SERONEGATIVE SPONDYLOARTHROPATHIES

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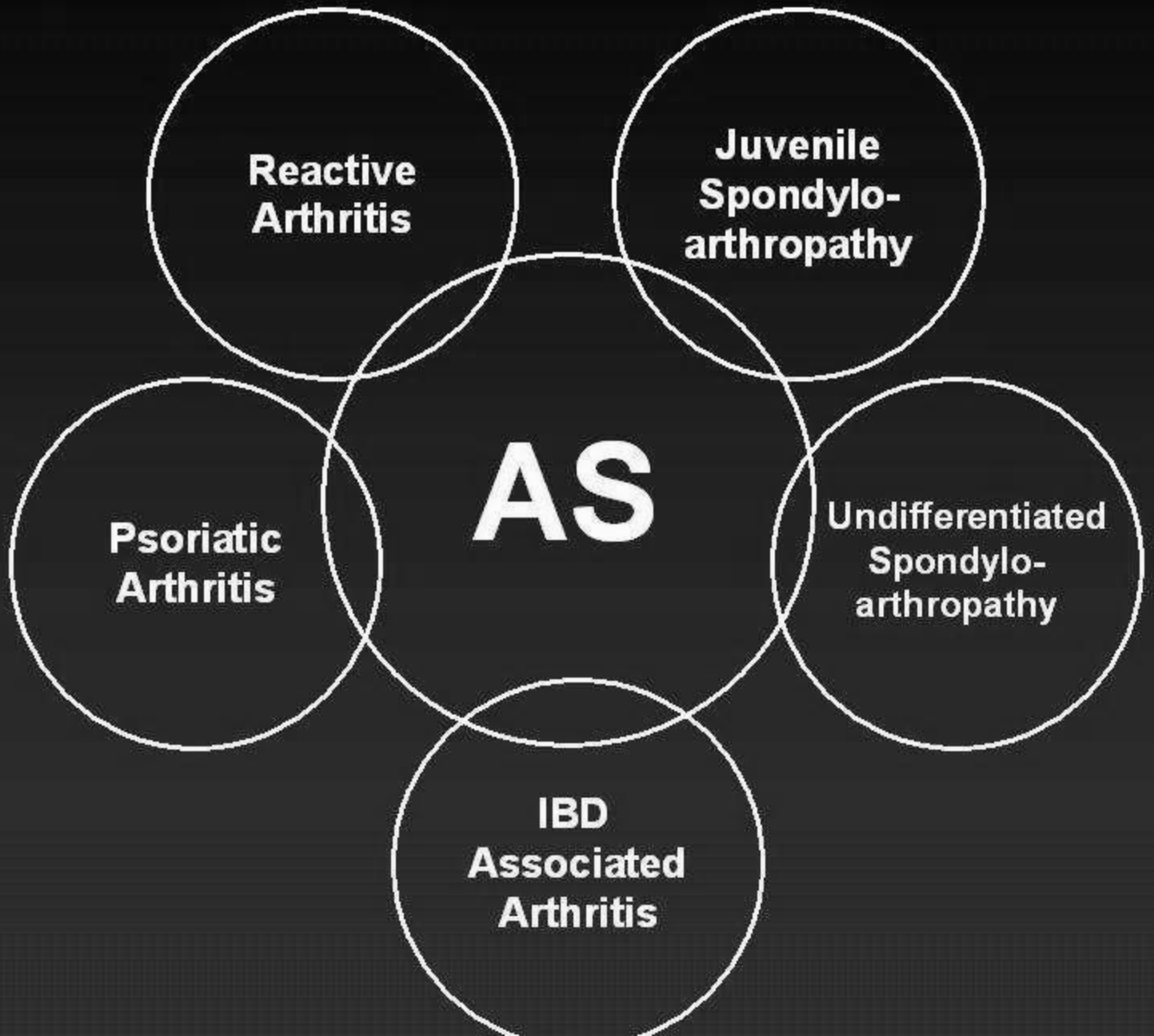
INTRODUCTION

- The Seronegative Spondyloarthropathies are a group of overlapping disorders that share certain clinical features and genetic associations.

Family of Spondyloarthropathies



What are the common features...

- Seronegative (i.e. rheumatoid factor is absent).
- Rheumatoid nodules are absent.
- Frequent association of HLA-B27.
- A tendency to occur in same family(familial aggregation).
- Inflammatory axial arthritis, generally Sacroiliitis and Spondylitis.
- Oligoarthritis generally with asymmetrical presentation.
- Enthesitis (inflammation of the entheses, the sites where tendons or ligaments insert into the bone) e.g. Plantar fasciitis, Achilles tendonitis, costochondritis.
- Extra-articular features, such as involvement of eyes (anterior uveitis), skin, genitourinary tract.

ANKYLOSING SPONDYLITIS

- Ankylosing Spondylitis (AS) is an inflammatory disorder of unknown cause that primarily affects the axial skeleton,peripheral joints and extra-articular structures.
- Marie-Strumpell's Disease/Bechterew Disease.

Epidemiology

- Males are affected more frequently than females (estimates vary from 2:1 to 10:1).
- Onset is between 15 and 25 years.
- There is a strong tendency to familial aggregation and association with the genetic marker HLA-B27.

Pathology

- Sacroiliitis is the earliest manifestation of AS.
- Synovitis, Pannus, Myxoid marrow, subchondral granulation tissue and marrow edema are found.
- In Spine, there is inflammatory granulation tissue at the junction of annulus fibrosis and vertebral bone.
- The outer annular fibers are eroded and replaced by bone, forming a *syndesmophyte*.

Pathogenesis

- The pathogenesis of AS is thought to be immune-mediated, but there is no direct evidence for autoimmunity. There is uncertainty regarding the primary site of disease initiation.

Clinical Manifestations

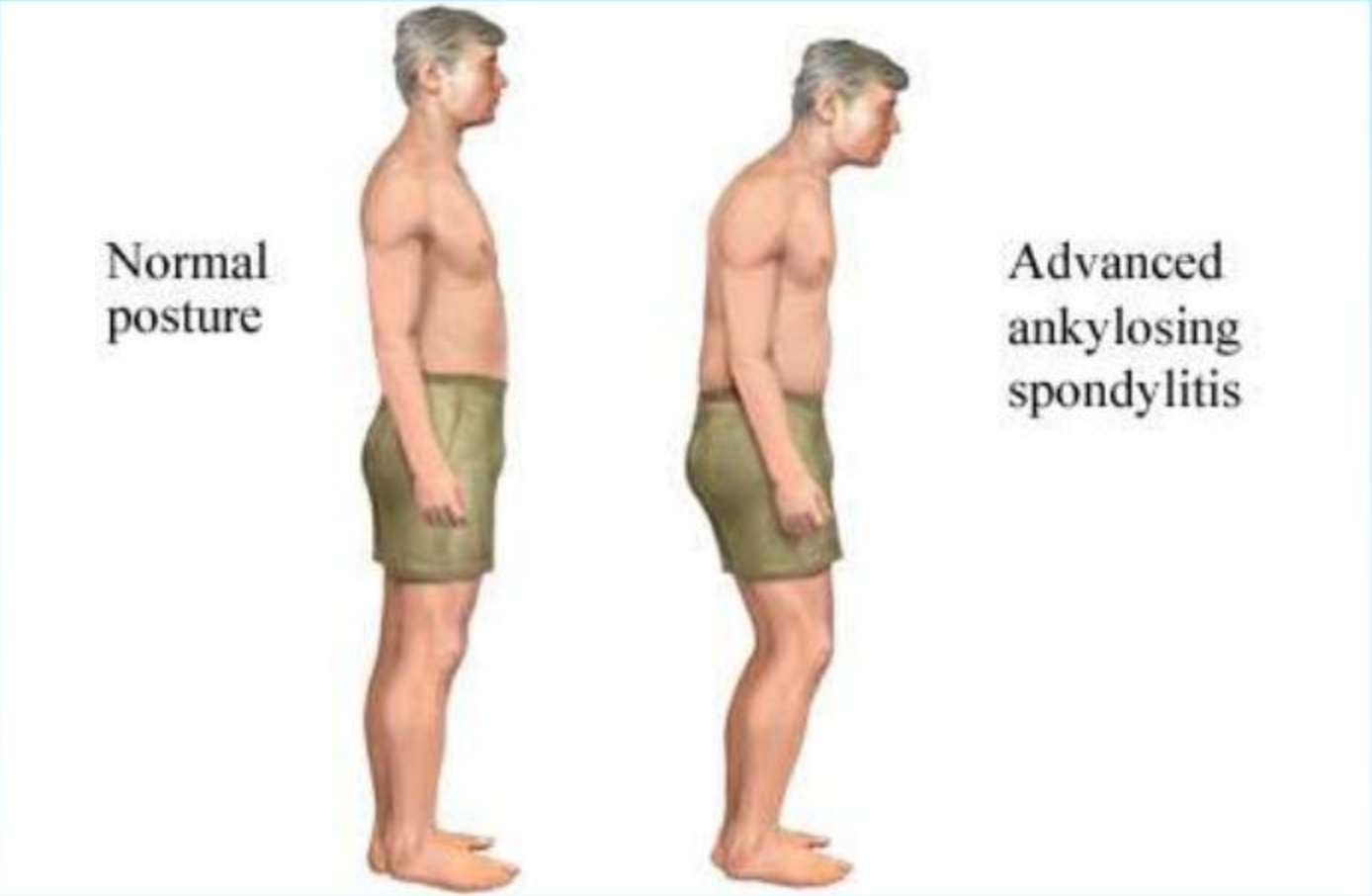
- The symptoms of the disease are usually first noticed in late adolescence or early adulthood median age being 23.
- The initial presentation of AS generally occurs in the SI joints; involvement of the SI joints is required to establish the diagnosis.
- SI joint involvement is followed by involvement of the diskovertebral, apophyseal, costovertebral, and costotransverse joints.

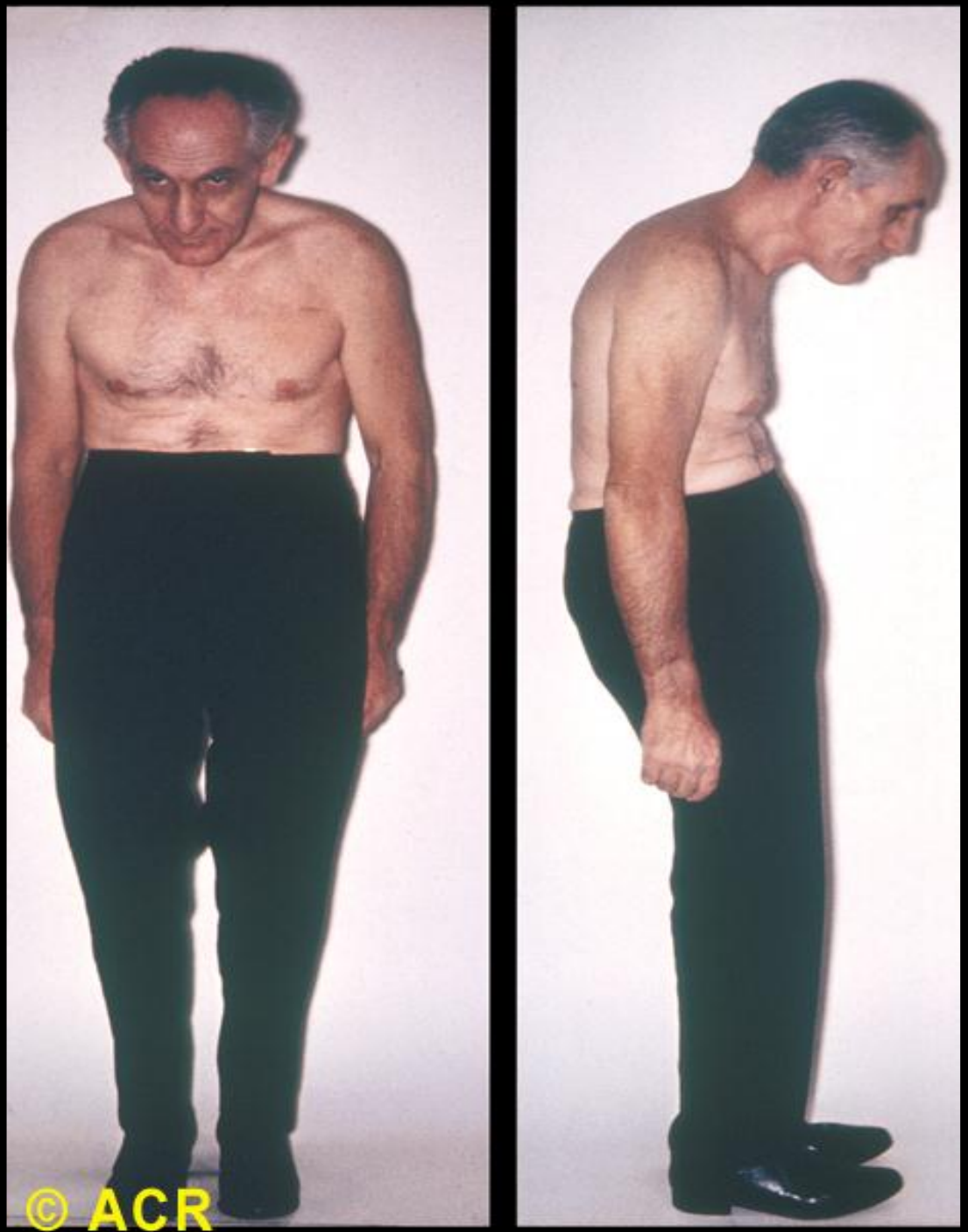
- The initial symptom is usually dull aching pain, insidious in onset, felt deep in the lower lumbar or gluteal region, accompanied by ***low-back morning stiffness*** of up to a few hours duration that *improves with activity and returns following inactivity.*

- Arthritis in the hips and shoulders occurs in 25–35% of patients.

- Arthritis of peripheral joints other than the hips and shoulders, usually *asymmetric*,occurs in another30% of patients.

STOOPED OVER POSITION

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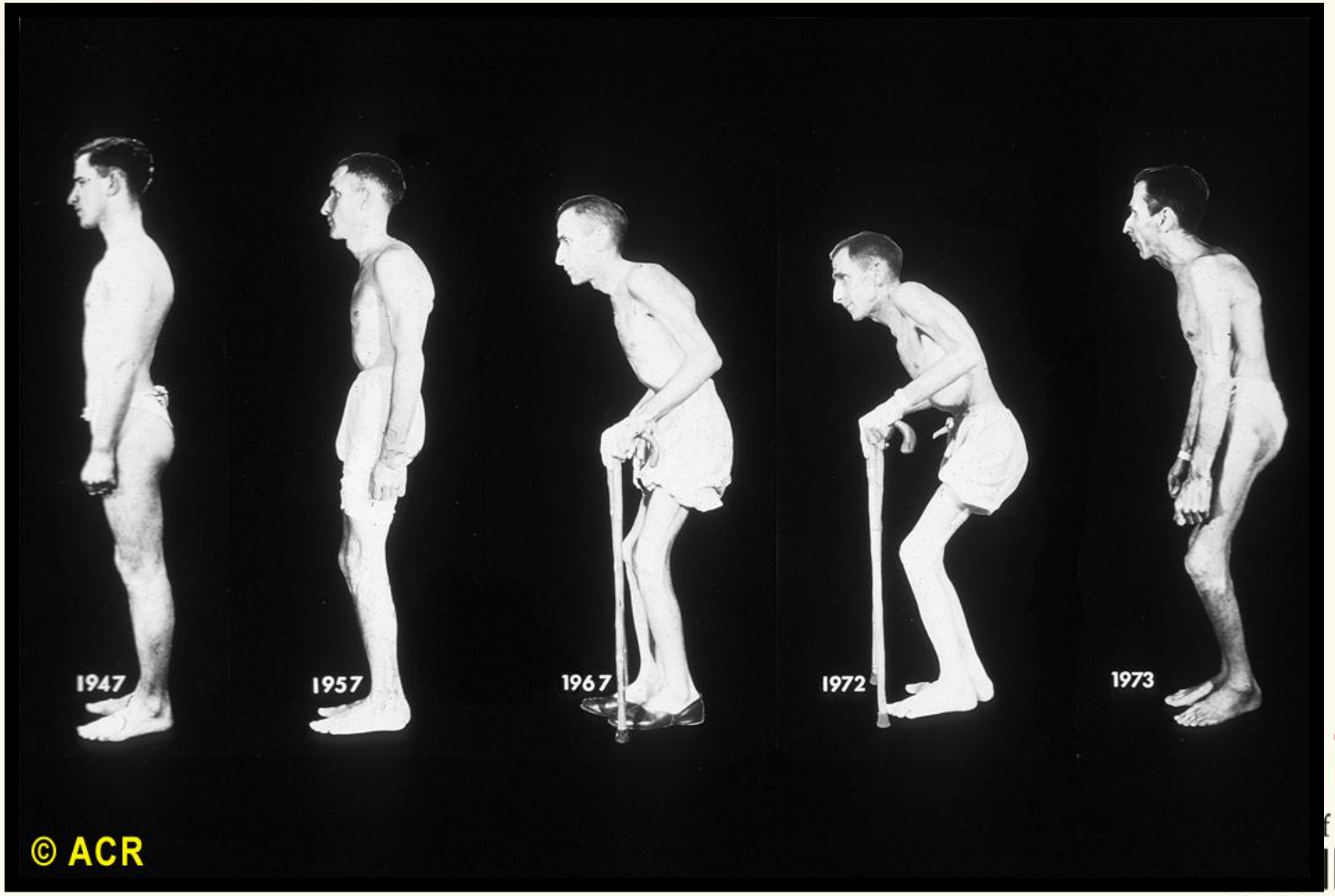
Ankylosing spondylitis: progression of deformities

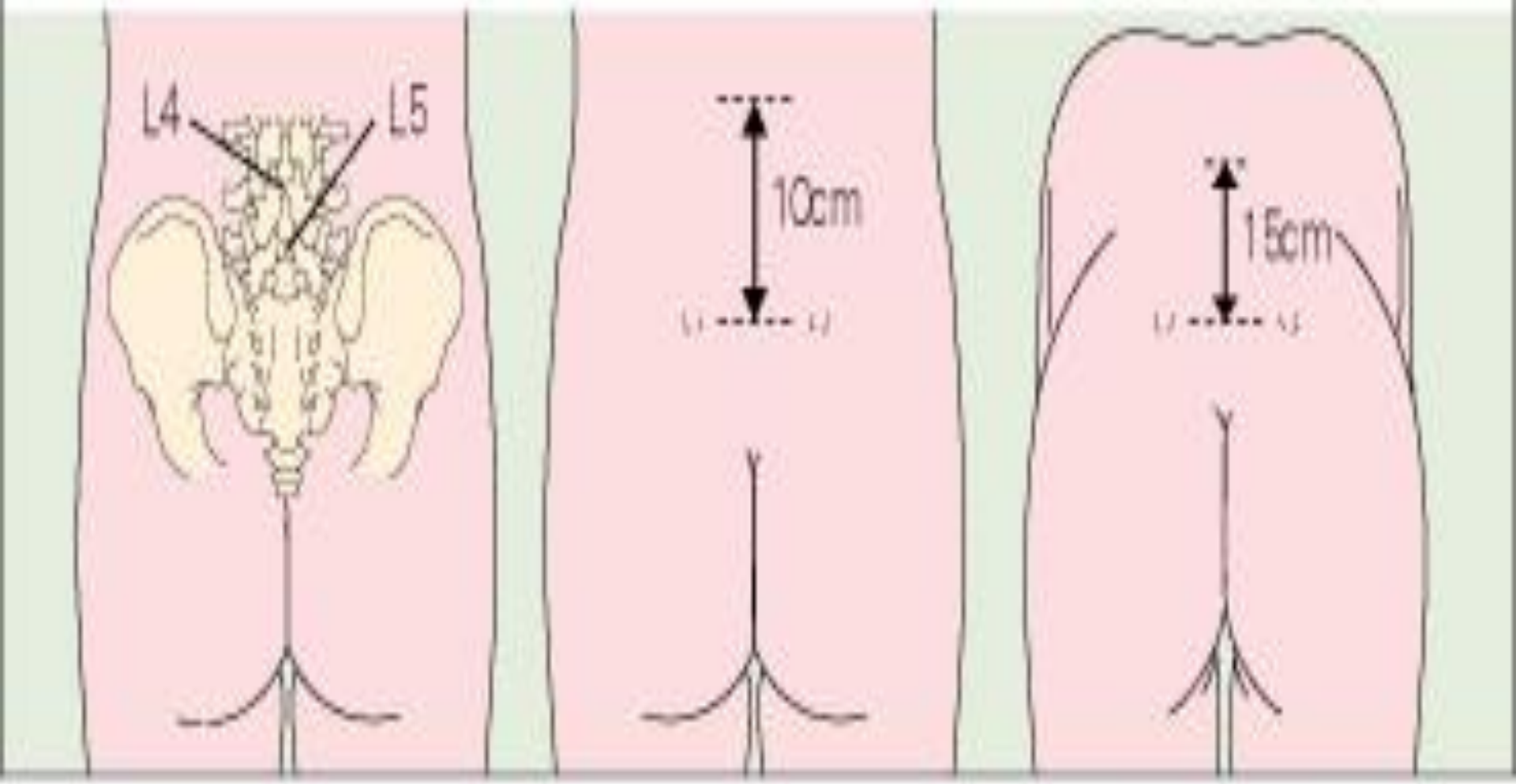


- Neck pain and stiffness from involvement of the cervical spine are late manifestations.

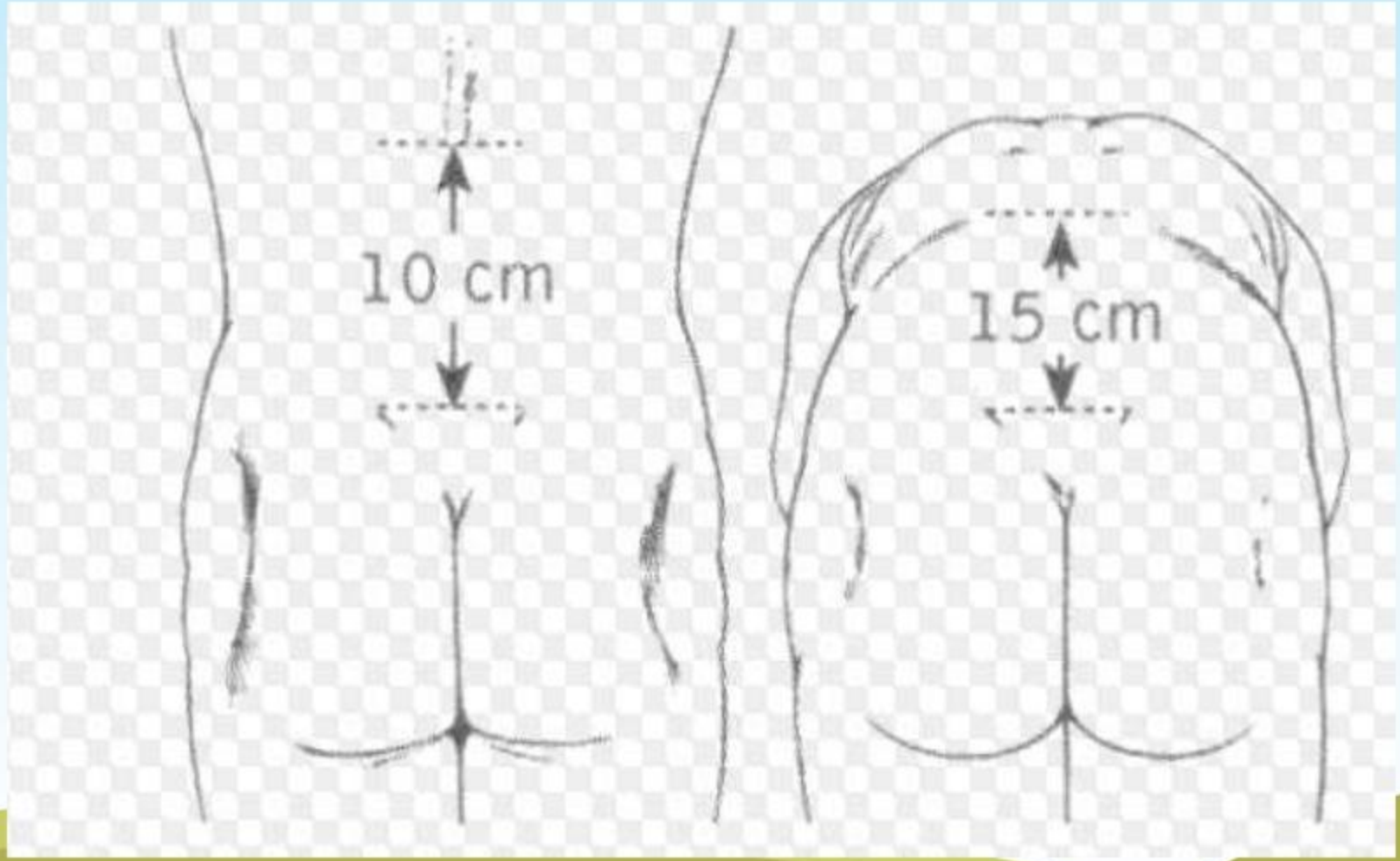
- Chest expansion is measured as the difference between maximal inspiration and maximal forced expiration in the fourth intercostal space. Normal chest expansion is 5 cm.

- Restriction of lumbar movement
  - Shober's test – mark the patient's back at the level of the posterior iliac spine. Place one finger 5 cm below this mark and a 2nd finger 10 cm above this mark. Patient is instructed to touch his toes. If the distance between finegrs increases < 5 cm, lumbar flexion is limited.

SCHOBER TEST

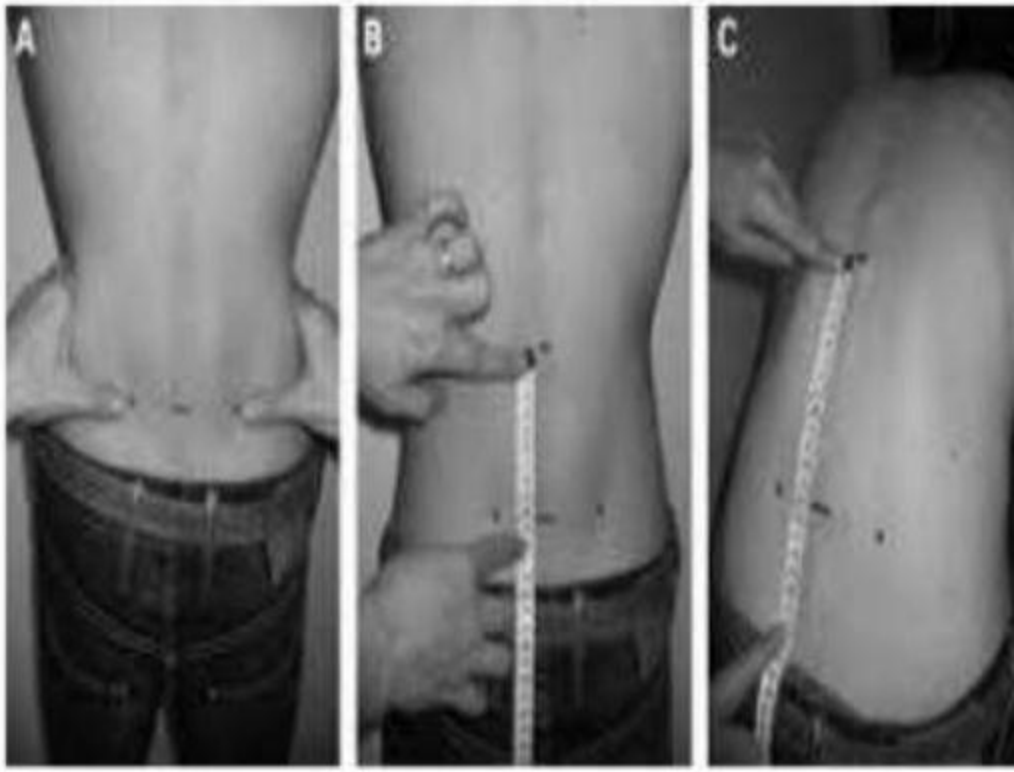


Original Schober test



Modified Schober test

- In this test marks are made 5 cm below and 10 cm above the sacral dimples.
- The distance between these marks should increase from 15 cm to at least 20 cm with lumbar flexion.
- The distance less than 5 cm is abnormal.



- Peripheral musculoskeletal involvement occurs in 30-50% of all patients.

The following are common:

- Achilles tendinitis.
- Plantar fasciitis.
- At the tibial tuberosity.
- Superior and inferior poles of the patella.
- Iliac crests.

Extra-articular manifestations

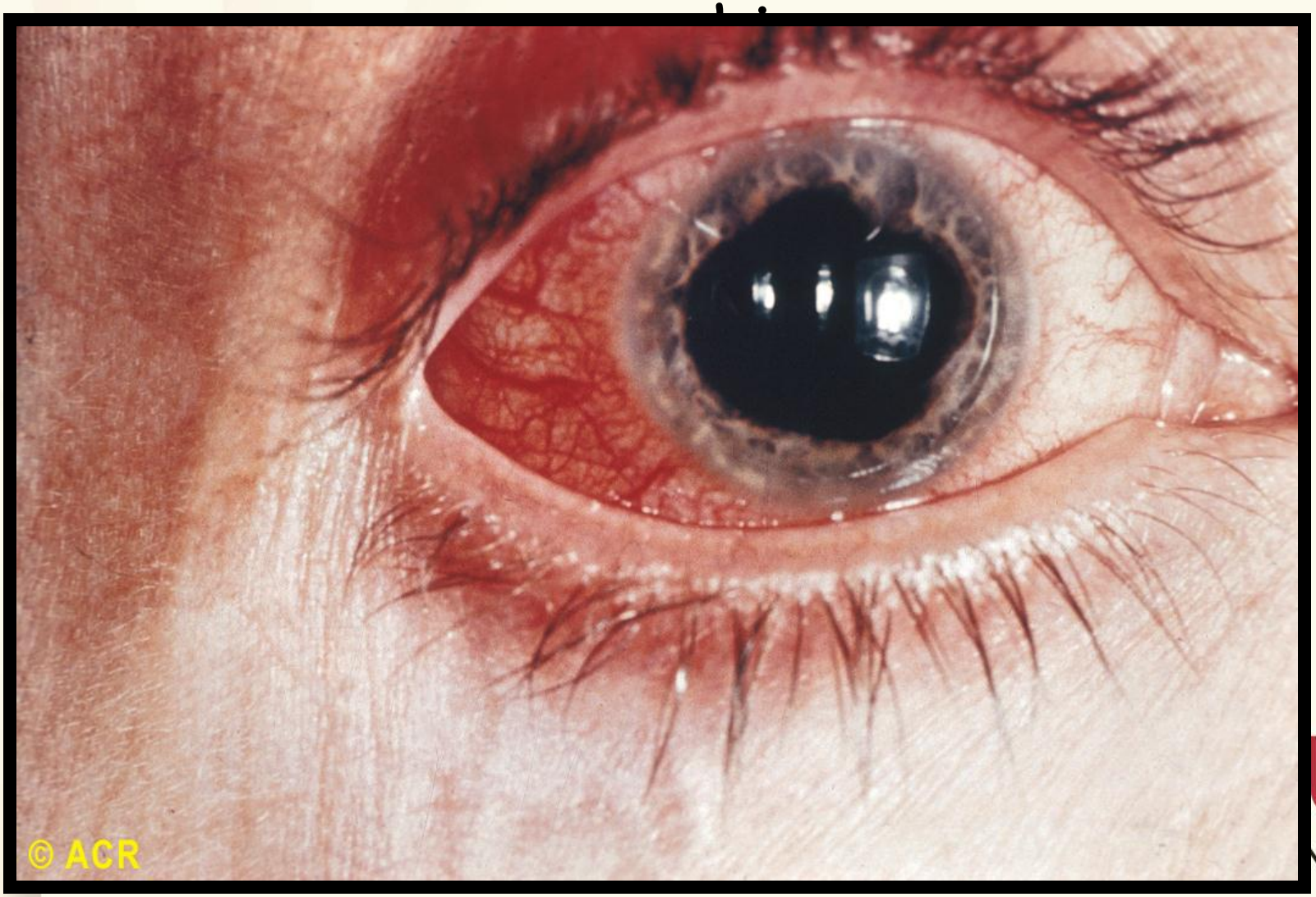
- Uveitis
- Cardiovascular disease
- Pulmonary disease
- Renal disease
- Neurologic disease
- GI disease

Uveitis

- Uveitis (also called iritis or iridocyclitis) is *the most common* extra-articular manifestation of AS, occurring in 20-30% of patients.

- Usually acute,unilateral and non granulomatous.

Ankylosing spondylitis: iridocyclitis with



Cardiovascular involvement

- Aortitis of the ascending aorta resulting in aortic valve insufficiency.
- Mitral valve insufficiency .
- Atrioventricular block.

Pulmonary involvement

- Restrictive lung disease.
- Bilateral apical pulmonary fibrosis.

Renal involvement

- Amyloidosis is a very rare complication of AS in patients with severe, active, and long-standing disease.

Gastrointestinal involvement

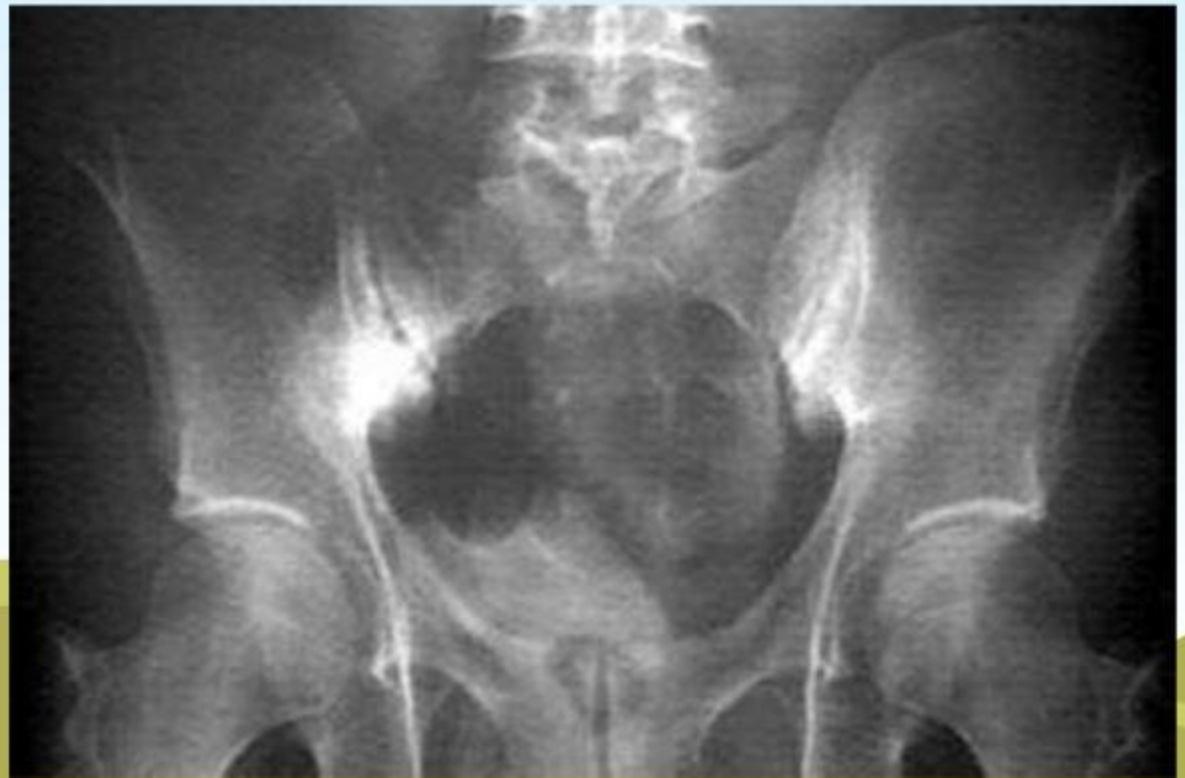
- Asymptomatic inflammation of the proximal colon and terminal ileum has been observed.

Laboratory Findings

- No laboratory test is diagnostic of AS.
- HLA-B27 is present in 90% of patients.
- Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are elevated.
- Mild anemia may be present.
- Patients with severe disease may show an elevated alkaline phosphatase level.
- Elevated serum IgA levels are common.
- Rheumatoid factor ,Anti-Cyclic Citrullinated peptide (CCP), and Antinuclear Antibodies (ANAs) are absent.

Radiographic Findings

- The earliest signs can be detected by 3-6 months after the onset.
- ***SacroIliac Joints***-Early patchy osteoporosis develop around the distal third of both the bones.Joint margins become illdefined and the joint intervals become widened.Subchondral erosions start and when multiple produce a rosary effect.



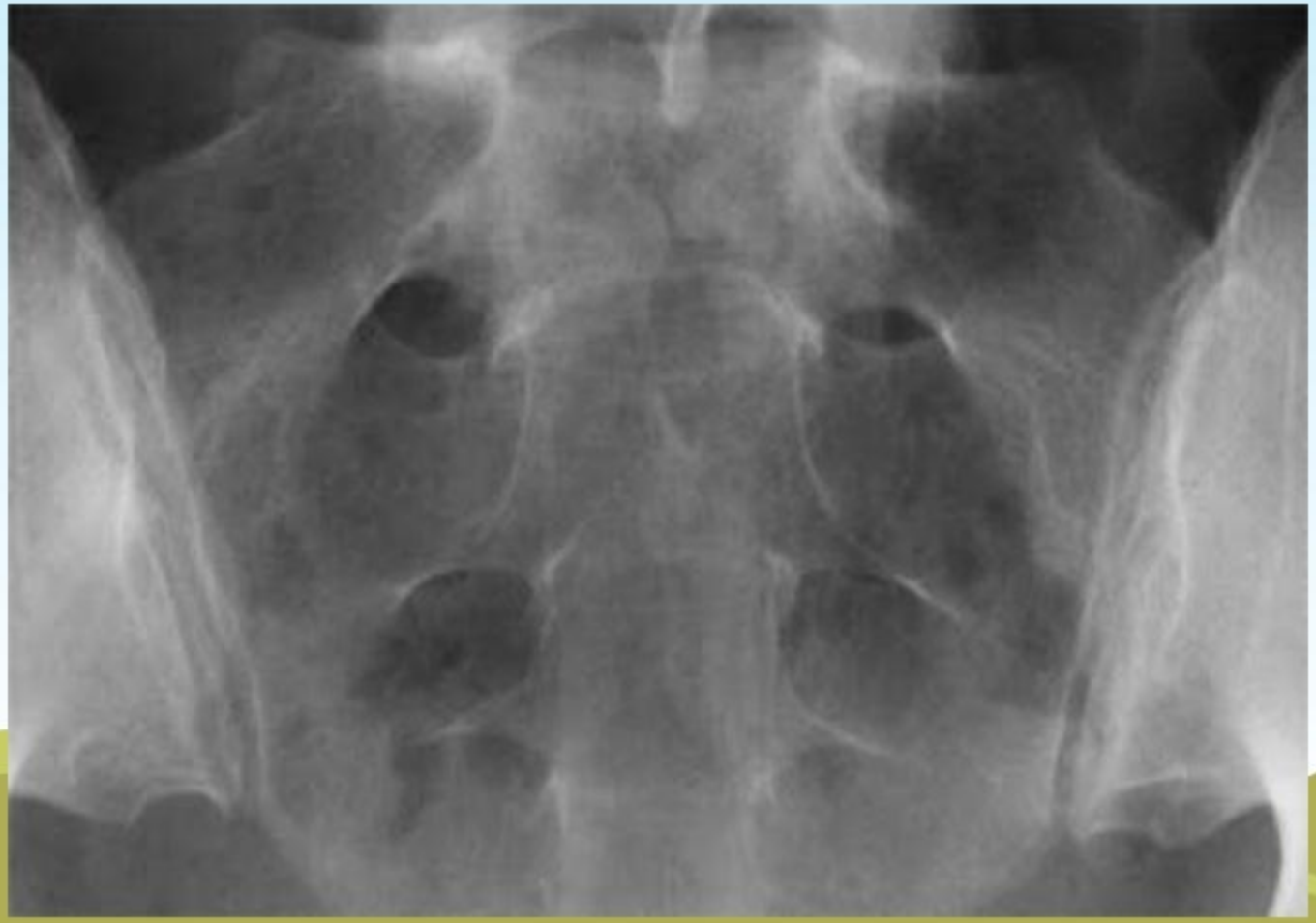
Ankylosing spondylitis

Radiographic evaluation

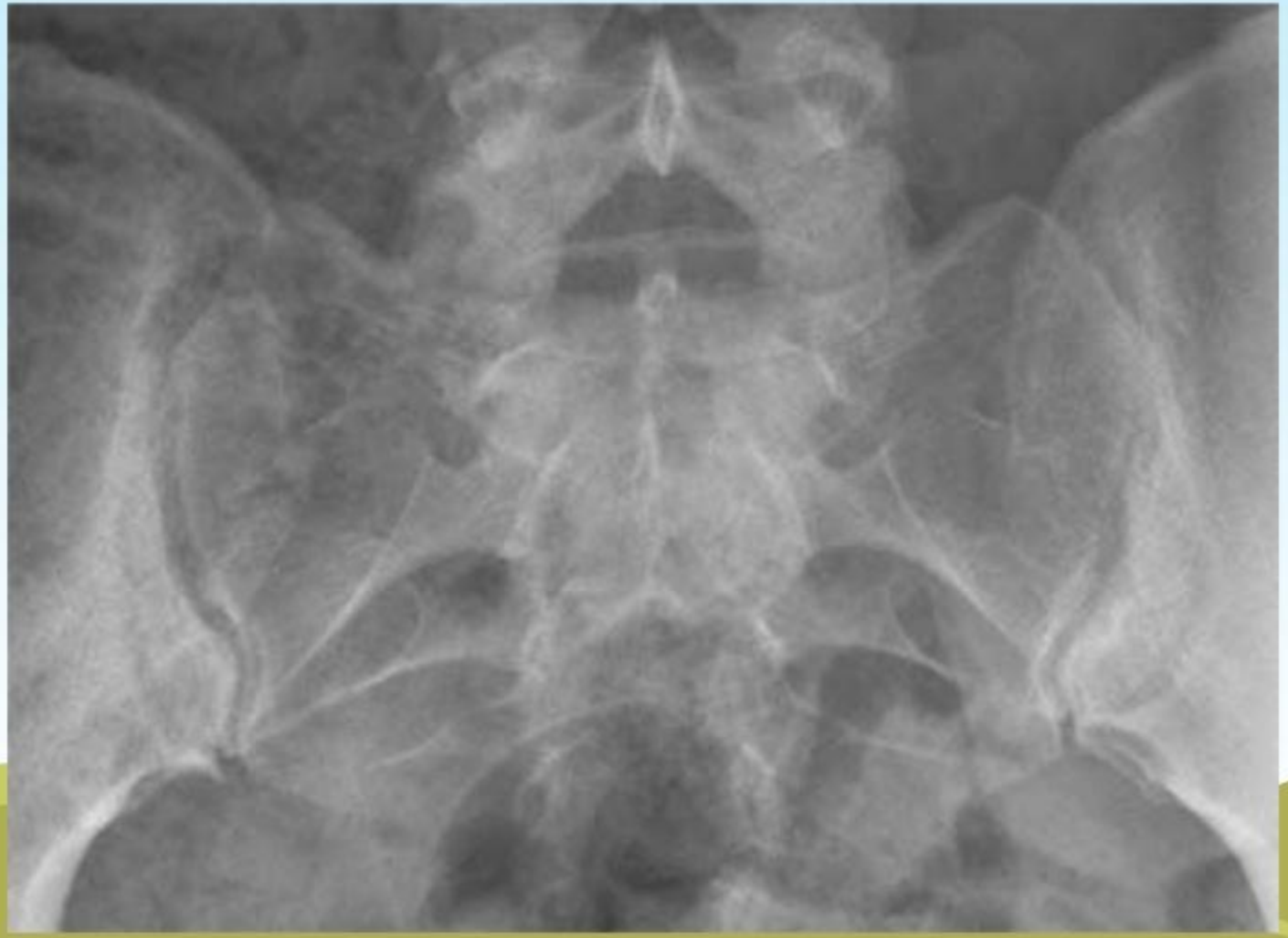
Sacroiliac joints	
Grade 0	Normal
Grade 1	Suspicious changes
Grade 2	Minimal abnormality – small localized areas with erosion or sclerosis without alterations in joint width
Grade 3	Unequivocal abnormality – moderate or advanced sacroiliitis with ≥ 1 of the following: erosions, sclerosis, widening, narrowing, or partial ankylosis
Grade 4	Severe abnormality – total ankylosis

Grades of Sacroiliitis- according to the New York criteria

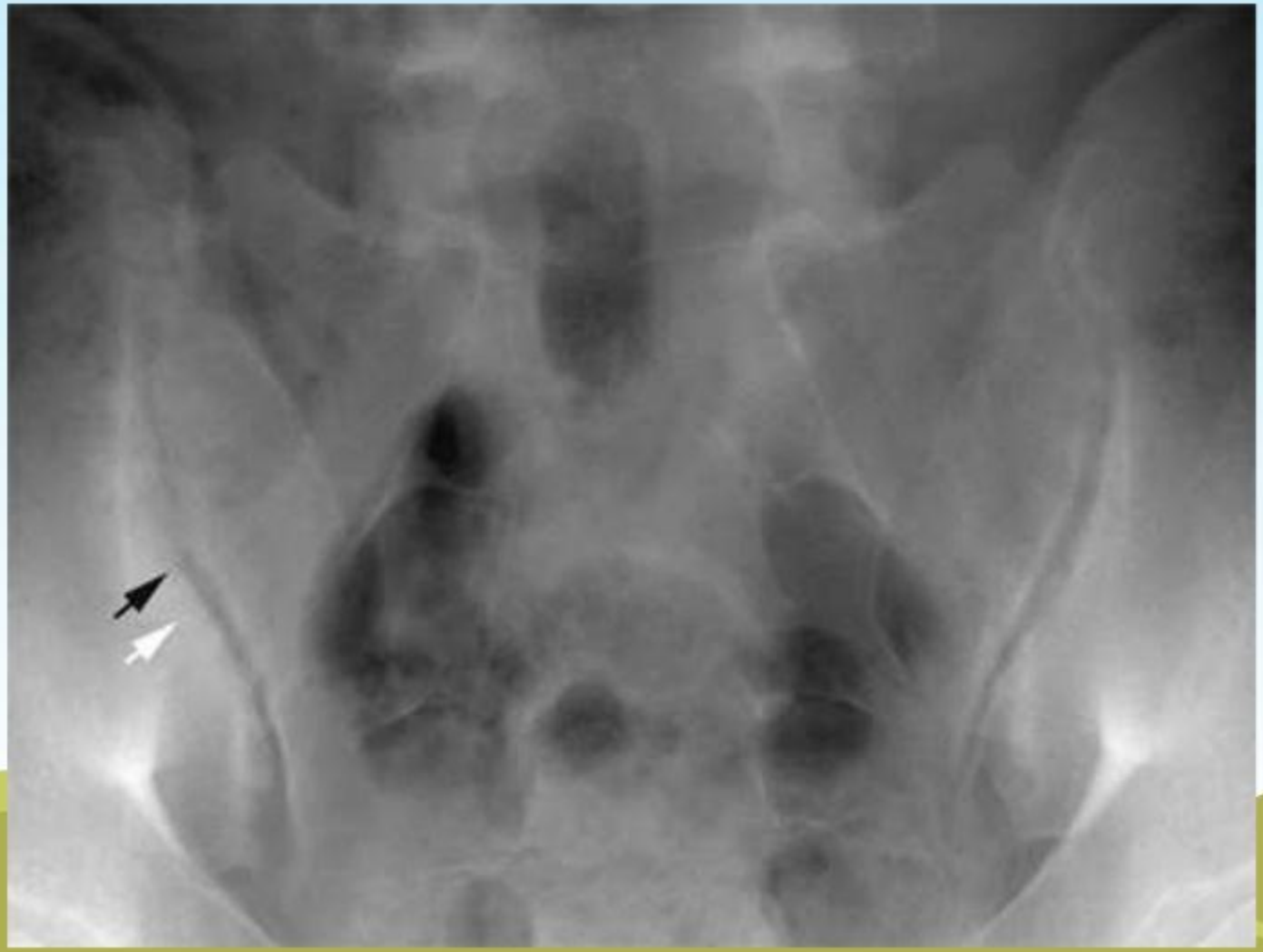
Grade 0-Normal



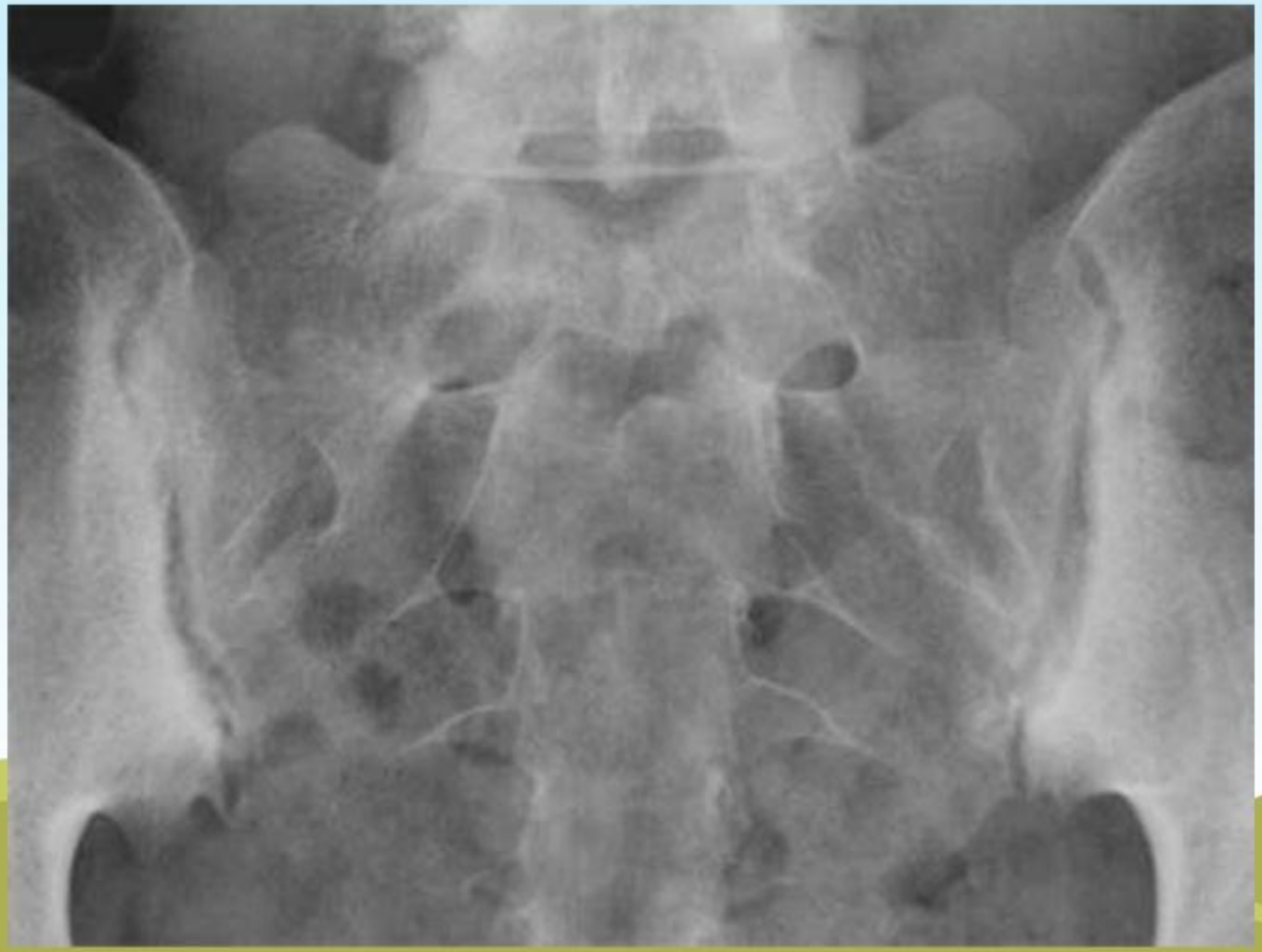
- **Grade 1-***Suspicious changes at the left sacroiliac joint in the form of slightly irregular joint facets.*



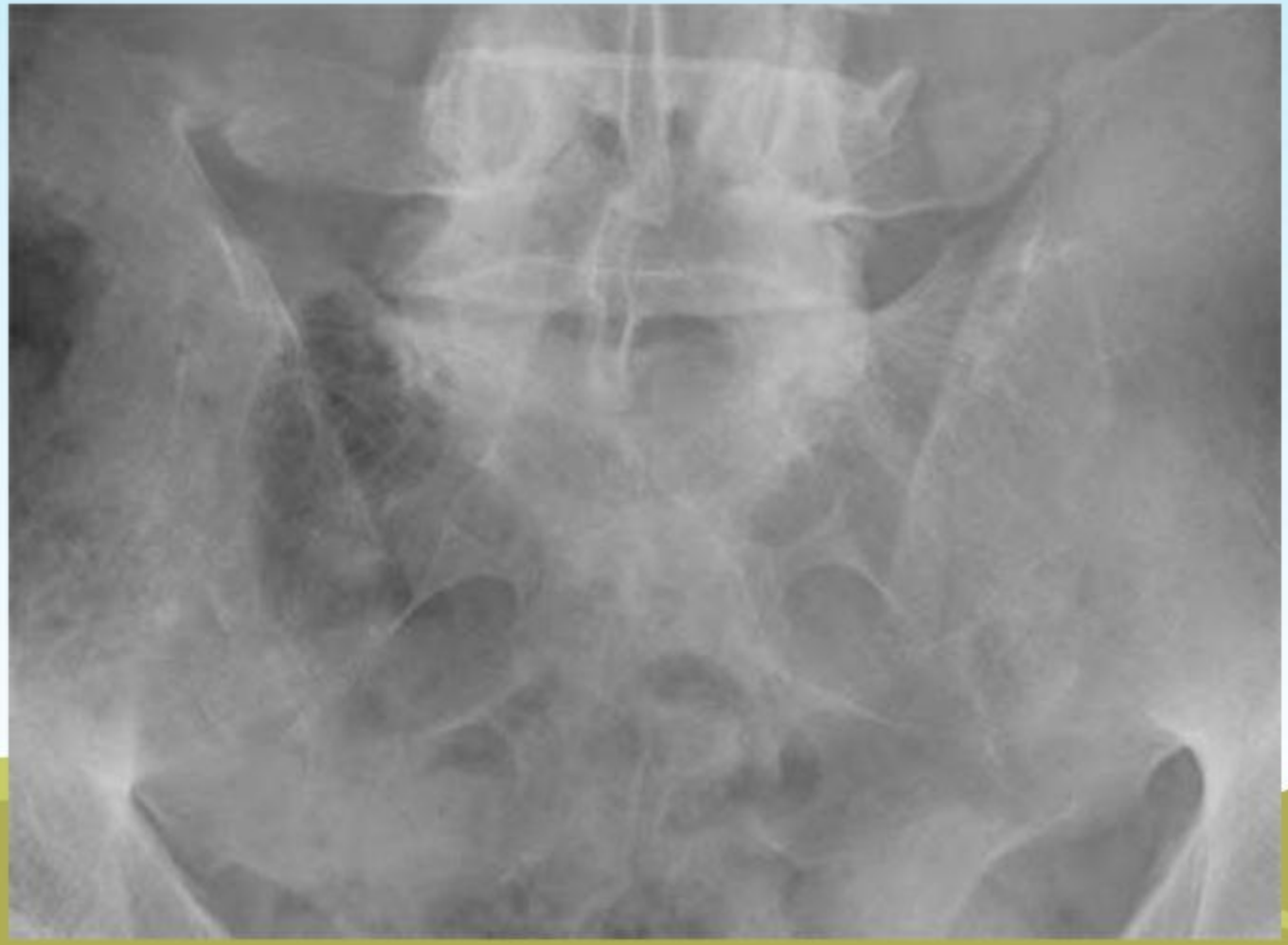
- **Grade 2**-*Minimal abnormalities in the form of small erosions (black arrow) and slightly condensed bone (sclerosis)(white arrow)*



- **Grade 3-***Manifest abnormalities in the form of erosion and sclerosis in addition to widening of the middle part of both sacroiliac joints.*

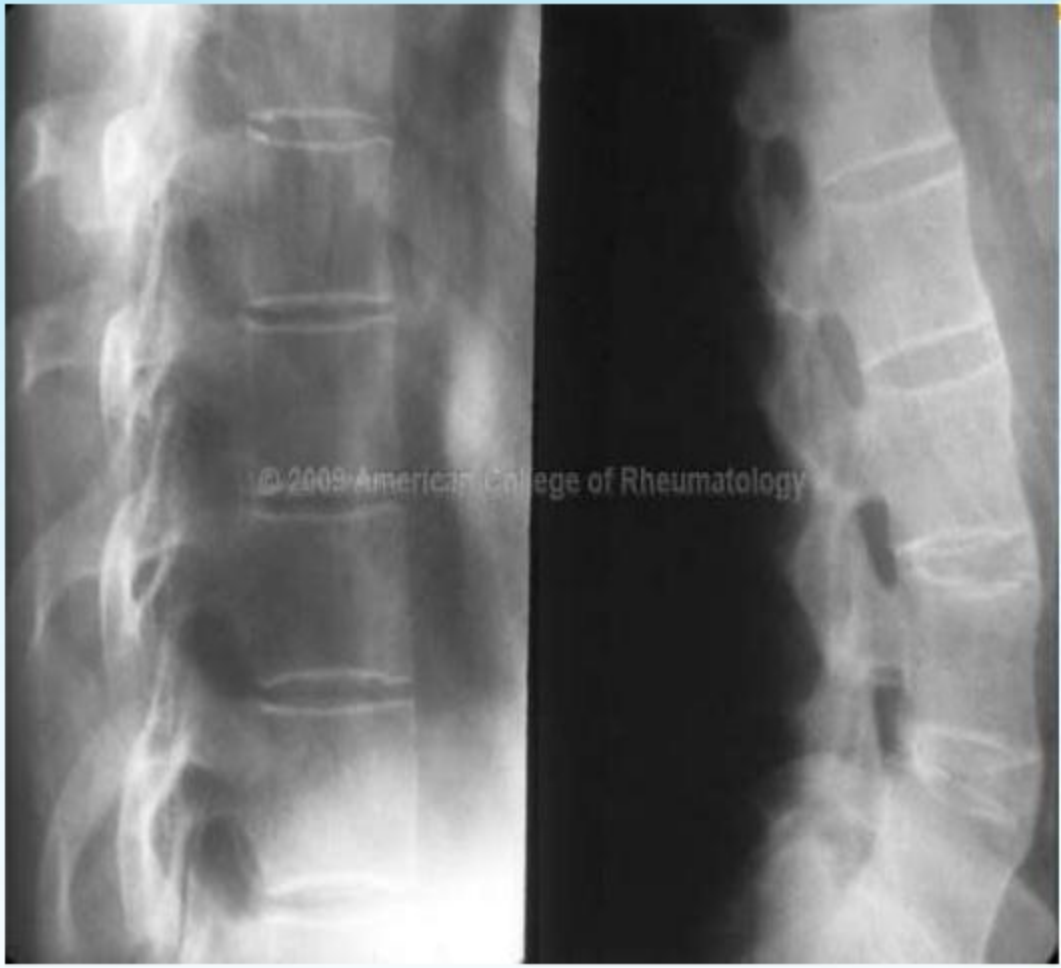


- **Grade 4-***Total ankylosis of both sacroiliac joints*

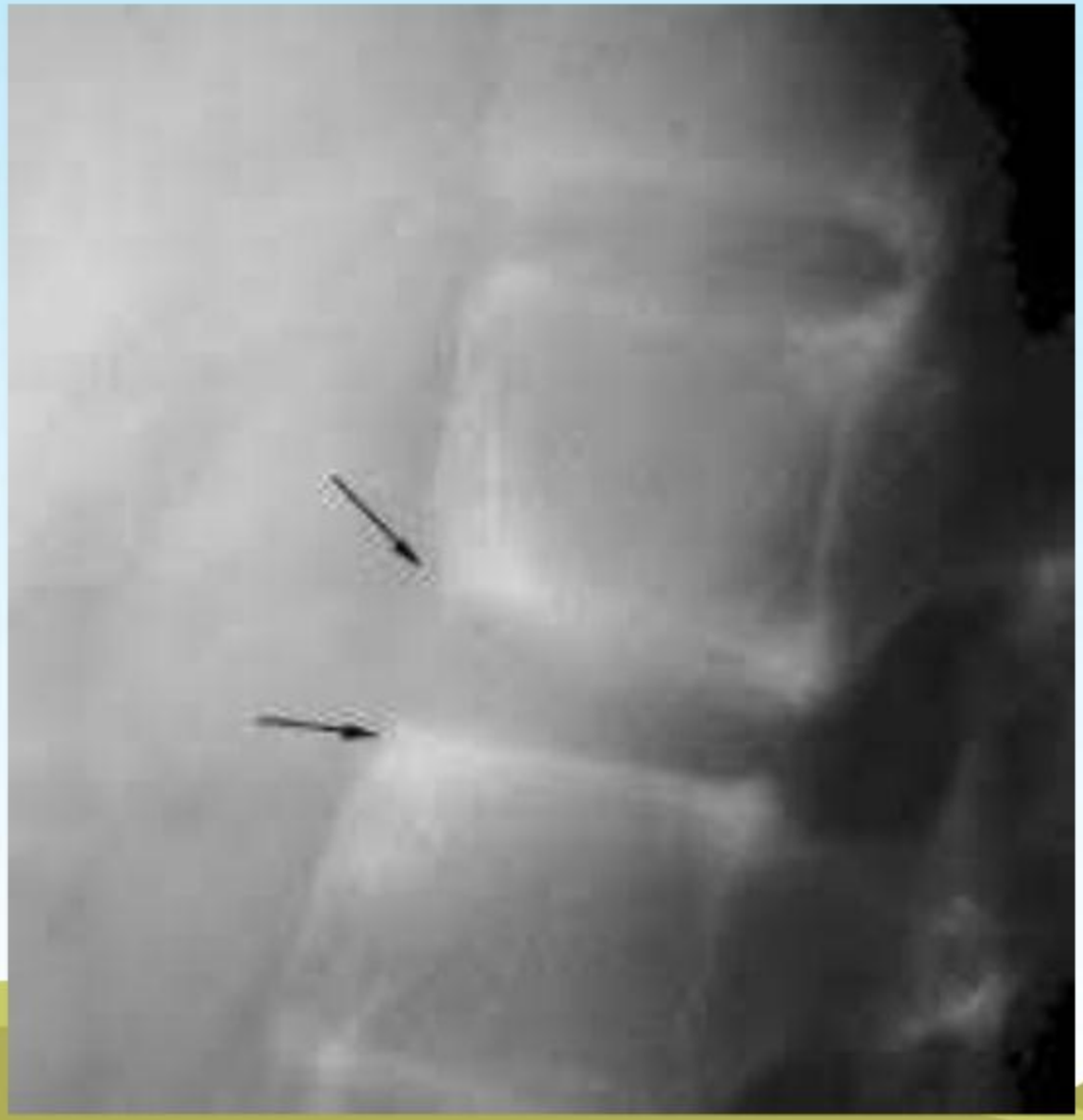


Lumbar Spine-

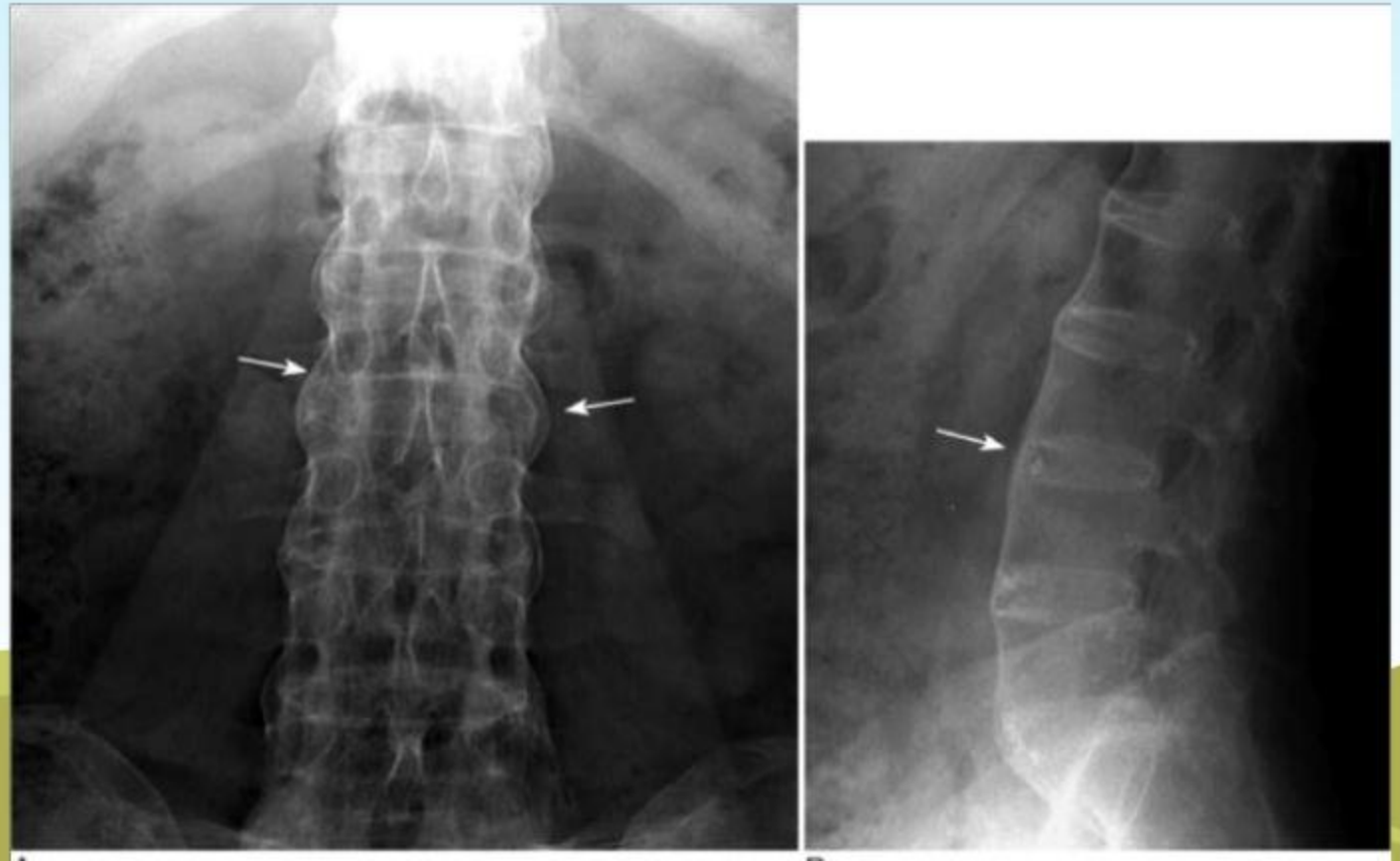
- The earliest change is ***squaring*** of the anterior portion of the vertebral bodies.The anterior concavity of the body is lost.
- This is found initially at the upper lumbar and lower thoracic regions.
- There will be loss of lumbar lordosis.



Shiny Corner Sign/Romanus sign



- Paravertebral ossification develops beneath the anterior longitudinal ligaments ***within the annulus*** at each level.The ossification develops vertically in contrast to those developed in the OA.Finally the appearance is of **Bamboo spine**.



- ***Cervical Spine***-Extreme bony bridging extends along the anterior aspect of the vertebral bodies.There will be loss of lordosis and apophyseal joints become ankylosed.

- ***Hips***-Severe Osteoporosis occurs in both sides of the joints.Erosions develop and the joint space becomes reduced.

Diagnosis-ESSG Criteria

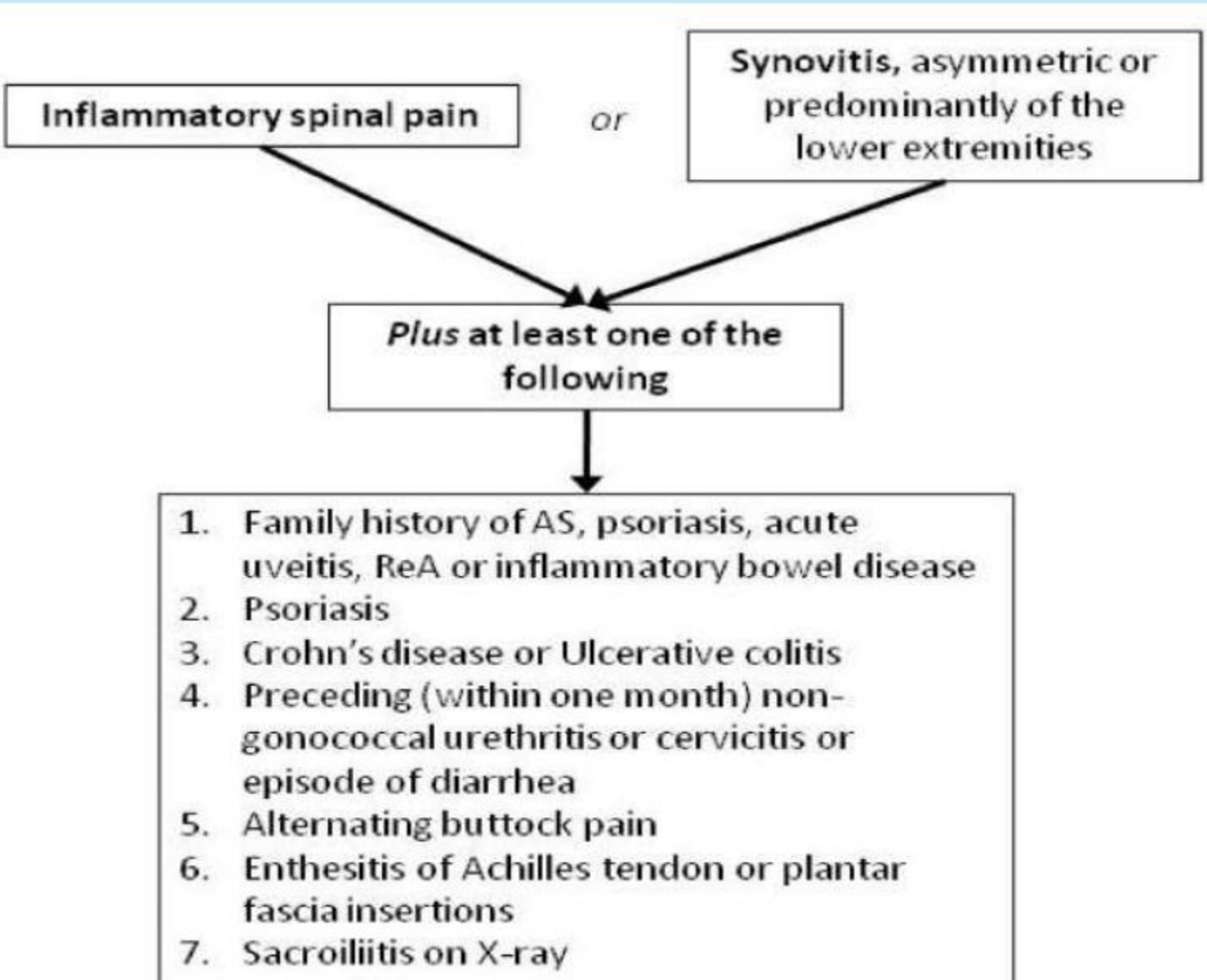


Table 1. Modified New York criteria for AS [11]. AS is diagnosed if the radiological criterion plus at least one clinical criterion is met.

Clinical criteria	Radiological criterion
Low back pain and stiffness persisting for >3 months, improved by exercise but not by rest Limitation of movement in the lumbar spine in both frontal and sagittal planes Limitation of chest expansion relative to normal values for age and sex	Grade ≥2 sacroiliitis bilaterally on plain radiography Or Grade 3 or 4 sacroiliitis unilaterally on plain radiography

AS: ankylosing spondylitis.

Image courtesy of Remedica Journals
http://www.remedicajournals.com/CML-Rheumatology/BrowseIssues/Volume-32-Issue-1/Article-Whole-Body-Magnetic-Resonance-Imaging-in-Ankylosing-Spondyli

ASAS classification criteria for axial SpA

(in patients with back pain ⩾ 3 months 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
- Arthritis
- Enthesitis (heel)
- Uveitis
- Dactylitis
- Psoriasis
- Crohn's disease/ulcerative colitis
- Good response to NSAIDs
- Family history for SpA
- HLA-B27
- Elevated CRP

* Sacroiliitis on imaging:

- Active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA

  or

- Definite radiographic sacroiliitis according to mod. New York criteria

Sensitivity 82.9%, specificity 84.4%; n = 649 patients with chronic back pain and age at onset < 45 years.
Imaging arm (sacroiliitis) alone has a sensitivity of 66.2% and a specificity of 97.3%.

** Note: Elevated CRP is considered a SpA feature in the context of chronic back pain

- To qualify as the criterion for inflammatory back pain of axial SpA the chronic (3 months) back pain should have four or more of these characteristic features

(1) age of onset below 40 years.

(2) insidious onset.

(3) improvement with exercise.

(4) no improvement with rest and

(5) pain at night with improvement upon getting up.

Treatment

General measures

- Patients are encouraged to remain active and follow their normal pursuits as far as possible.
- They should be taught to maintain satisfactory posture and to perform spinal extension exercises every day.
- Swimming, dancing and gymnastics are ideal forms of recreation.
- Rest and immobilization are contraindicated because they tend to increase the general feeling of stiffness.

Low Back Pain Exercises

Standing hamstring stretch

Quadruped arm/leg raise

Side plank

Gluteal stretch

Cat and camel

Pelvic tilt

Partial curl

Extension exercise

Non-steroidal anti-inflammatory drugs

- NSAIDs improve spinal pain, peripheral joint pain, and function over a short period of time (6 weeks).
- They dont prevent or retard the progress to ankylosis.

TNF inhibitors

- Etanercept,Infliximab,Adalimumab, Golimumab,and Certolizumab pegol-have all been approved by the US Food and Drug Administration (FDA) as therapies for AS and are indicated after NSAID therapy has failed.

- ***Infliximab(Remicade)*** -Adult dosage-5 mg/kg IV at 0, 2, and 6 weeks, then every 6 weeks.
- ***Etanercept (Enbrel)***-Adult dosage- 50 mg SC once weekly or 25 mg SC twice weekly; if twice weekly, doses should be given on same day or 3-4 days apart.
- ***Adalimumab(Humira)***-40 mg SC q2wk.
- These therapies are generally reserved for individuals who have failed to be controlled with non-steroidal anti-inflammatory drugs.

SURGICAL TREATMENT

OSTEOTOMIES OF THE LUMBAR SPINE

- Described by Smith-Petersen, Larson, and Aufranc in 1945.
- If the flexion deformity is severe, the patient's field of vision is limited to a small area near the feet.
- Respiration becomes almost completely diaphragmatic.
- Gastrointestinal symptoms like dysphagia or choking may occur.
- In addition to improvement in function, the improvement in appearance made by correcting the deformity is achieved.

- The safest and most efficient position for this procedure is with the patient lying on his or her side.
- This lateral position has several advantages:

(1) it is easier to place the grossly deformed patient on the table.

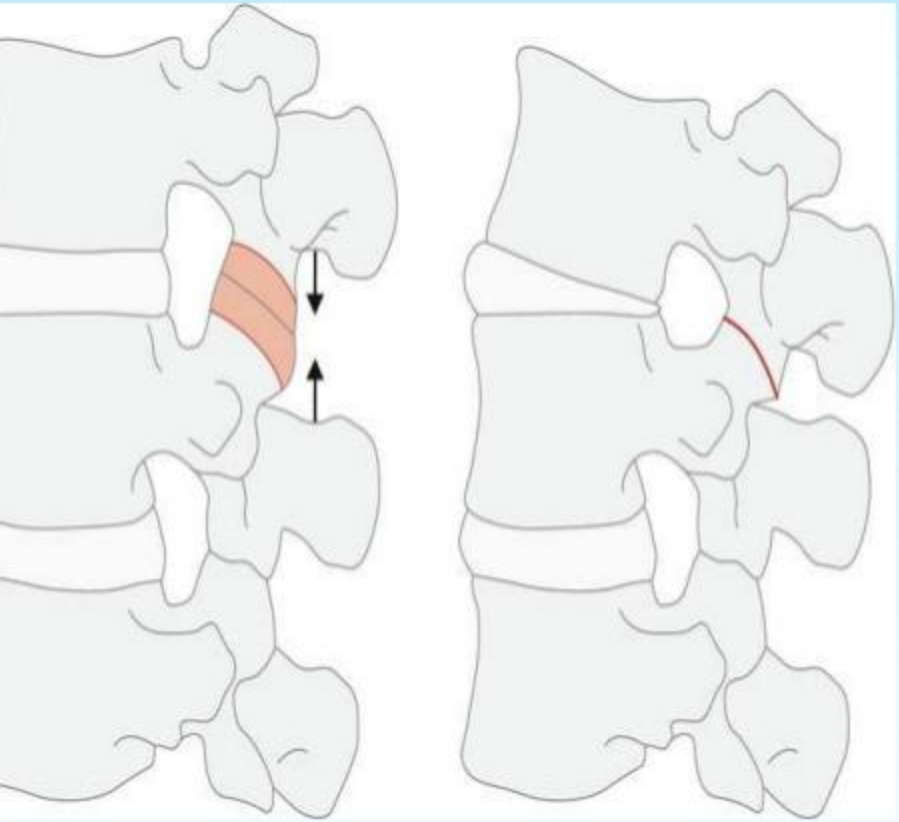
(2) the danger of injuring the ankylosed spine by pressure of the forehead against the table is eliminated.

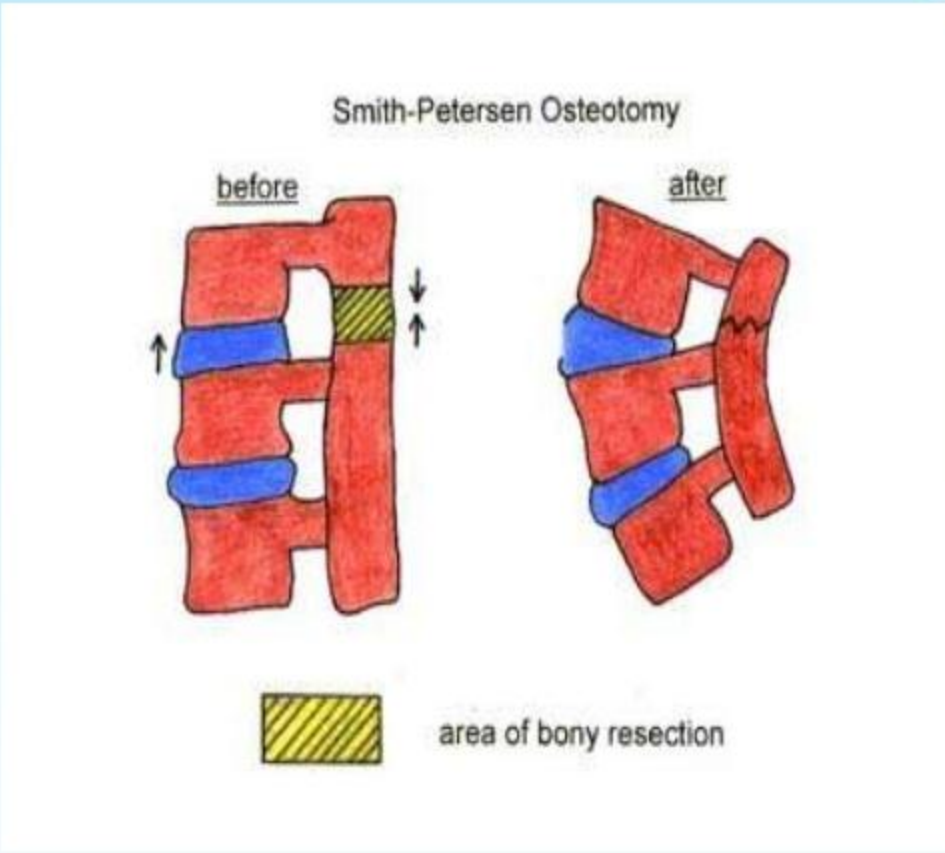
(3) the anesthesia is easier to manage because maintaining a clear airway and free respiratory exchange is less difficult, and

(4) the operation is easier because any blood would flow out from the depth of the wound rather than into it.

1.SMITH-PETERSEN OSTEOTOMY

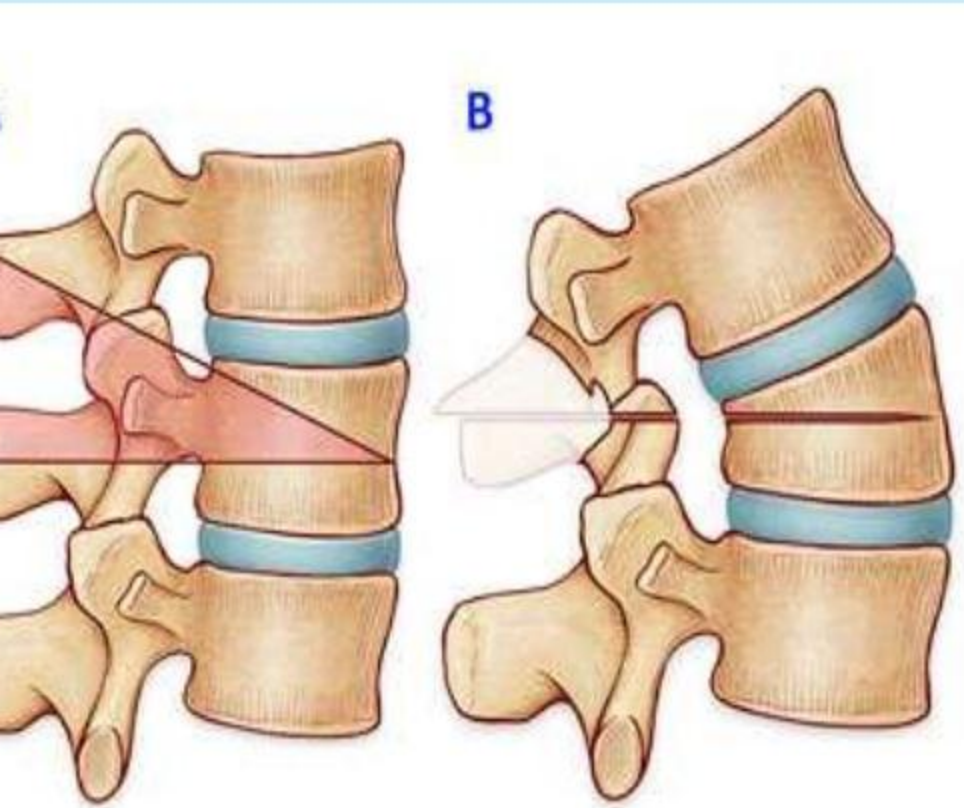
- Excellent option for correction of smaller degrees of spinal deformity.
- ***Bone is removed through the pars and facet joints*** .
- Symmetrical resection is necessary to prevent creating a coronal deformity.
- Approximately 10 degrees of correction can be obtained with each 10 mm of resection.
- The osteotomy is closed with compression or with in situ rod contouring, and bone graft, is applied




Smith-Petersen Osteotomy
before
after
area of bony resection

PEDICLE SUBTRACTION OSTEOTOMY

- Three Column Osteotomy.
- Best suited for patients who have significant sagittal imbalance of 4 cm or more and immobile or fused discs.
- An inherently safer procedure than the Smith-Petersen osteotomy because it avoids multiple osteotomies.
- Typically,30 degrees or more of correction can be obtained with a single posterior osteotomy,at the level of the deformity.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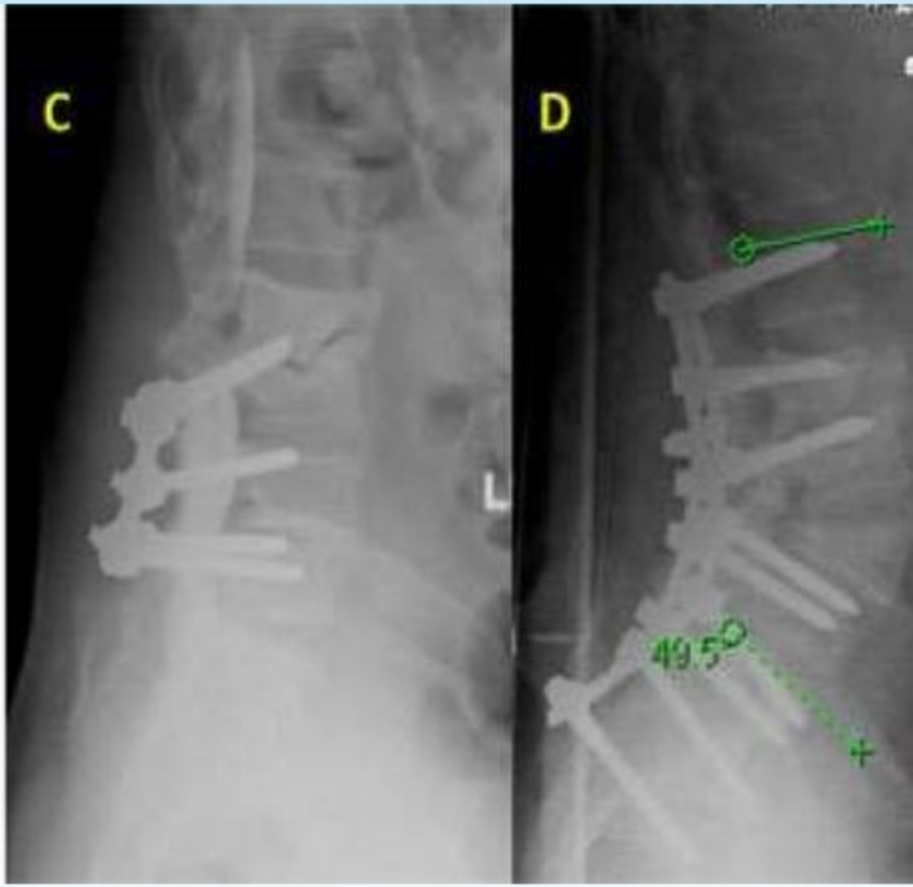
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EGGSHELL OSTEOTOMY

- Reserved for severe sagittal or coronal imbalance of more than 10 cm from the midline.
- Requires both anterior and posterior approaches .

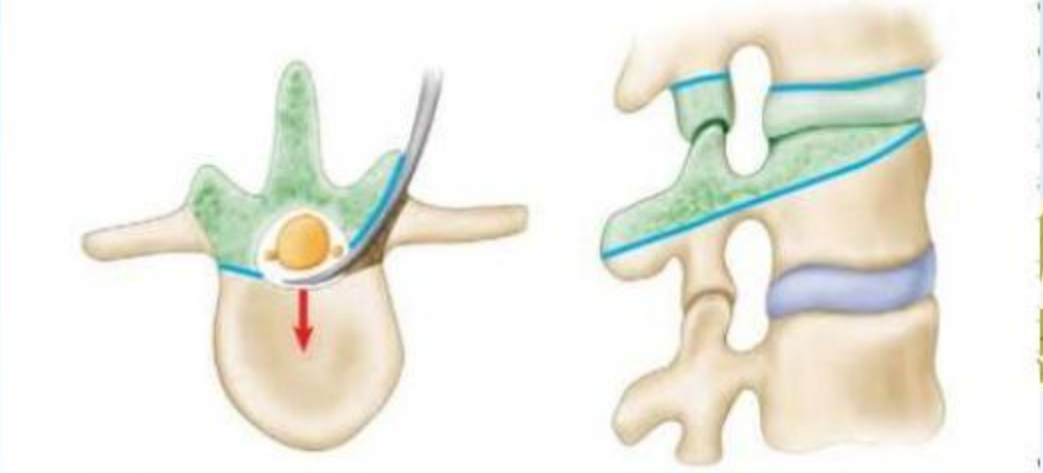


FIGURE 44-27 Heinig eggshell procedure. After posterior elements have been removed and pedicles have been collapsed outward, long, sharp curet is used to collapse "eggshell."

JOINT REPLACEMENT

- Patients with significant involvement of the hips may benefit from total hip arthroplasty.
- Heterotopic bone formation may occur after total joint replacement, especially around the hip. Heterotopic bone formation can be reduced by giving NSAIDs (eg, indomethacin) or employing radiation therapy postoperatively.

REACTIVE ARTHRITIS/REITERS SYNDROME

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

Etiology

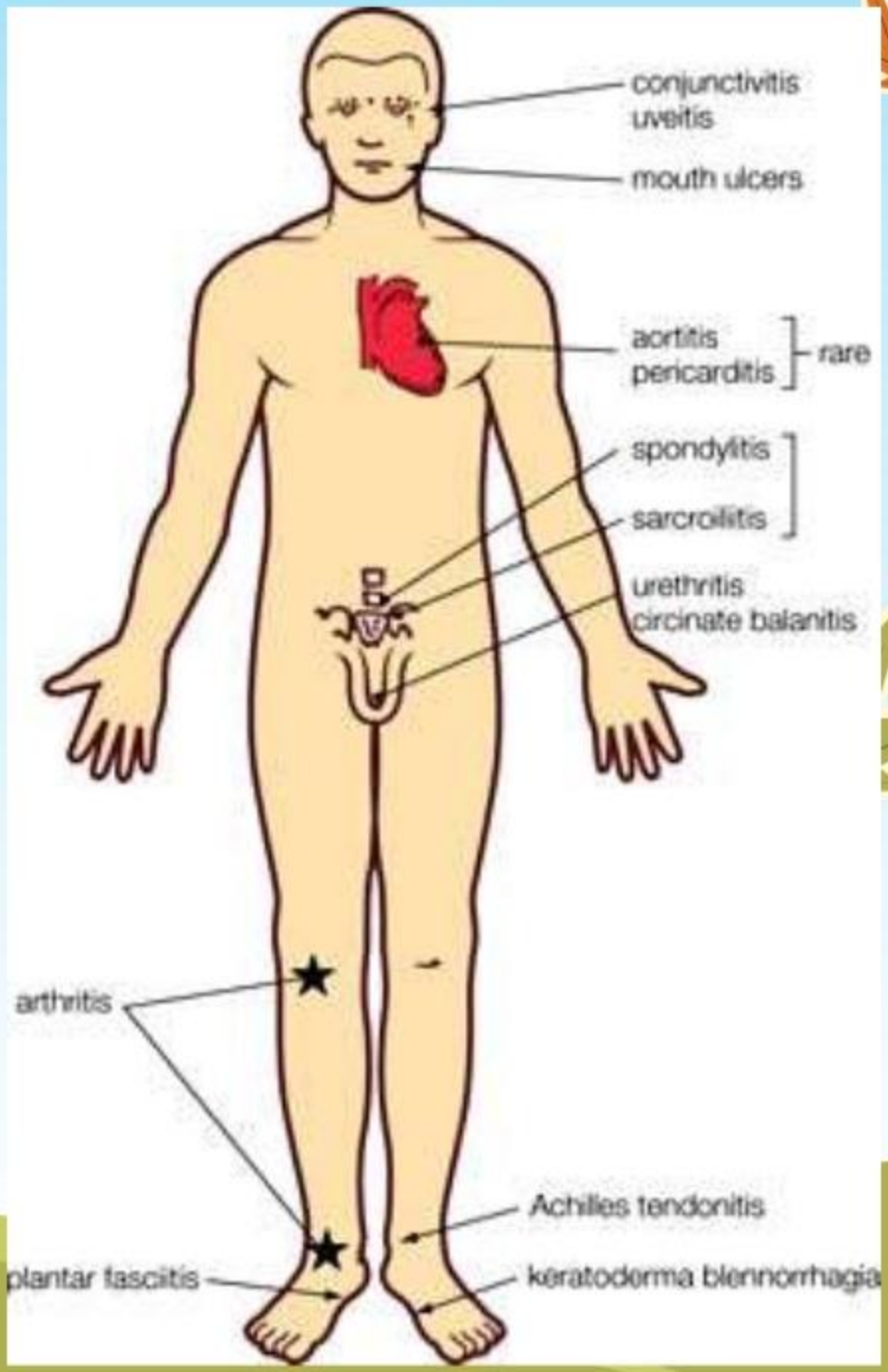
- Gut pathogens include *Shigella flexneri*, *Salmonella, Campylobacter* species and *Yersinia enterocolitica.*
- *Lymphogranuloma venereum* and *Chlamydia trachomatis* have been implicated as sexually transmitted infections.

Pathology

- The pathological changes are essentially the same as those in ankylosing spondylitis, with the emphasis on large-joint synovitis and a chronic disease course tending towards Sacroiliitis and Spondylitis.

Clinical features

- The most common age group is 18–40 years.
- Can occur in children over 5 years of age and in older adults.
- Men are affected more often than women (the ratio is about 10:1).

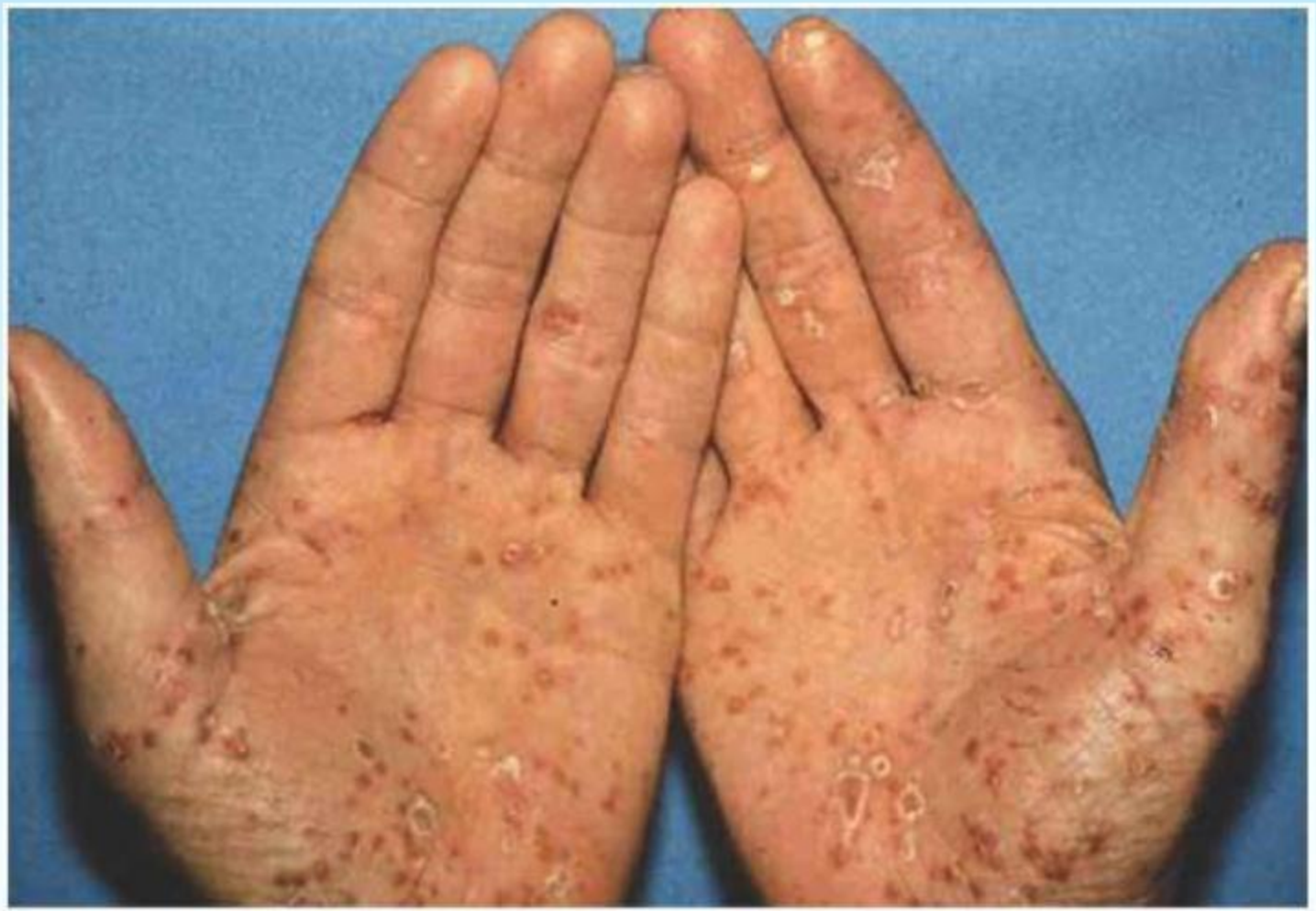


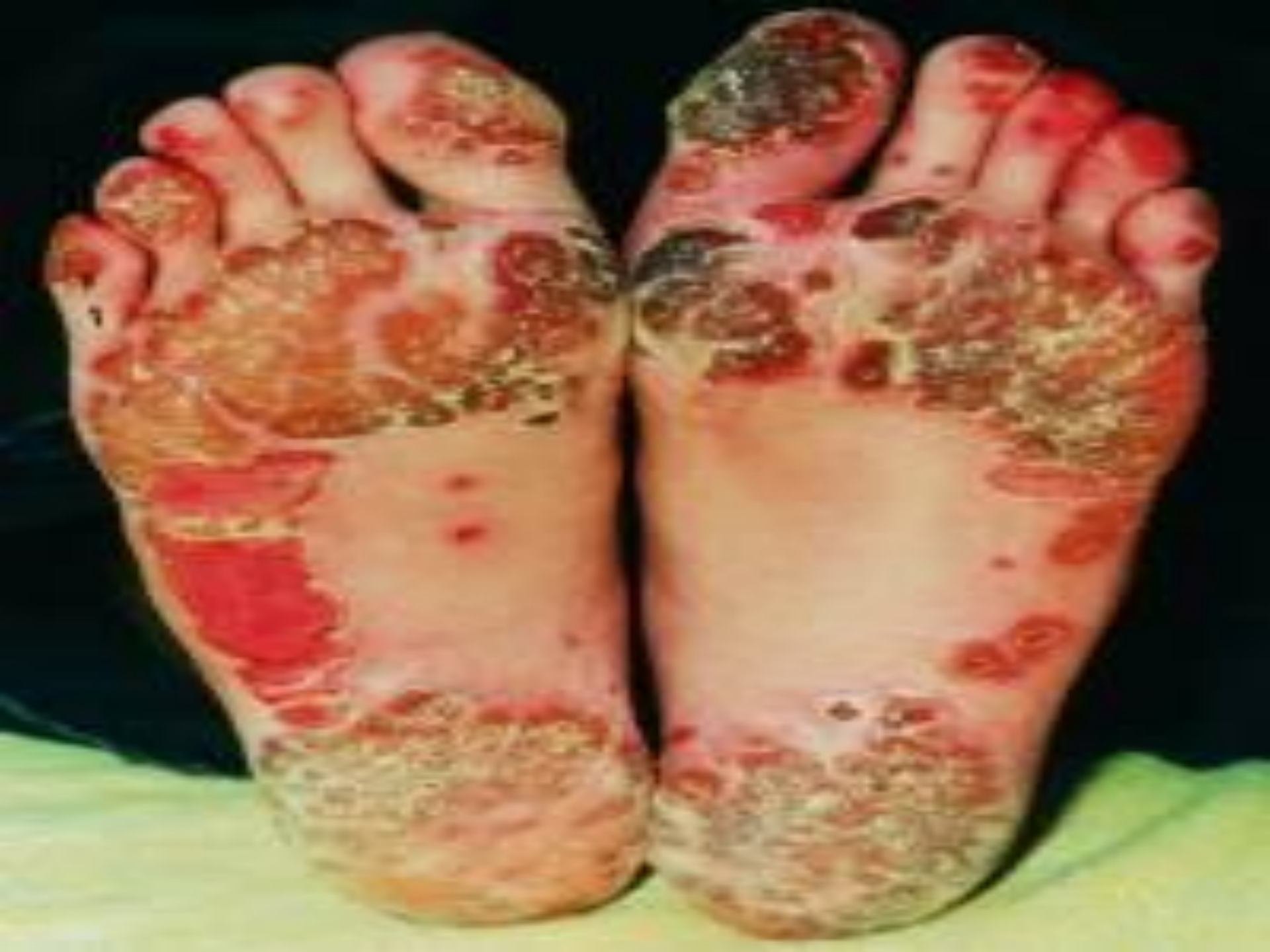
- *The **acute phase*** of the disease is marked by an asymmetrical inflammatory arthritis of the lower limb joints.
- Knee, Ankle, Subtalar, Metatarsophalangeal, and toe interphalangeal joints, are most commonly involved, but the wrist and fingers can be involved as well.
- Dactylitis, or "sausage digit," a diffuse swelling of a solitary finger or toe, is a distinctive feature of ReA.

Dactylitis or Sausage Fingers

It is a pathological condition in which there is inflammation of the fingers or toes giving them the shape of a sausage, which gives it its name. The fingers appear swollen and plump and the affected individual finds it difficult to adequately use the fingers.

- Tendo Achilles tendinitis and Plantar fasciitis are common.
- In males, urethritis and in females, cervicitis or salpingitis are common.
- Ocular disease is common, ranging from asymptomatic conjunctivitis to an aggressive anterior uveitis.
- The characteristic skin lesions, are *keratoderma blenorrhagica*.





- The ***chronic phase*** is more characteristic of a spondyloarthropathy,with features resembling those of ankylosing spondylitis.

Laboratory Findings

- Tests for HLA-B27 are positive in 75 per cent of patients with sacroiliitis.
- ESR may be high in the active phase of the disease.

Radiographic Findings

- In early or mild disease, radiographic changes may be confined to juxtaarticular osteoporosis.
- With long-standing persistent disease, marginal erosions and loss of joint space can be seen in affected joints.
- Sacroiliitis and spondylitis may be seen as late sequelae.
- Sacroiliitis is more commonly ***asymmetric*** than in AS, and spondylitis, can begin anywhere along the lumbar spine.
- The syndesmophytes may be asymmetric, coarse and nonmarginal

Treatment

- Most patients with ReA benefit to some degree from high-dose NSAIDs.
- Indomethacin, 75–150 mg/d in divided doses, is the initial treatment of choice, but other NSAIDs may be tried.
- Majority of patients with chronic ReA due to *Chlamydia* benefited significantly from a 6-month course of rifampicin 300 mg daily plus azithromycin 500 mg daily for 5 days then twice weekly, or 6 months of rifampicin 300 mg daily plus doxycycline 100 mg twice daily.

- Tendinitis and other enthesitic lesions may benefit from intralesional glucocorticoids.
- Topical steroids may be used for uveitis.
- TNF inhibitors like Infliximab may be used in refractory cases.

PSORIATIC ARTHRITIS

- *Psoriatic arthritis* (PsA) refers to an inflammatory arthritis that characteristically occurs in individuals with Psoriasis.
- 60 per cent of those with psoriatic spondylitis or sacroiliitis have HLA-B27.

Pathology

- The inflamed synovium in PsA resembles that of RA, although with somewhat less hyperplasia and cellularity than in RA, and greater vascularity.
- Unlike RA, PsA shows prominent enthesitis, with histology similar to that of the other spondyloarthritides.

Clinical Features

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

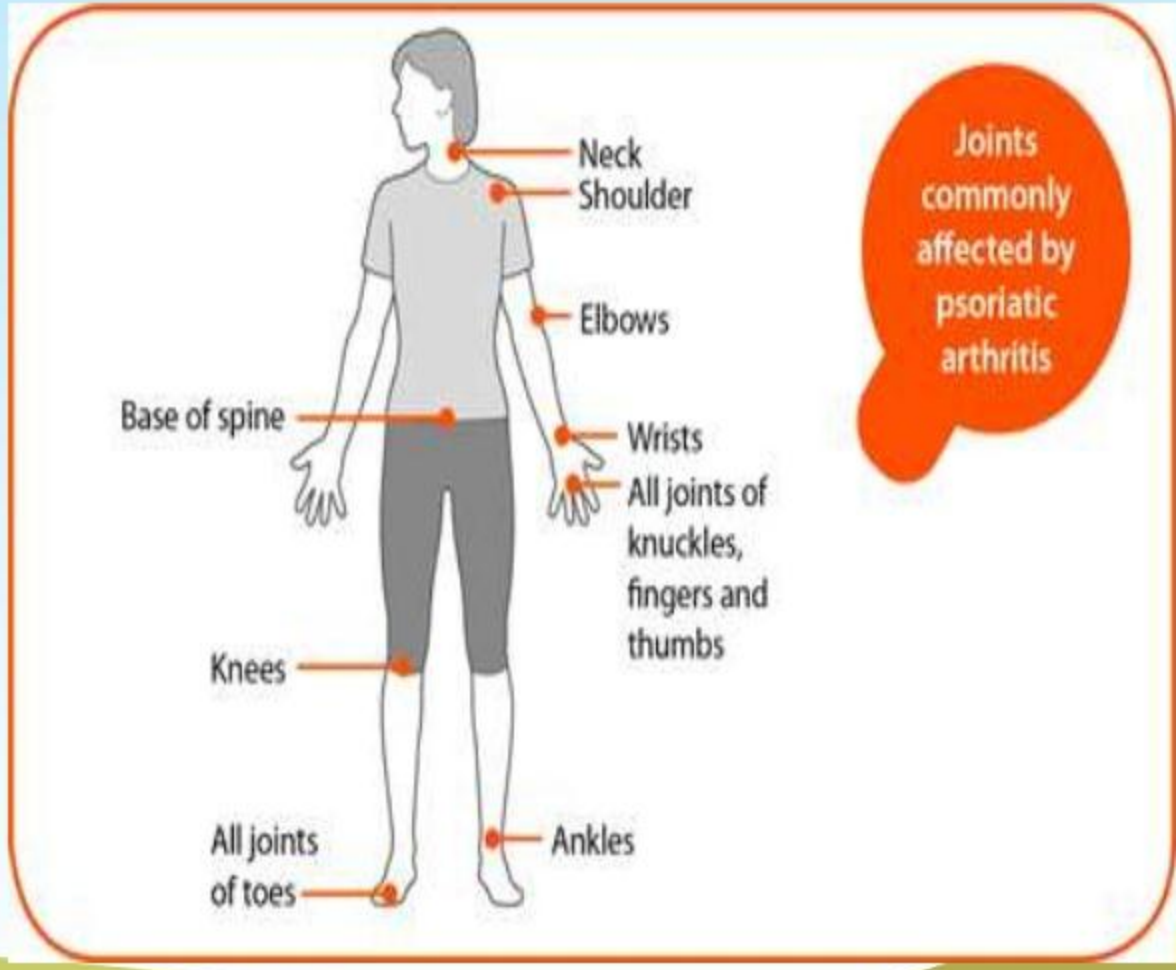


Table – Features that distinguish PsA from RA and OA[a]

Feature	PsA	RA	OA
Inflammatory arthritis	Yes	Yes	No
Peripheral involvement	Yes	Yes	Yes
Axial involvement (sacroiliac joint, spine)	Yes	No (only C1-2 and occasional C spine)	Possible
Symmetrical involvement	Rare	Yes	Variable
DIP joint involvement	Yes	No	Yes
Enthesitis	Yes	No	No
Dactylitis	Yes	No	No
Erosions and new bone formation	Yes	No	No
Skin involvement	Most of the time	No	No

PsA, psoriatic arthritis; RA, rheumatoid arthritis; OA, osteoarthritis; DIP, distal interphalangeal.

[a] One variant, inflammatory OA, may manifest focal erosion and new bone formation.

- The spectrum of arthropathy associated with psoriasis is broad.
- Five patterns are described

(1) arthritis of the DIP joints.

(2) asymmetric oligoarthritis.

(3) symmetric polyarthritis similar to RA.

(4) axial involvement (spine and sacroiliac joints).

(5) arthritis mutilans, a highly destructive form of disease.

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

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

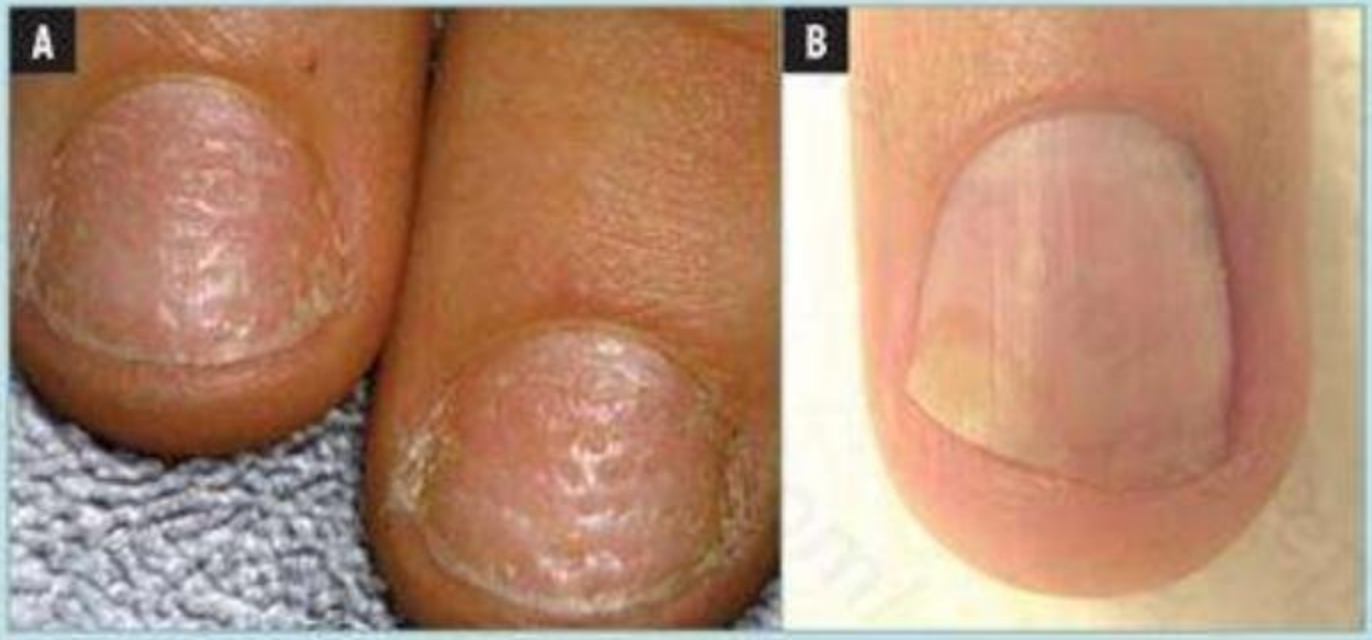
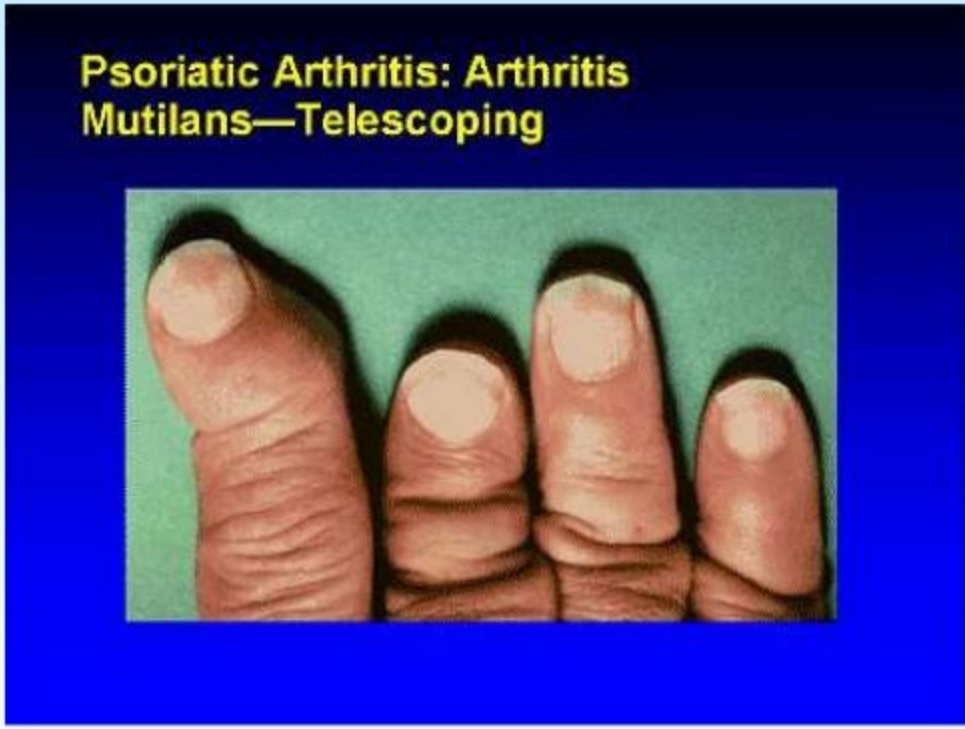


Image courtesy of International Journal of Clinical Reviews
http://www.remedicajournals.com/International-Journal-of-Clinical-Reviews/BrowseIssues/November-2010/Article-Nail-Psoriasis-topical-and-systemic-therapies

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

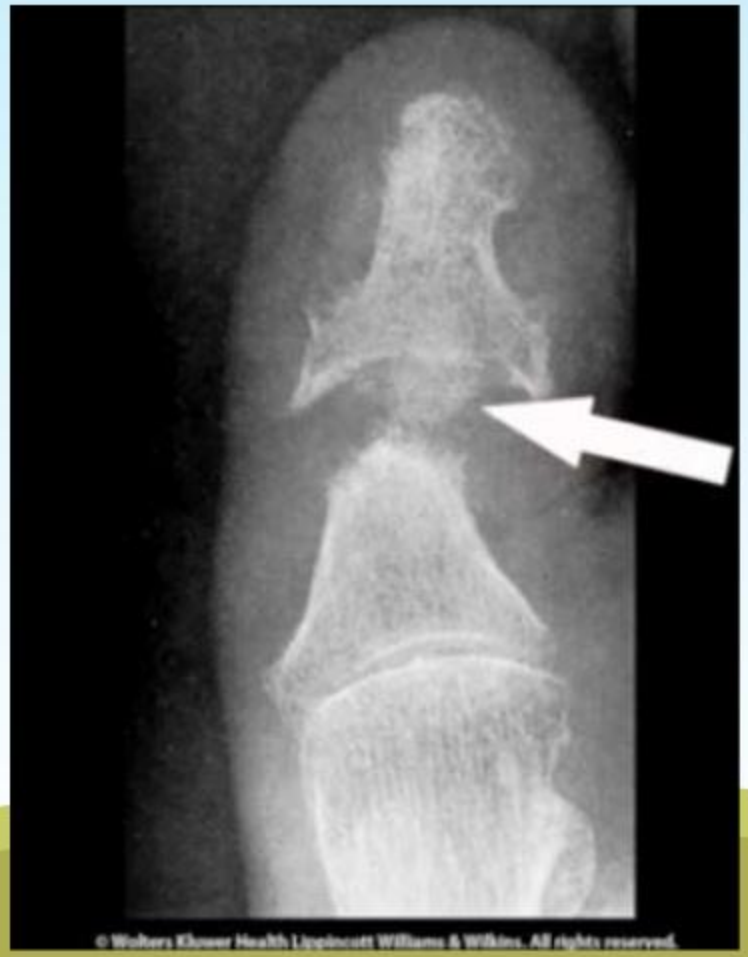


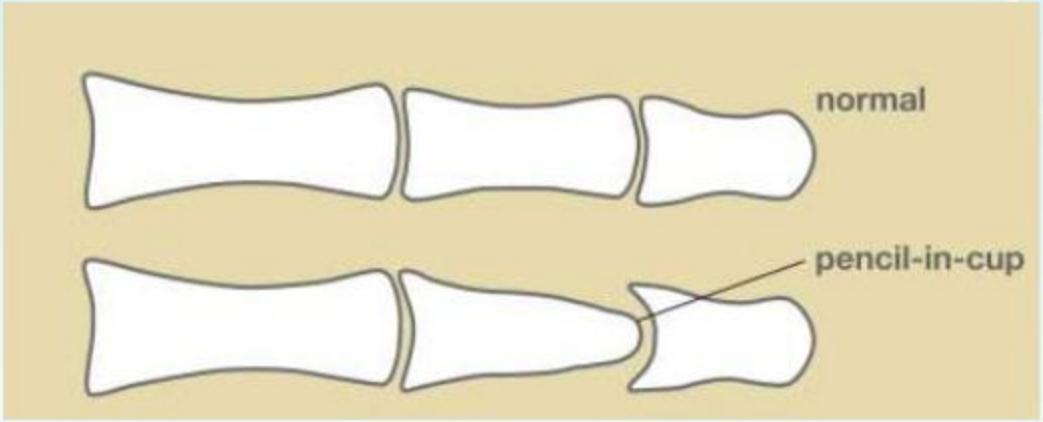
Laboratory Findings

- ESR and CRP are elevated.
- About 10% of patients have anti-CCP antibodies.
- Uric acid may be elevated in the presence of extensive psoriasis.
- HLA-B27 is found in 50–70% of patients with axial disease, but 20% in patients with only peripheral joint involvement.

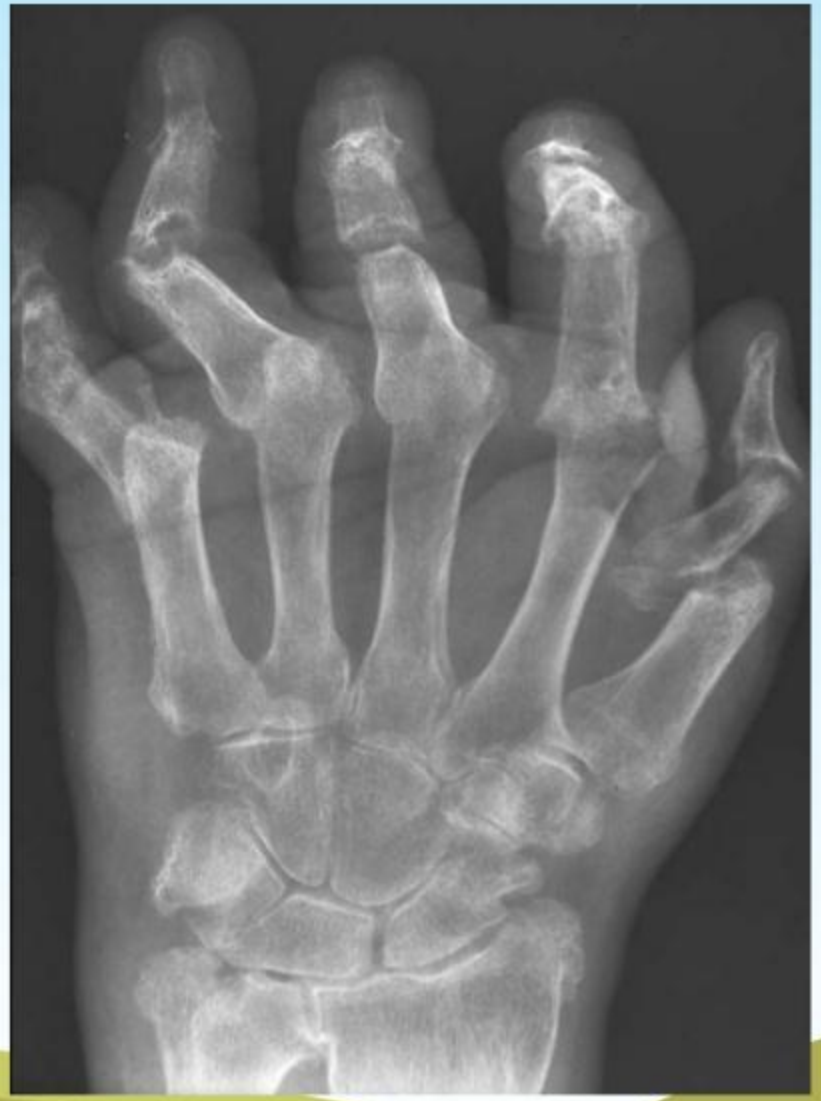
Radiographic Findings

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





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



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

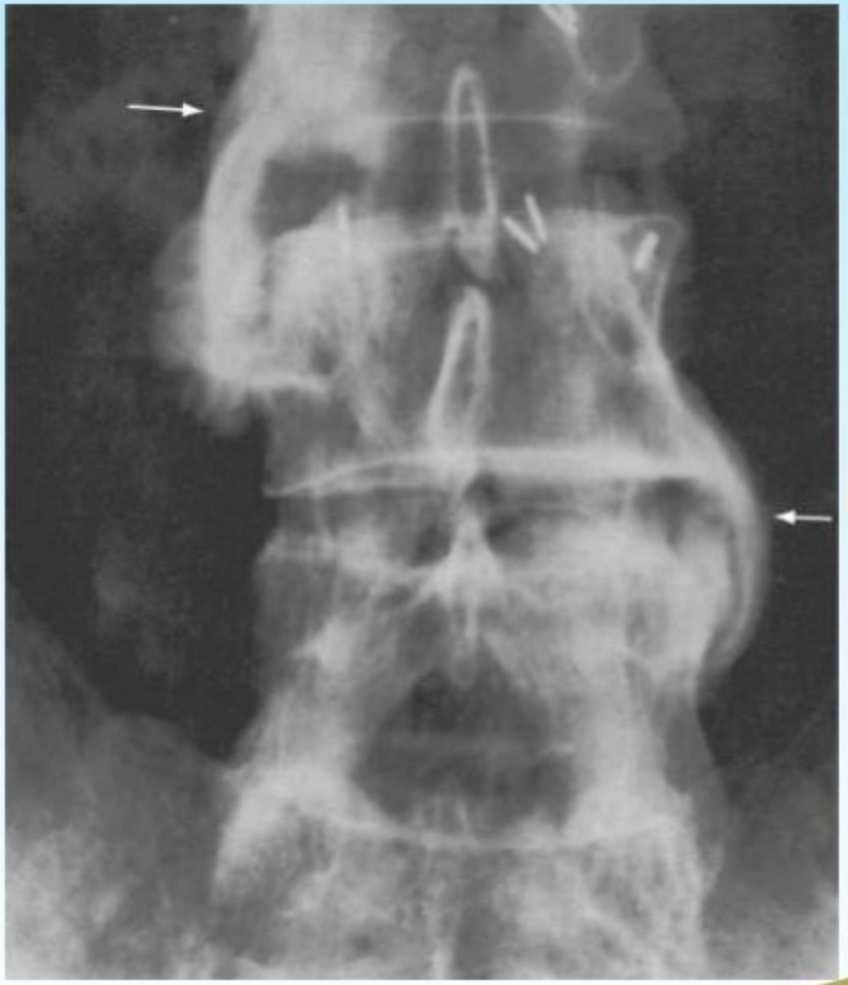


Table 6 – Classification criteria for psoriatic arthritis[a]

Criterion	Points
1. Evidence of current psoriasis, a personal history of psoriasis, or a family history of psoriasis	
Evidence of current psoriasis on examination	2
Personal history	1
Family history	1
2. Typical psoriatic nail dystrophy (onycholysis, pitting, hyperkeratosis) on examination	1
3. Negative test for rheumatoid factor	1
4. Dactylitis (inflammatory swelling of an entire finger or toe)	
Current dactylitis on examination	1
Personal history	1
5. Radiographic evidence of juxta-articular new bone formation on plain radiographs of hands or feet	1

[a] To meet **CASPAR** (**C**l**AS**sification criteria for **P**soriatic **AR**thritis) criteria, a patient must have inflammatory articular disease (joint, spine, or entheseal) with ≥ 3 total points from any of the 5 categories.

Adapted from Taylor W et al; CASPAR Study Group. *Arthritis Rheum.* 2006.[47]

Treatment

- In mild disease no more than topical preparations to control the skin disease and NSAIDs for the arthritis are needed.
- In resistant forms of arthritis, immunosuppressive agents (methotrexate) and TNF inhibitors (infliximab, etanercept and adalimumab) have are effective.
- *Etanercept*- 50 mg SC once weekly or 25 mg SC twice weekly; if twice weekly, doses should be given on same day or 3-4 days apart.
- Adalimumab- 40 mg SC q2wk.
- Infliximab- 5 mg/kg IV at 0, 2, and 6 weeks, then every 8 weeks.

ENTEROPATHIC ARTHRITIS

- Both forms of IBD, Ulcerative Colitis (UC) and Crohn's disease (CD) are associated with SpA.
- Two types of involvement.

1.Peripheral Arthritis.

2.Sacroiliitis and Spondylitis.

1.Peripheral arthritis

- Peripheral arthritis occurs in about 15 per cent of patients with inflammatory bowel disease.
- Typically larger joints are involved in asymmetric fashion.
- Synovitis and joint erosion can occur.
- Men and women are affected with equal frequency and there is no particular association with HLA-B27.

2. Sacroiliitis and Spondylitis

- This pattern is seen in about 10 per cent of patients with inflammatory bowel disease,.
- HLA-B27 is positive in 60 per cent and there is an increased incidence of ankylosing spondylitis in close relatives.
- Unlike the peripheral arthritis, sacroiliitis shows no temporal relationship to gastrointestinal inflammation and its course is unaffected by treatment of the bowel disease.

Laboratory Findings

- Of patients with AS and IBD, 30–70% carry the HLA-B27 gene.

Radiographic Findings

- Radiographic changes in the axial skeleton are the same as in uncomplicated AS.

Treatment

- Infliximab and adalimumab are effective for induction and maintenance of clinical remission in CD and UC.
- Treatment for IBD, including sulfasalazine and related drugs, systemic glucocorticoids, and immunosuppressive drugs, are also usually of benefit for associated peripheral arthritis.

UNDIFFERENTIATED AND JUVENILE-ONSET SPONDYLOARTHRITIS

- Patients who do not meet the classification criteria are included in this.
- Approximately one-half of the patients with undifferentiated SpA are HLA-B27-positive.
- In familial cases, which are much more frequently B27-positive, there is often eventual progression to classical AS.

- Juvenile-onset SpA, begins between ages 7 and 16, most commonly in boys (60–80%).
- An asymmetric, predominantly lower-extremity oligoarthritis and enthesitis occurs.
- Extraarticular features are absent.

- The prevalence of B27 in this condition,is approximately 80%.
- Many of these patients go on to develop AS in late adolescence or adulthood.

- Management of undifferentiated SpA is similar to that of the other spondyloarthritides.

THANK YOU

FOR ATTENTION