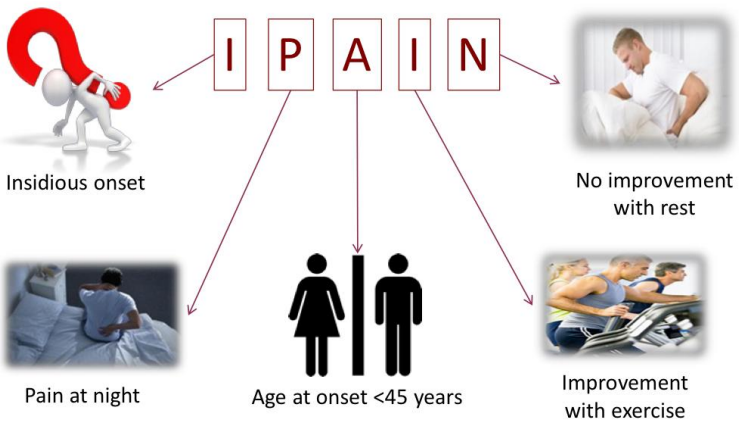
Insidious onset

Pain at night

Age onset <45

Improves with Exercise

No improvement with rest



Ankylosing spondylitis (AS) Axial Spondyloarthritis

General:

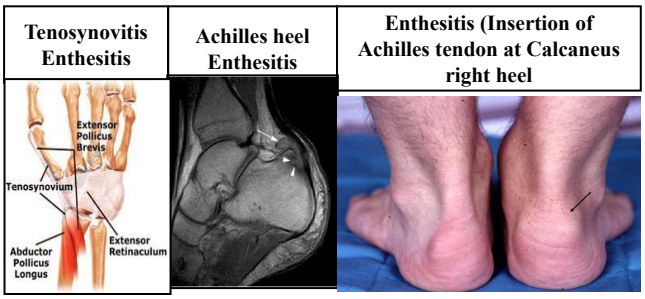
- Inflammatory Disorder of the spine. **Bilateral sacroiliitis** characterized by fusion of the spine in an ascending manner (lumbo-cervical direction) with secondary Lower back pain and stiffness.
- characteristically worse in the morning and better as the day progresses.
- Improve with activity and a hot shower and worsen with rest.
- Loss of lumbar lordosis and increased kyphosis
- It is a progressive disease that can lead to deformity over time

Clinical Features: Important

The most important clinical feature is **inflammatory back pain.**
Pain might extend to the buttock

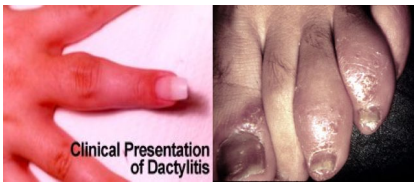
Heel Pain - Enthesitis:

- Enthesitis is inflammation of **Entheses.**
  Entheses are sites where tendons, ligaments, joint capsules, or fascia attach to bone.
- **Achilles Heel Enthesitis is the most common site.**
  (Achilles tendon)



Dactylitis

Inflammation of the entire finger "sausage shaped"



Acute Anterior Uveitis

- What is the most common extra-articular manifestation of SA?
  Acute Anterior Uveitis!

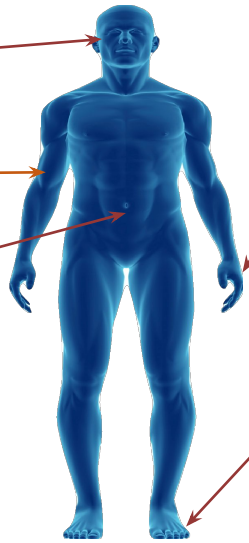
- Acute onset
- Unilateral
- Anterior
- Spontaneous remission "self limited"
- Recurrent
- Related to HLA_B27
- Unrelated to disease activity!!
- Has no complication

Extra-articular Manifestations

Anterior Uveitis
25-40% of patients affected

Psoriasis
16% of patients affected

Inflammatory bowel Disease (IBD)
10% of patients affected
(UC & CD)



Dactylitis
21.5% of patients affected

Enthesitis
25-58% of patients affected

Investigation:

ESR & C-reactive protein

- Levels are increased up to 70% in most As. Patient.
- No relation with disease activity.
- If ESR or CRP is normal this doesn't reflect that there is no AS.
- Only 60% correlation

HLA-B27

"هلا عمرها ٢٧ سنة"

It's important to order HLA-B27 gene when suspecting spondyloarthropathies

- 90% to 95% of AS patient.
- Is neither necessary nor sufficient for the diagnosis of patient that their history and physical examination suggest AS.
- If the radiographic finding is not clear the lab, Test may be confirmatory.

Rule of 10:
10% of AS patients will not have the HLA-B27 Gene
10% of the population will have the gene.

Imaging - X-ray

The **sacroiliac joint** in the most commonly involved joint. However, AS can involve any part of the spine and some large joints.

Grading of Radiographic Sacroiliitis (1966)

Changes seen on x-ray:
- Sclerosis (appears white on x-ray)
- Widening of SI joint
- Fusion

Grade 0	Normal	
Grade 1	Suspicious changes	
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"

X ray is always the 1st step but not diagnostic. But gold standard is MRI
-The earliest Radiological sign Blurring of the upper or lower vertebral rims.

Grade 0

- 22 y.o male.
- Inflammatory back pain for a year.
- Recurrent iritis.
- Family Hx of SpA
- Good response to NSAIDs
- What's the diagnosis
- What's the next step? MRI

Sacroiliitis Grade 0 (Normal)

Grade 3

Bilateral Grade 3 Radiographic Sacroiliitis:
Bony Changes
Inflammation is not Visible on Plain X-ray

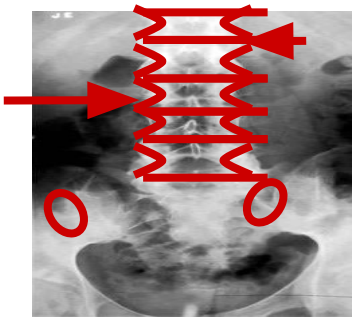
Sclerosis seen as white areas

***Note loss of the clear SI joint line and "fluffy" white area surrounding both SI joints**

Spondylitis *(Inflammation of the vertebra)*

Normal

Bridging: fusion of spinal vertebrae

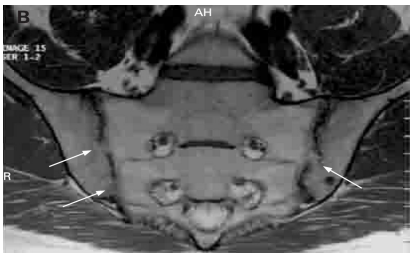


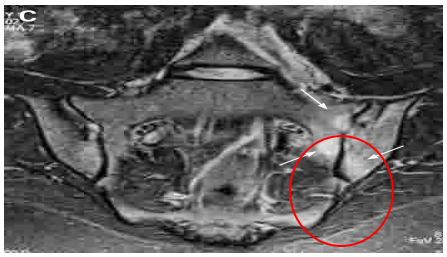
Ankylosing Spondylitis:
Bamboo Spine "result of vertebral body fusion"
Lumbar Vertebrae

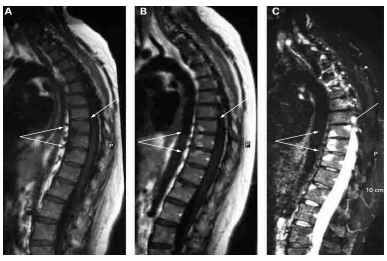
Extra

Imaging- MRI

X-ray changes takes two years to appear but MRI changes shows within weeks.
X-ray changes? **Ankylosing spondylitis (AS)**
X-ray changes have not appeared yet? (but appears in MRI) **Non-radiographic axial spondyloarthritis (nr-axSpA)**
MRI is the gold standard. Very sensitive & Specific







Extra from the Doctor:
T1 shows: Bone (structural) changes "Erosion or fusion"
T2 shows: Bone marrow inflammation

Diagnostic Criteria

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

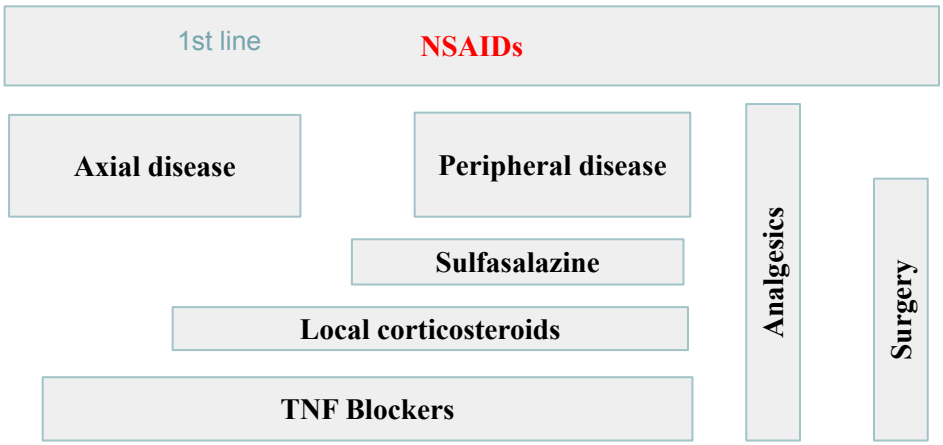
SpA features
- inflammatory back pain (IBP)
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

Sensitivity: 79.5%, Specificity: 83.3%;

Management *Important!!!*

ASAS/EULAR Recommendations for the Management of Ankylosing Spondylitis:

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



Golden therapeutic duration 8-12 months

Treatment:
1st line is NSAIDs to all patients.
If NSAIDs failed =>
For Axial AS: Biological Therapy (TNF blockers/IL-17 Inhibitors) "Corticosteroids & Sulfa won't work on spine!!"
For Peripheral AS: Sulfasalazine (Failed?) => Local corticosteroids (failed?) => Biological Therapy (TNF blockers/IL-17 Inhibitors)

Psoriatic Arthritis (PsA)

- **Arthritis** associated with **psoriasis**,
  - (a scaly rash, most frequently occurring on the elbows, knees, and scalp)
- **Identifying features:**

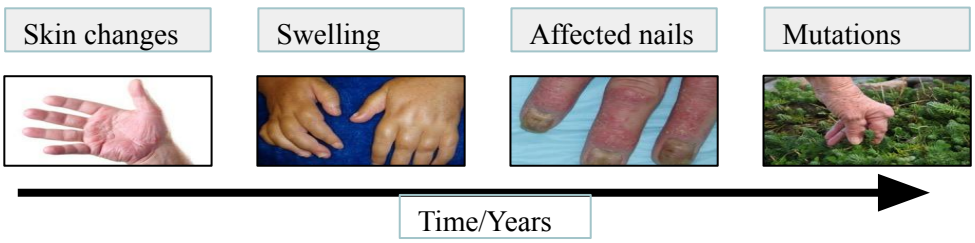
  Psoriasis: plaques typically precede development of the arthritic component. Skin changes starts before Joints symptoms.

  peripheral (PsA is mainly a peripheral disease) **arthritis** 30% will have back pain (Axial involvement)
- **Other manifestations**: spondylitis, tenosynovitis, **enthesitis**, **dactylitis** + **Nail pitting are characteristic**.
- **20-30%** of psoriasis patients will develop psoriatic arthritis
- No correlation between the severity of psoriatic plaques and PsA has been identified.
- Equal gender distribution. (♂ : ♀) - Peak years of onset typically between the ages of 20 and 40

Pathogenesis of PsA

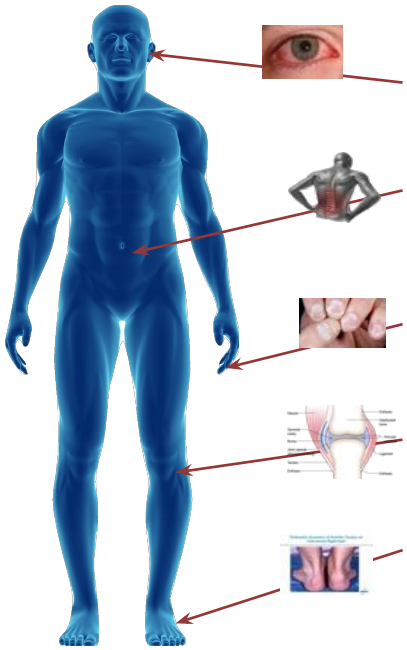
- Synovial hyperplasia and cellular infiltration.
  - **Pannus formation**
  - Cartilage erosion
  - **Prominent role for cytotoxic (CD8+) T cells**
- **Increased levels of TNFα found in joint.**
  - Pro-inflammatory effect
  - Stimulation of proteases
- Associated **enthesitis** present.

PsA is a chronic progressive disease



Clinical Features of PsA

Clinical feature	Patients (%)
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



Uveitis
25% of patients affected

Axial Disease
40% of patients affected

Nail Psoriasis
80-90% of patients affected at some point

Synovial joint involvement

Enthesitis
20% of patients affected

scaly rash, most frequently occurring on the scalp, elbows and knees

Moderate to severe nail changes in patient with Psoriasis

Fingernail **pitting**

Patterns (types) 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	• Usually involves small joints, less frequently involves large joints • Normally oligoarthritis (≤4 joints) • Arthritis Onset usually develop after the psoriasis.	~ 47%
Symmetrical	• Involves small joints and large joints • May be RF positive (clinically similar to RA) • Arthritis onset may develop concurrently with psoriasis	~ 25%
Spondylitis	• SIJ and vertebrae affected asymmetrically • More common in men • May coexist with peripheral PsA • Enthesitis prevalent • Arthritis Onset usually develop after the psoriasis.	~ 23%
DIP synovitis	• Restricted to only DIP joints	
Arthritis mutilans	• Joint lysis • Telescoping movement	

Asymmetric Psoriatic Arthritis

- Asymmetric psoriatic arthritis typically involves one to three joints in the body -- large or small (usually small)-- such as the knee, hip, or one or several fingers.
- Asymmetric psoriatic arthritis does not affect matching pairs of joints on opposite sides of the body.

Symmetric Psoriatic Arthritis

- Symmetric psoriatic arthritis affects the same joints -- usually in multiple matching pairs -- on opposite sides of the body.
- 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.
- Symmetric psoriatic arthritis **resembles rheumatoid arthritis.**

Distal Interphalangeal Predominant (DIP)

Usually the PIP is with RA

- 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.

- DIP psoriatic arthritis is sometimes confused with osteoarthritis, a chronic disease that causes the deterioration of joint cartilage and bone at the joints.
  DIP joints are usually spared in RA+Lupus !!

Arthritis Mutilans

- Arthritis mutilans is a severe, 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.
- Fortunately, this severe type of psoriatic arthritis is **rare**.

The onset of arthritis depends on the subtype:

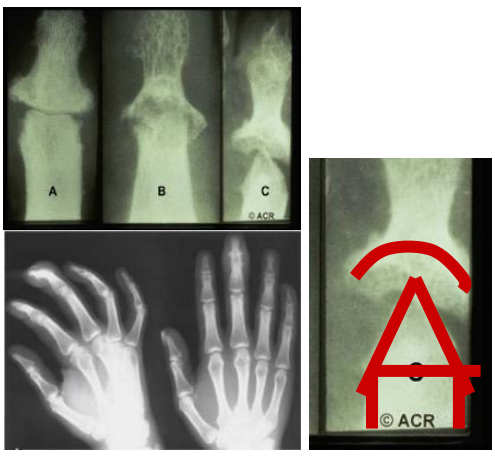
Delayed after psoriasis onset:
- asymmetrical, spondylitis.

Concurrent with psoriasis:
- symmetrical.

PsA Radiologic Features

- Characteristic peripheral joint destruction progresses to cause a **"pencil in cup"** Appearance with arthritis mutilans pattern

- In spondylitis subtype, may also see sacroiliitis and changes in the spine.



Diagnosis:

- Arthritis in the presence of psoriasis is the key to clinical diagnosis.
- Diagnosis is **clinical** and **radiographic**.

Symptoms at presentation determine which pathway

Axial ± peripheral symptoms at time of presentation

- Apply ASAS Criteria for **Axial** SpA

Purely peripheral symptoms at time of presentation*

- Apply ASAS Criteria for **Peripheral** SpA

ASAS Classification Criteria for Spondyloarthritis (SpA)

Axial

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

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

Peripheral

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

ASAS

Management of PsA:

- **NSAIDs 1st line**
- If failed give **Methotrexate**
- If failed give **Biological Therapy** (TNF blockers/IL-17 Inhibitors)
- Local synovitis respond to intra-articular corticosteroids.

Reactive Arthritis (ReA)

Was not mentioned in the slides but doctor said its important. He also explained it in the lecture.

Reactive arthritis is a **sterile** synovitis.which occurs following:

Gastrointestinal infection: Shigella, Salmonella, Yersinia or Campylobacter
Urinary Tract Infection "usually an STD"**:** Chlamydia trachomatis, Ureaplasma realyticum.

- Symptoms of ReA takes **at least 14 days** from the time of infection to appear. After UTI or GI infection only!!!
- Occurs mostly in **HLA-B27** positive individuals.

Test yourself:
A 33-year-old man has a 3-month history of:

- right ankle pain and a left inflamed second toe (Asymmetric + mainly lower limbs).
- He had 4 days of bloody diarrhea(GI infection probably shigella) 3 months ago.

Clinical Features:

- Asymmetric inflammatory oligoarthritis of **lower extremities** (upper extremities less common); the knees, ankles and feet are the most common sites.
- Arthritis progresses **sequentially** from one joint to another. (New joints may be involved sequentially over days).
- skin lesions resemble psoriasis!:
  - Circinate balanitis
  - keratoderma blennorrhagica

Additional features:

- Classic triad of **Reiter's syndrome** (urethritis, reactive arthritis and conjunctivitis)
- Acute anterior uveitis
- Enthesitis (plantar fasciitis, Achilles tendonitis)
- Few patients develop sacroiliitis and spondylitis.

Undifferentiated spondyloarthropathy: when a patient has features of reactive arthritis but there is no evidence of previous infection (in the GI or genitourinary tract) and the classic findings of Reiter syndrome are absent.

Diagnosis:

Diagnosis is clinical.
No specific test for reactive arthritis,

- ESR is raised in the acute stage
- Send synovial fluid for analysis (to rule out infection or crystals)
- Aspirated synovial fluid is **sterile,** with a **high neutrophil** count.
- Good prognosis

Management:

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

Basically: ★
NSAIDs are 1st line therapy
Failed? Give sulfasalazine.

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. Used only to treat the actual infection and not the arthritis.

Summary:

Disease	Ankylosing spondylitis	Psoriatic arthritis	Reactive arthritis	Enteropathic arthritis
Most commonly involved joint	Sacroiliac	Asymmetrical involvement of the small joints of the hand, including the DIPs.	Asymmetrical involvement of the knees, ankles and feet.	-Arthritis of patients with ulcerative colitis or crohn's disease. - It parallels the activity of the disease.
Clinical features	-Low back pain And Early morning stiffness radiating to the buttocks or posterior thighs. - Enthesitis -transient peripheral arthritis - extra-articular manifestations like psoriasis and anterior uveitis.	-arthritis in the presence of psoriasis. -Dactylitis -Nail changes: onycholysis, ridging, and pitting.	-Acute arthritis shortly (within 2-4 weeks) after an enteric or sexullay acquired infection. -Enthesitis -Dactylitis	
Diagnosis	Best initial : X-Ray Most accurate: MRI	Best initial :X- Ray	Clinical diagnosis Synovial fluid analysis: sterile with high neutrophils.	
Treatment	First line: NSAIDs If NSAIDS failed : Axial disease -> TNF-a Blockers Peripheral disease -> sulfasalazine	First line: NSAIDs Severe cases: methotrexate	First line: NSAIDs Severe cases: sulfasalazine	

Summary :

Inflammatory Back Pain	Mechanical Back Pain
Insidious onset	Variable onset; may be acute
Pain at night	-
Age <45 years	Any age
Improves with exercise and movement	Worsens with exercise and movement
Not relieved by rest	Relieved by rest
Morning stiffness lasting >30 mins	-

Quiz:

Q1: what is the most common complication associated with ankylosing spondylitis?
A. enthesitis of the Achilles tendon
B. anterior uveitis
C. enthesitis of the plantar fascia
D.posterior uveitis

Q2: 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.Reactive arthritis
C.Osteoarthritis
D.Psoriatic arthritis

Q3: 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. Ankylosing spondylitis
C. Enteropathic arthritis
D. Reactive arthritis

Q4: 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

Q5: All spondyloarthropathies have an immunogenetic association with which of the following antigens?

A. HLA DR4
B. HLA B24
C. HLA B27
D. HLA DR7

Answers:

1- B
2- D
3- D
4- A
5- C