ANKYLOSING SPONDYLITIS: Diagnostic Criteria,Imaging & Medical Management

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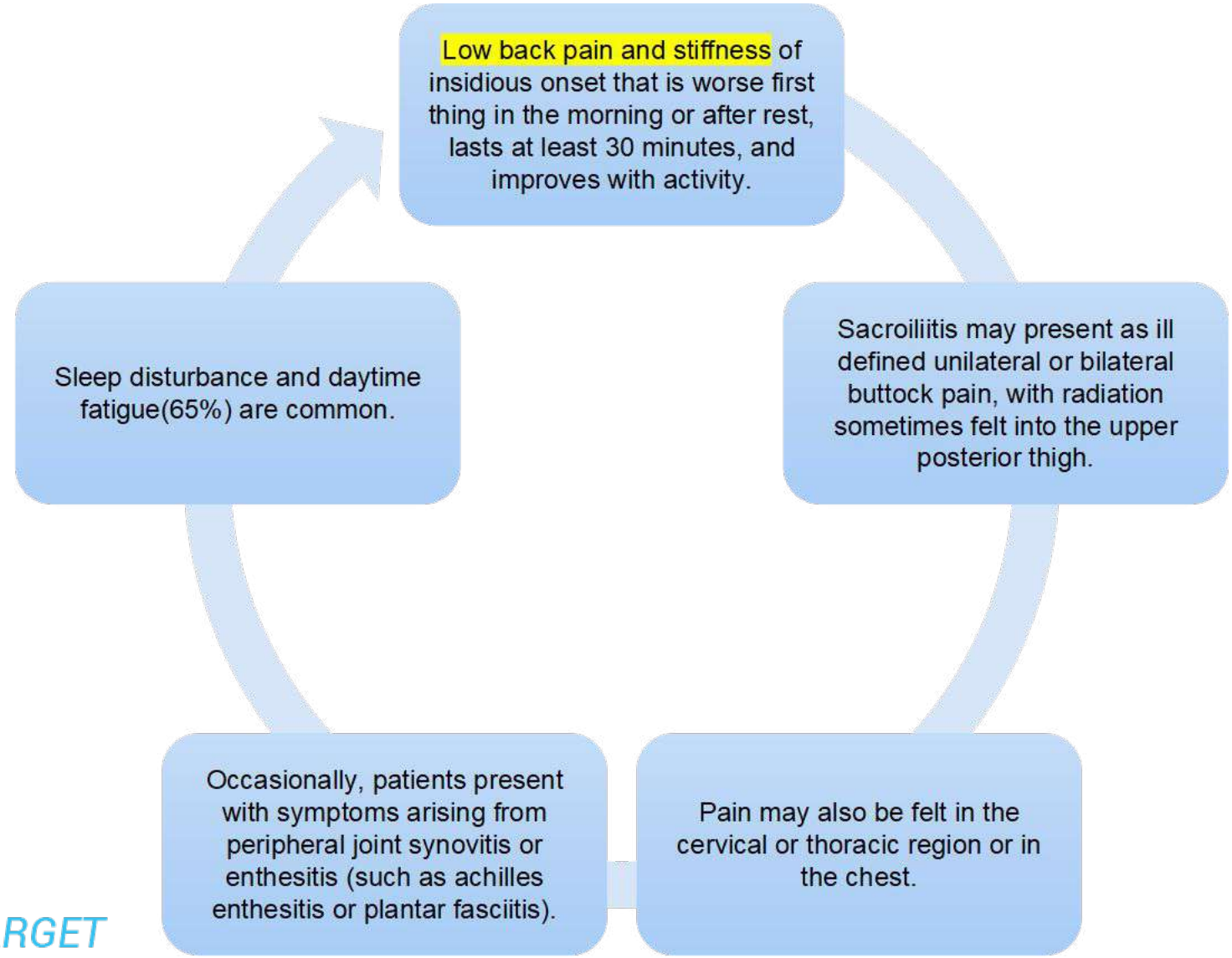
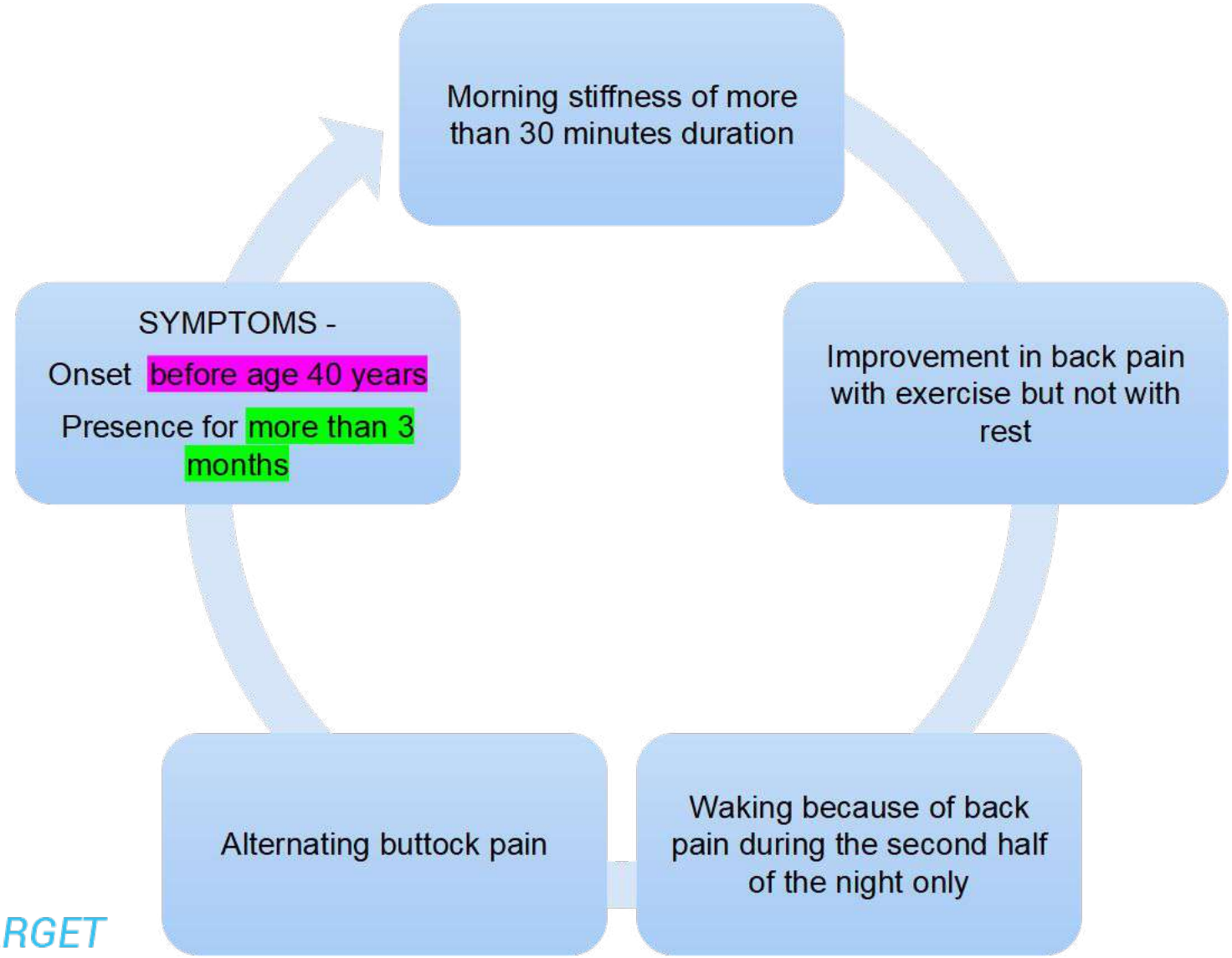
How is it diagnosed?





CLASSIFICATION CRITERIA

- The most commonly used criteria for the classification of ankylosing spondylitis were developed in

Modified New York criteria for ankylosing spondylitis (1984)

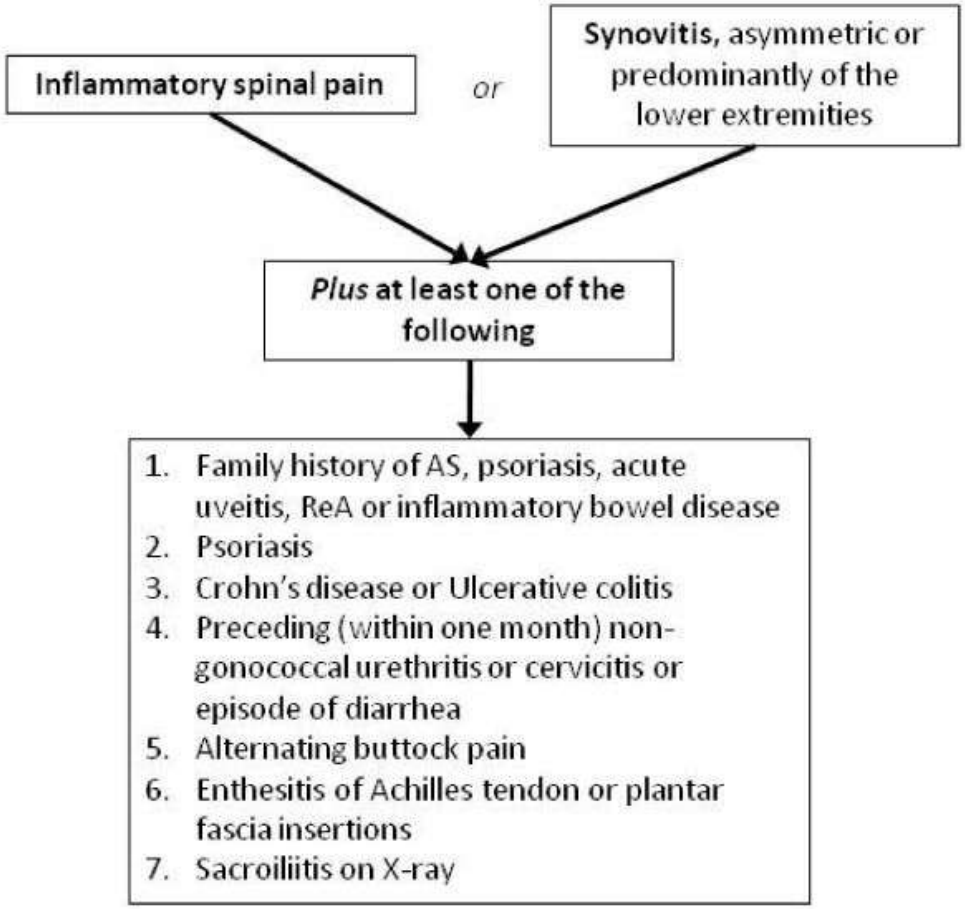
1. Low back pain (insidous onset) of at least three months duration with inflammatory characteristic
2. Limitation of lumbar spine motion in sagittal and frontal planes
3. Decreased chest expansion (relative to normal values for age and sex)
4. Bilateral sacroiliitis grade 2 or higher
5. Unilateral sacroiliitis grade 3 or higher.

- Definite ankylosing spondylitis ---4th & 5th criterion presents with any clinical criteria.
- However, radiological sacroiliitis may not develop for many years, and the development of new cri

Amor criteria for spondyloarthritis

Table 1. Spondyloarthropathies Amor Criteria 1990.	
Clinical characteristic	**Score**
Lumbar pain at night or lumbar morning stiffness	1
Asymmetric oligoarthritis	2
Buttock pain (or bilateral alternating buttock pain)	1 (2)
Sausage-like toe or digit(s)	2
Heel pain or other well-defined enthesities	2
Iritis	2
Nongonococcal urethritis/cervicitis within 1 month of onset	1
Acute diarrhea within 1 month of arthritis onset	1
Psoriasis, balanitis or inflammatory bowel disease (Crohn's or ulcerative colitis)	2
Sacroiliitis (bilateral grade 2 or unilateral grade 3)	2
HLA-B27(+) or (+) family history of a spondyloarthropathy	2
Rapid (<48 h) response to NSAIDs	2
Diagnosis of a spondyloarthropathy requires a score of ≥6.	
Data taken with permission from [11].	

European Spondyloarthropathy Study Group (ESSG) criteria



ASAS criteria for classification of axial spondyloarthritis

ASAS classification criteria for axial 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#

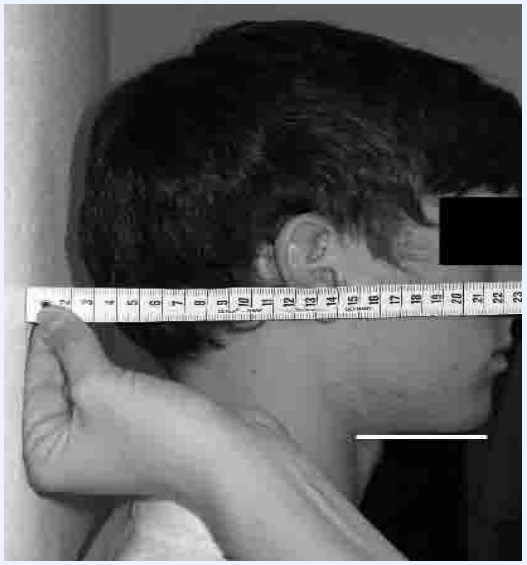
#SpA features
- inflammatory back pain
- arthritis
- enthesitis (heel)
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- good response to NSAIDs
- family history for SpA
- HLA-B27
- elevated CRP

*Sacroiliitis on imaging
- active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA
- definite radiographic sacroiliitis according to mod NY criteria

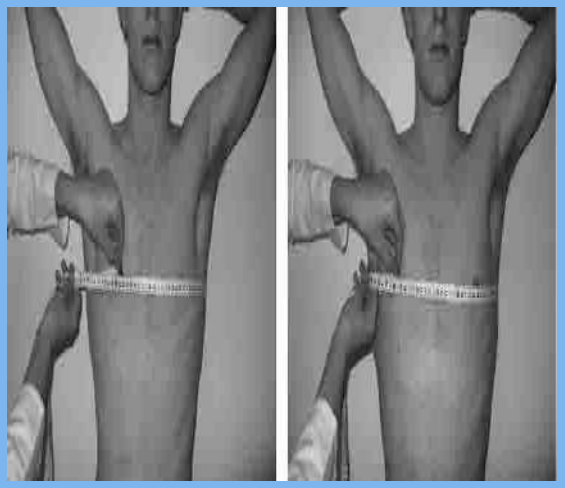
CALIN Criteria for LBP

Parameter	Criteria
1	Age at onset , 40 years
2	Insidious onset
3	Improvement with exercise
4	No improvement with rest
5	Pain at night (with improvement upon getting up)

Physical Examination

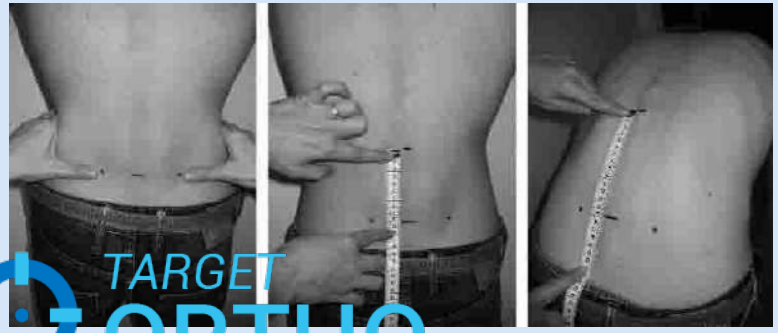
Appearance of the Patient	Patients with ankylosing spondylitis usually appear normal.
Vital Signs	Vital signs are within normal limits in patients with AS
Cervical spine 	I. Forward stooping of the thoracic and cervical spine. II. The degree of flexion deformity is measured by asking the patient to stand erect with heels and buttocks against a wall and to extend the neck while keeping the mandible in the horizontal position and ask the patient to touch the wall. III. The degree of flexion deformity is measured by the distance between the occiput and the wall.

Thoracic spine



I. The degree of chest expansion is measured by the range of motion of the costovertebral joints and is measured at the level of the xiphoid process(**fourth intercostal level anteriorly)**
II. The physician must ask the patient to raise their arms beyond their heads and then ask the patient to **maximal forced expiration how much they can and that is followed by a maximal inspiration.**
III. In normal individuals the expansion is usually >2 cm.
IV. In normal individuals it is greater than 10 cm.

MOD. Schober test



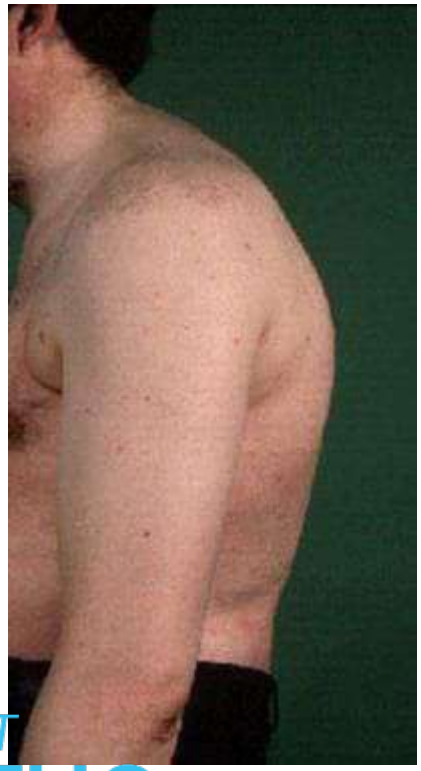
I. In patients with AS Schober test is used to measure forward flexion of the lumbar spine.
II. Physician must ask the patient to stands erect then a point is placed at the middle of a line joining the posterior superior iliac spines, another mark is made above 10 cm in the midline then ask the patient to bends forward how much they can without bending the knees and measure the distance.
III. In normal individuals should exceed 2 cm.

Lateral spinal flexion

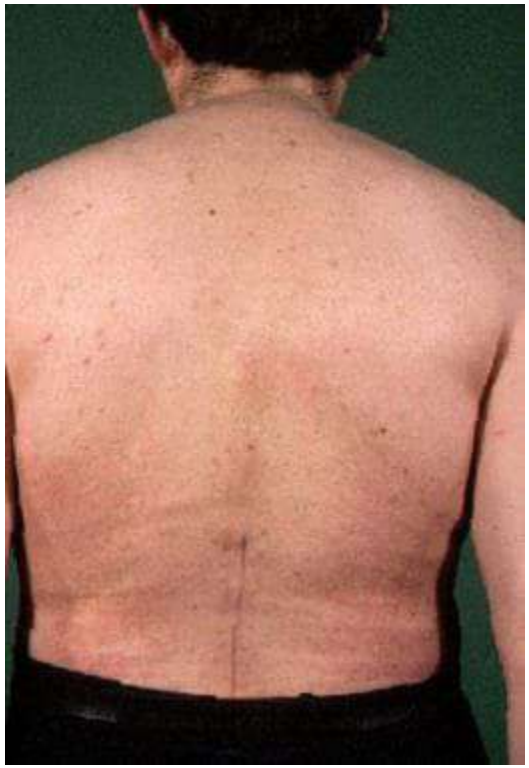
- Patient's heels and back rest against the wall. No flexion in the knees, no bending forward.
- Place a mark on the thigh , bend sideways without bending knees or lifting heels , place a second mark and record the difference.
- Alternatively, measure the distance between the patient's middle fingertip and the floor before and after bending sideways , and record the difference.
- The better of two tries is recorded for left and right separately.
- The mean of left and right is reported for lateral spinal flexion (in cm to the nearest 0.1 cm).

Sacroiliac joint tenderness	Pain apply direct pressure over the sacroiliac joint/ASIS and, at the same time apply force on iliac spine laterally. LATERALLY-Apply pressure to compress the pelvis. SUPINE- FABER TEST
Hip joint	Flexion deformities and can be assessed by internal and external rotation of the hip.
Dactylitis	Dactylitis also called as sausage digits.
Lungs	Restrictive lung disease Upper lobe fibrosis
Cardiovascular	Valvular heart disease Aortitis Conduction disturbance

The patient's spine has been fused in flexed position.

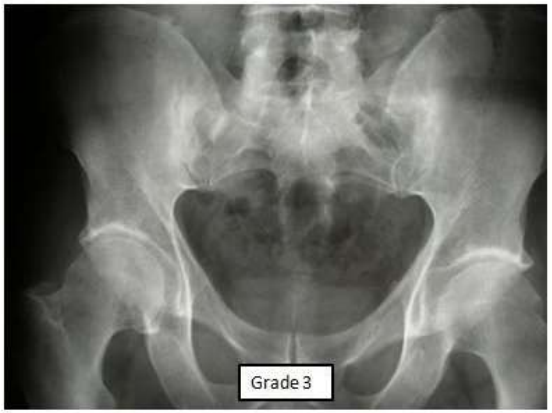


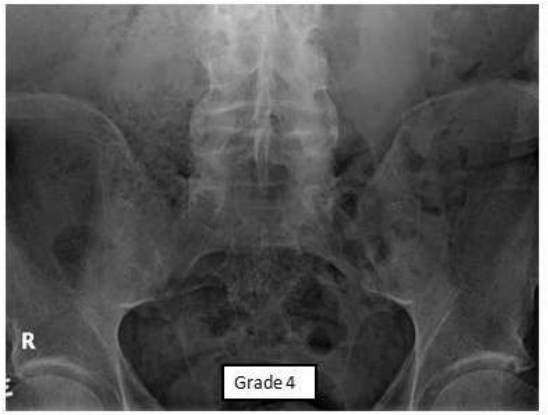
The patient's spine has been fused in a flexed position.



Radiography

- This disease generally begins in the distal portions of the spine and progresses more proximally with time in a continuous fashion.
- Involvement of the SI joint is a requirement for the diagnosis of AS.
- Sacroilitis-Bilateral, symmetric, and gradually progresses over years.





Grade 0	normal
Grade 1	suspicious changes
Grade 2	minimal definite changes: circumscribed areas with erosions or sclerosis with no changes of the sacroiliac joint space.
Grade 3	distinctive changes, sclerosis, change of joint space (decrease or widened), partial ankylosis
Grade 4	ankylosis

Radiological criterion according to the modified New York criteria for AS (1984)
Sacroiliitis grade 2 bilaterally or grade 3-4 unilaterally.

Radiographic scoring methods in AS

1. BASRI (Bath Ankylosing Spondylitis Radiology Index)), a grading system that evaluates radiographs of the anteroposterior view of the pelvis, the anteroposterior and lateral views of the lumbar spine and the lateral view of the cervical spine .
2. Stoke Ankylosing Spondylitis Spinal Score (SASSS) that evaluates posterior and anterior corners of the lumbar spine for erosions, sclerosis, squaring, syndesmophytes and total bony bridging
3. mSASSS, which is a modification of the SASSS and evaluates only the anterior edges of both the lumbar and cervical spine on a lateral view
4. Radiographic Ankylosing Spondylitis Spinal Score (RASSS)

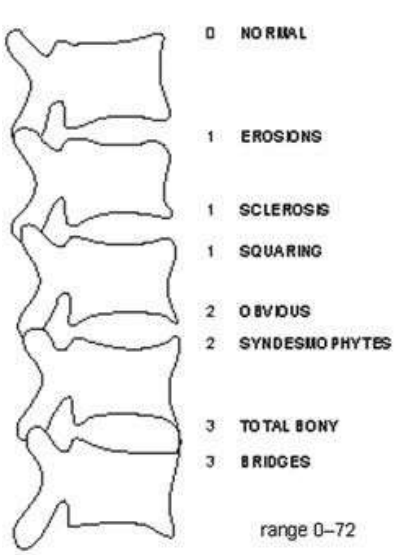
Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS).

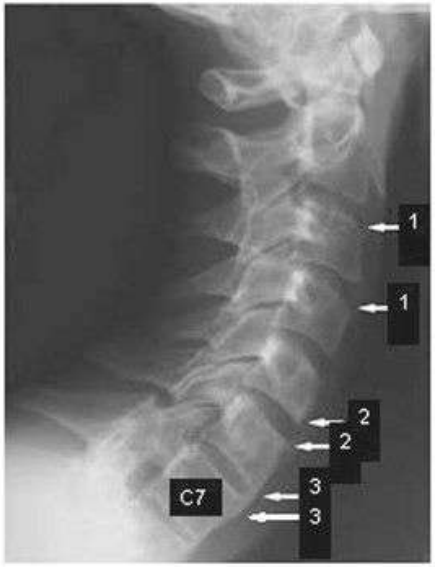
Outcome measure to assess the impact of treatment on structural progression in ankylosing spondylitis

A total of 24 sites are scored on the lateral cervical and lumbar spine

(A): the anterior corners of the vertebrae from lower border of C2 to upper border Th1 (including) and from lower border of Th12 to upper border of S1 (including).

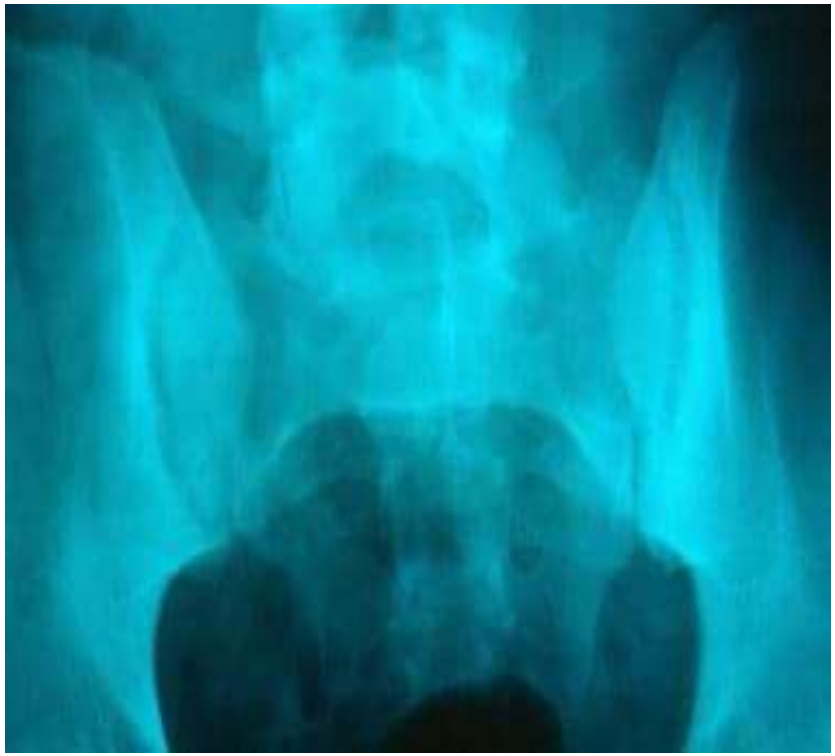
Each corner can be scored from 0 to 3, resulting in a range from 0 to 72 for the total mSASSS.



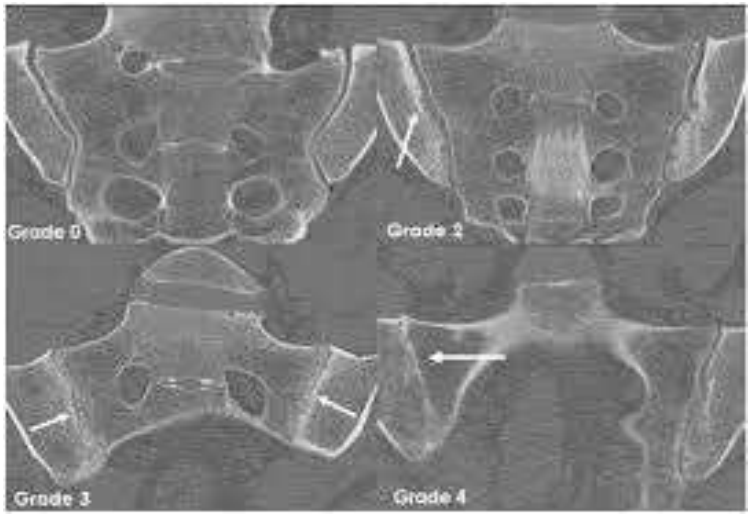


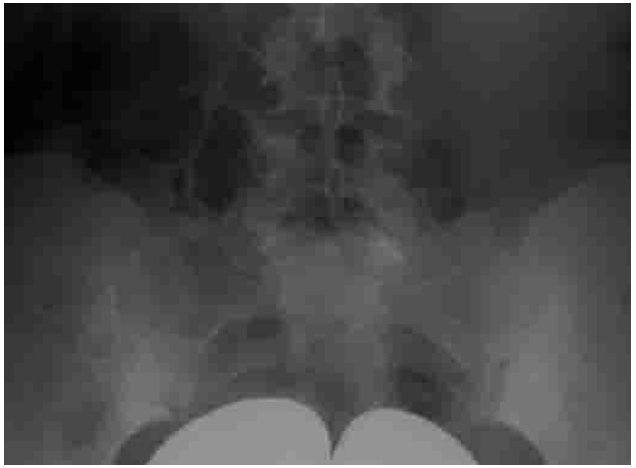
SACROILITIS

- The lesions progress from blurring of the subchondral bone plate to irregular erosions of the margins of the SI joints (pseudo-widening) to sclerosis, narrowing, and finally fusion.
- Erosions of the subchondral bone of the SI joint are generally seen earlier in the lower portion of the joint (because this portion is lined by synovium) and on the iliac side (because of the thinner cartilage covering this side of the joint).

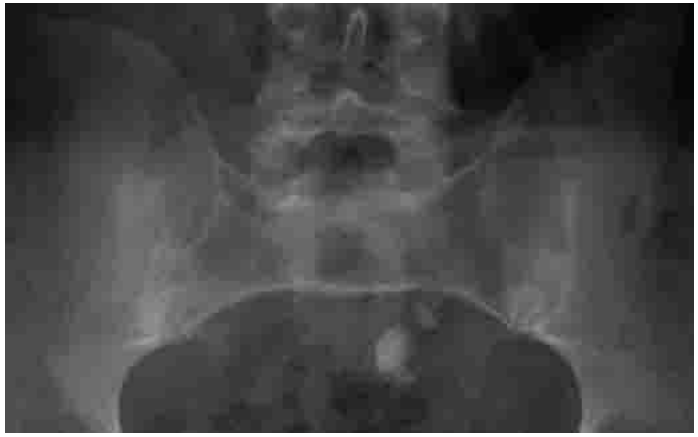


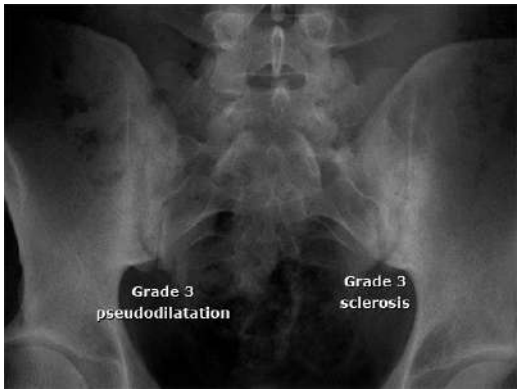
Bilateral symmetric sacroiliitis in a patient with AS showing blurring of the margins of the joints and pseudo-widening.



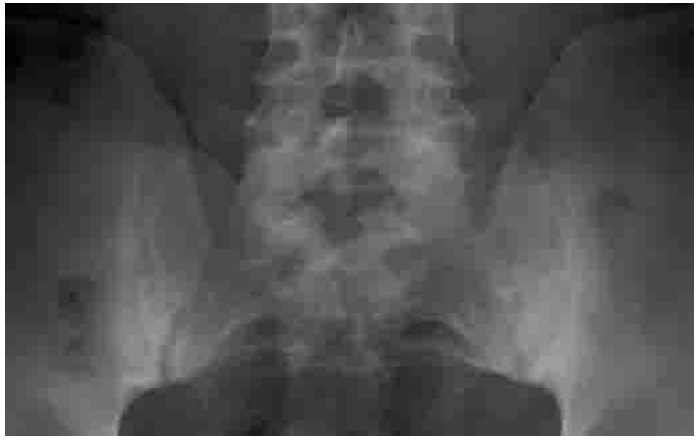


Both sacroiliac (SI) joints (right more than left) show some erosions, irregular joint space and ill-defined margins. (right grade 3, left grade 2).

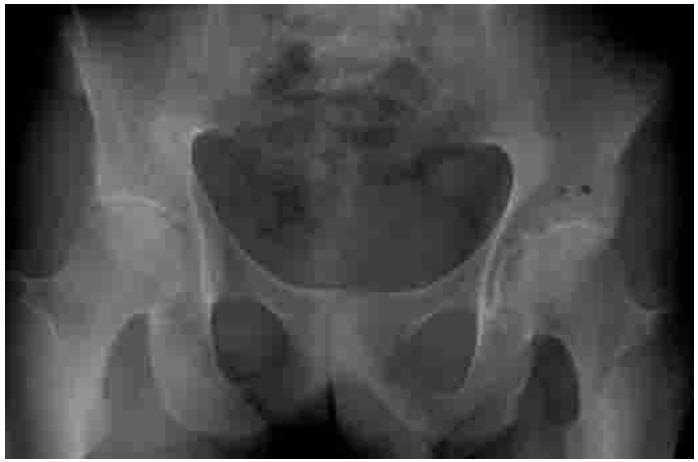




The left sacroiliac (SI) joint does not show specific changes but the joint does not appear completely normal (grade 1). At the site of the arrow at the right SI joint there is a minimal erosion and minimal sclerosis and ill defined margins at the iliac side of the joint (grade 2)

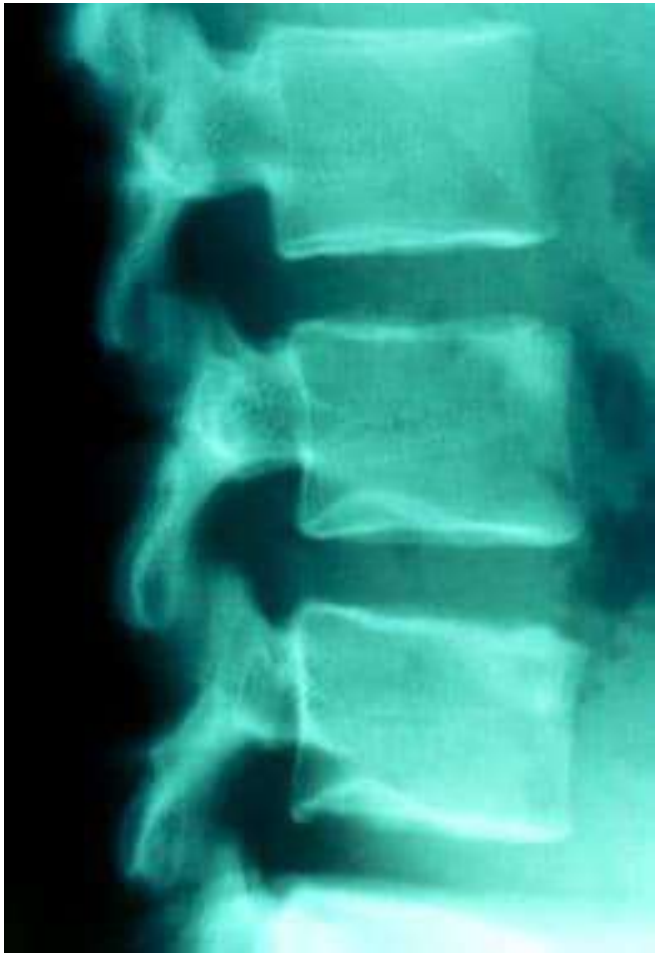


Both sacroiliac (SI) joints show ill-defined margins, sclerosis, and especially at the left SI joint an irregular joint space (grade 2 bilaterally)



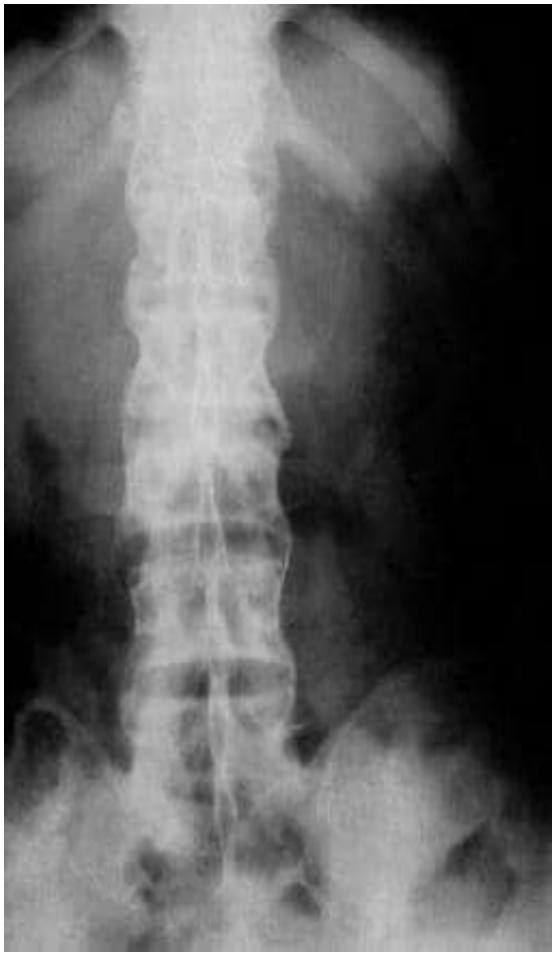
Both sacroiliac (SI) joints show a complete ankylosis (grade 4 bilaterally).
The symphysis pubis (horizontal arrow) shows a partial ankylosis. At the insertion of the ligaments at the os pubis thereare signs of blurry margins.
The left hip shows severe joint space narrowing.

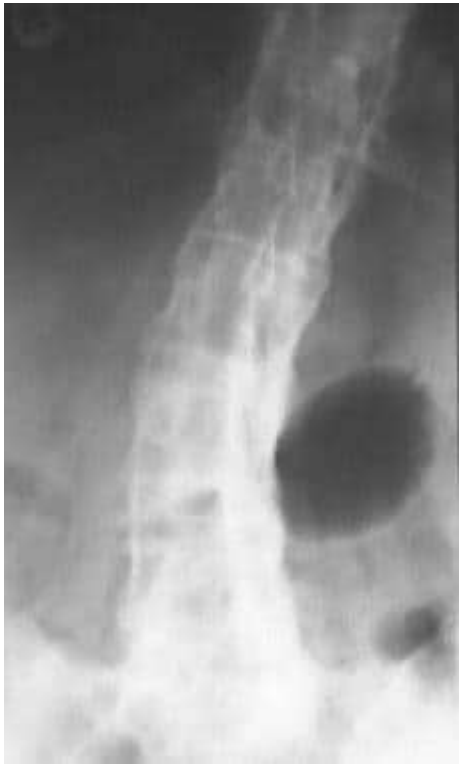
- The radiographic signs of AS are due to enthesitis (annulus fibrosus).
- Early radiographic signs include squaring of the vertebral bodies caused by erosions of the superior and inferior margins of the vertebral bodies.
- The inflammatory lesions at vertebral entheses may result in sclerosis of the superior and inferior margins of the vertebral bodies, called shiny corners (Romanus lesion).



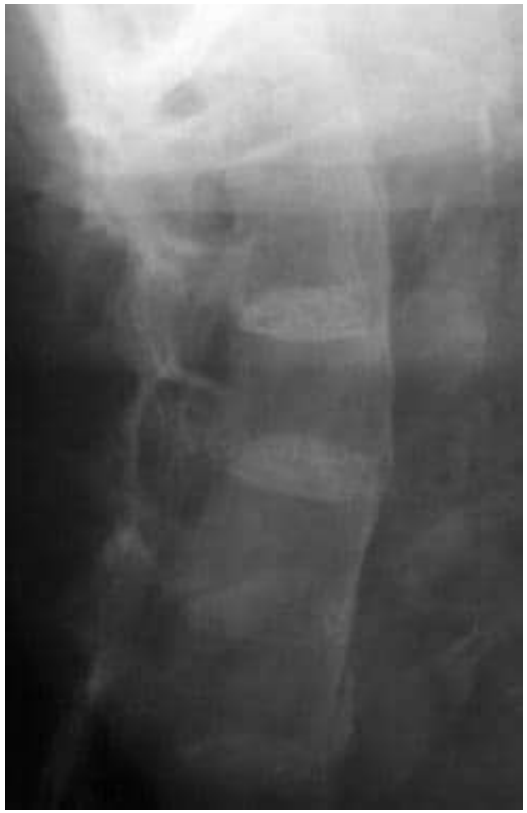
Enthesitis at the site of the insertion of the annulus fibrosis on the corners of the vertebral bodies, shiny corner (Romanus) lesions.

- Ossification of the annulus fibrosus leads to the radiographic appearance of syndesmophytes, which in AS are typically marginal.
- Over time, the development of continuous (bridging) syndesmophytes may result in complete fusion (bamboo spine)

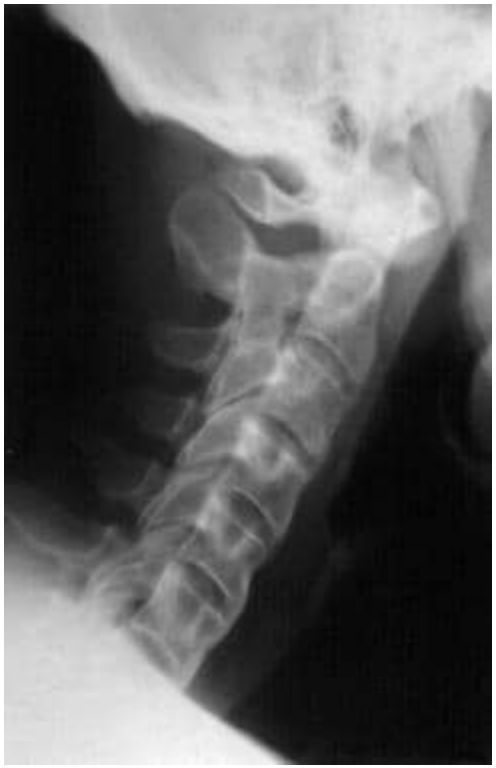




Anteroposterior radiograph of spine of a patient with AS. Ossification of annulus fibrosus can be observed at multiple levels, which has led to fusion of spine with abnormal curvature.



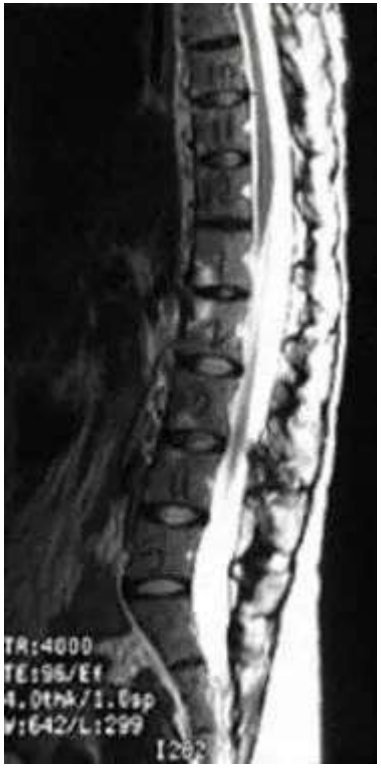
This radiograph of the lumbar spine of a patient with end-stage AS shows bridging syndesmophytes, resulting in bamboo spine



This radiograph of the cervical spine of a patient with AS shows fusion of the vertebral bodies due to bridging syndesmophytes.

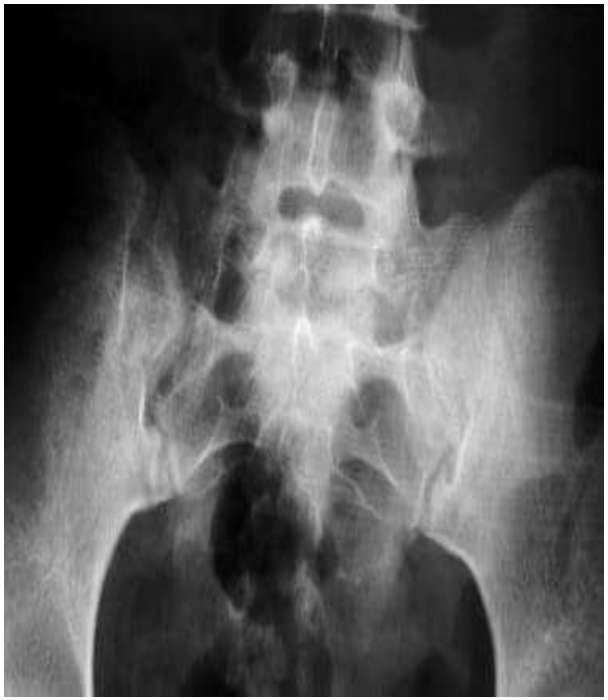
MRI and CT

- Fat-saturating techniques such as short tau inversion recovery (STIR) or MRI with gadolinium is sensitive for inflammatory lesions of enthesitis.

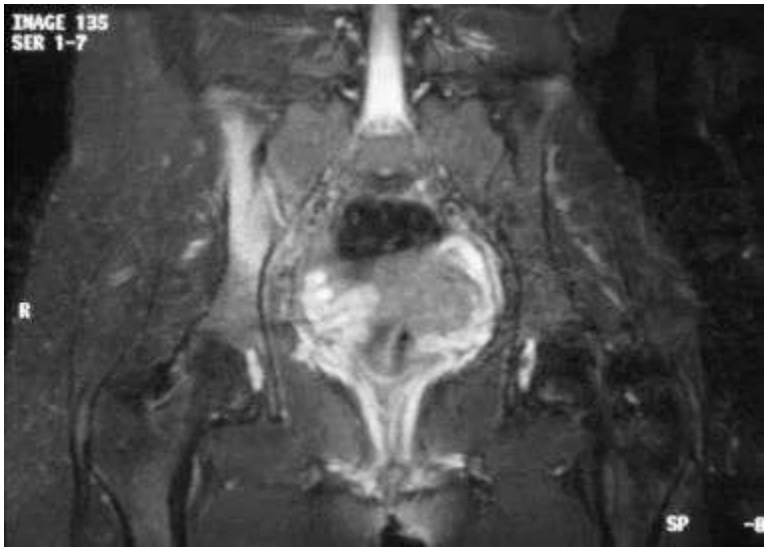


Sagittal MRI of thoracolumbar spine of a patient with AS. Syndesmophytes and anterior corner lesions can be seen.

- In patients with inflammatory back pain who have normal plain radiographs, MRI imaging of the pelvis (sacroiliac joints) may be very useful to confirm a diagnosis of axial SpA.

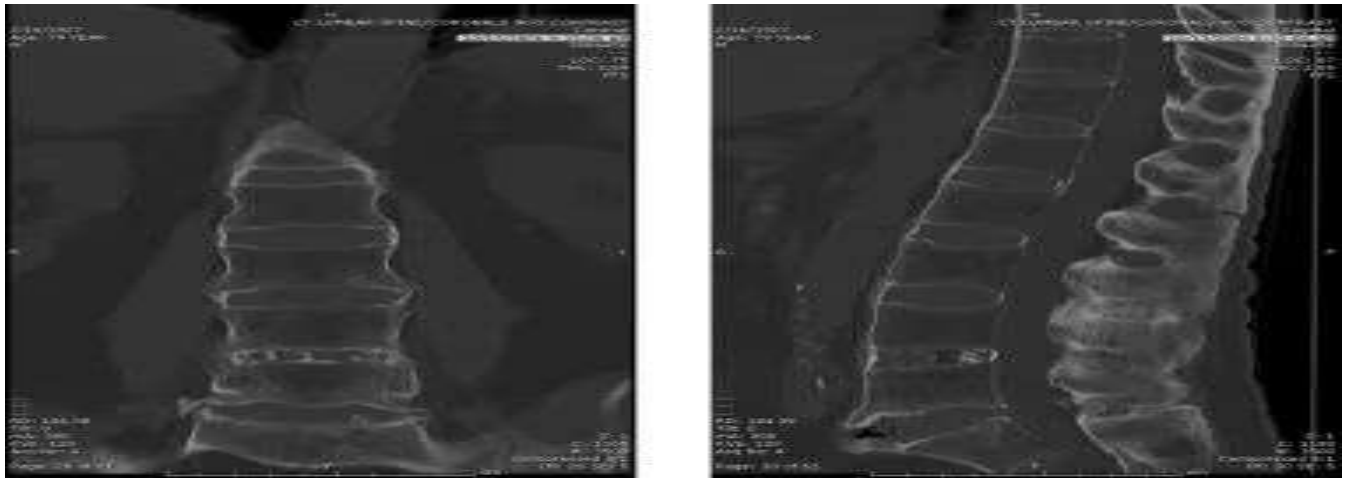


This15-year-old female patient presented with recent onset of right-sided low back pain. Plain radiography findings were normal.



Increased signal intensity in the right sacroiliac joint, revealing sacroiliitis.
Other laboratory study findings were essentially normal.
The patient was started on indomethacin and rapidly improved.

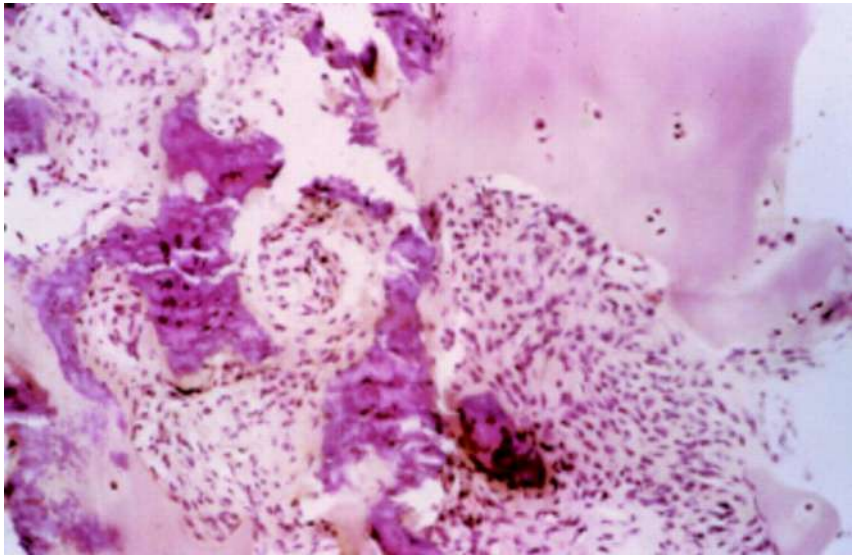
- Patients who develop bowel or bladder dysfunction should be evaluated immediately with MRI to assess for possible cauda equina syndrome secondary to spinal stenosis.



CT scan of the L-spine in a patient with AS showing bony syndesmophytes.

Histologic Findings

- Histopathologic evaluation is not generally part of the diagnostic workup in patients with ankylosing spondylitis.
- The basic pathologic lesion is inflammation at the enthesis (enthesitis
- The histologic picture is that of chronic inflammation with CD4+ and CD8+ T lymphocytes and macrophages.



Approach Considerations

1. No definite disease-modifying treatment exists for individuals with ankylosing spondylitis (AS) although biologic agents show evidence of such activity.
2. Early diagnosis is important.
3. Patient education is vital to familiarize the patient with the symptoms, course, and treatment of the disease.
4. No drugs have been proved to modify the course of the disease.
5. Symptoms are generally not affected by pregnancy or childbirth.

MANAGEMENT OF AP

Predominant manifestation	Axial manifestations: back pain and stiffness	Peripheral manifestations: arthritis, enthesitis, dactylitis
First-line therapy	NSAIDs	
	Non-pharmacological treatment: education, exercise, physical therapy, rehabilitation, patient associations, self help groups	
		Local steroids
		csDMARDs (Sulfasalazine)
Sesond-line therapy	bDMARDs: TNF α inhibitor or IL-17 inhibitor	
Additional therapy and therapy in special clinical situations	Analgesics	
	Surgery	

Pharmacologic treatment for peripheral spondyloarthritis includes the following:

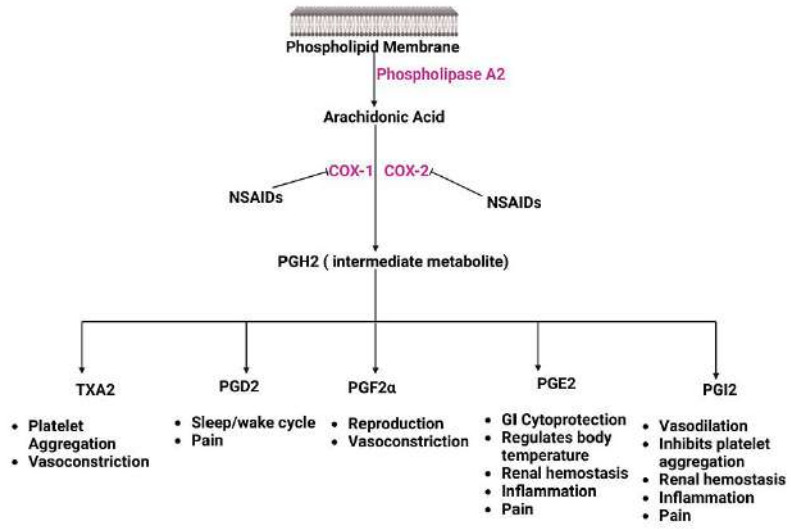
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Sulfasalazine
- Tumor necrosis factor–alpha inhibitors (TNFi)
- Interleukin-17A (IL-17A) inhibitors
- Corticosteroids
- Janus kinase (JAK) inhibitors
- Miscellaneous agents

Physical Therapy and Exercise

- Water therapy and swimming
- Postural training is also useful.
- Spinal extension and deep-breathing exercises help maintain spinal mobility, encourage erect posture, and promote chest expansion.
- Maintaining an erect posture during daily activities and sleeping on a firm mattress with a thin pillow also tend to reduce the tendency toward thoracic kyphosis.

Nonsteroidal anti-inflammatory drugs

- NSAIDs improve the symptoms of the disease by reducing pain and decreasing inflammation.If one NSAID is ineffective, another from a different family may provide relief.
- Indomethacin may be more effective than other NSAIDs
- Cyclooxygenase-2 (COX-2) inhibitors appear to be as effective as nonselective NSAIDs.



INDOMETHACIN(INDOCIN)

- Most effective NSAID for the treatment of AS
- Mild to moderate pain; it inhibits inflammatory reactions and pain

- Immediate release: 25-50 mg PO/PR q8-12hr; not to exceed 200 mg/day
- Extended release: 75-150 mg/day PO in single daily dose or divided q12hr; no

Ibuprofen(ADVIL,MOTRIN)

- Ibuprofen is used for relief of mild to moderate pain; it inhibits inflammatory reactions and pain by decreasing the activity of COX, which results in a decrease of prostaglandin synthesis.

Naproxen(Naprosyn,Naprelan,A Naprox)

- Mild to moderate pain; it inhibits inflammatory reactions and pain by decreasing the activity of COX, which results in a decrease of prostaglandin synthesis.

- Significantly impaired renal function: Monitor closely; consider reduced dosage if warranted

- Severe hepatic impairment: Avoid use

Diclofenac(Cataflam, Voltaren-XR)

- Diclofenac inhibits prostaglandin synthesis by decreasing COX activity, which, in turn, decreases formation of prostaglandin precursors. Liver function test abnormalities occur more often with diclofenac than with other NSAIDs.
- Diclofenac sodium: 25 mg PO 4 or 5 times daily

- Diclofenac potassium: 50 mg PO q12hr

Celecoxib

- Celecoxib is a COX-2 selective inhibitor that is associated with L**e**ss GI toxicity and **X** antiplatelet effect.
- 200 mg PO once daily or divided q12hr
- If no effect after 6 weeks, may increase to 400 mg/day
- If inadequate response observed after 6 weeks of taking 400 mg/day consider discontinuing therapy

5-Aminosalicylic Acid Derivatives

- 5-Aminosalicylic acid derivatives inhibit prostaglandin synthesis and reduce the inflammatory response to tissue injury.
- Delayed release:
- *0.5-1 g/day PO divided BID;*
- *Increase weekly to maintenance dose of 2 g/day PO divided BID;*
- *If response inadequate, may increase to 3 g/day after administering for 12 weeks*

Sulfasalazine

Sulfasalazine is useful in AS patients

I. who do not respond to OR

II. who have contraindications to NSAIDs,

III. Those with coexisting inflammatory bowel disease.

- Sulfasalazine reduces spinal stiffness, peripheral arthritis, and the erythrocyte sedimentation rate (ESR), but there is no evidence that it improves spinal mobility, enthesitis, or physical function.

- Sulfasalazine toxicities include rash, nausea, diarrhea, and agranulocytosis (rarely).

Corticosteroids

- Oral corticosteroids are occasionally helpful in controlling AS symptoms.
- They should be used only for short-term management; long-term management carries a high risk of adverse effects.

- No evidence has shown that corticosteroids alter the outcome of the disease, and these agents are known to increase the tendency toward spinal osteoporosis.

- Local corticosteroid injections are useful for symptomatic sacroiliitis, peripheral enthesitis, and arthritis, although the response is not typically as rapid as in patients with rheumatoid arthritis.

Immunosuppressants

- Methotrexate has an unknown mechanism of action in AS; it may affect immune function by inhibiting dihydrofolate reductase, interfering with purine synthesis.
- Effects are observed in the 3-6 weeks following administration.
- Methotrexate ameliorates symptoms (eg, pain, swelling, stiffness) but there is no evidence that it induces remission.

- Initial: 7.5 mg PO/IV/IM as a single weekly dose,
- 2.5 mg PO q12hr for 3 sequential doses per week

- Slingle dose not to exceed 20 mg/week PO (increased risk of bone marrow suppression)

Tumor necrosis factor–alpha inhibitors

- TNF-α (cachectin) is produced predominantly by macrophages, and TNF-β (lymphotoxin) is produced by lymphocytes.
- TNFi have a fairly rapid onset of action (2 weeks), and have been shown to reduce the inflammatory activity of spinal disease as assessed with magnetic resonance imaging.

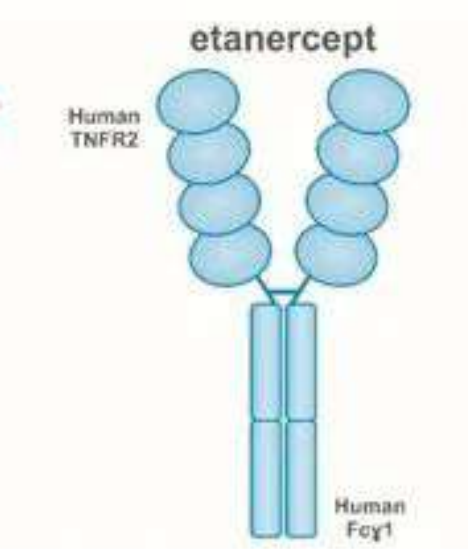
- TNFi are indicated after NSAID therapy has failed (two different NSAIDs for one month each).

- The following TNFi have been approved by the US Food and Drug Administration (FDA) as therapies for AS:

1) Etanercept
2) Infliximab
3) Adalimumab
4) Golimumab
5) Certolizumab pegol

ETaNercept

- Produced by **r DNA**
- Etanercept consists of a fusion protein of the extracellular portion of the p75 TNF-α receptor and the Fc portion of immunoglobulin G (IgG)... (TNF-α+ IgG1Fc)
- It INTERCEPTS TNF-α, reducing inflammation and symptoms of ankylosing spondylitis.
- sc. 50 mg weekly
- It is also approved for rheumatoid arthritis, PsA, psoriasis, and juvenile idiopathic arthritis.



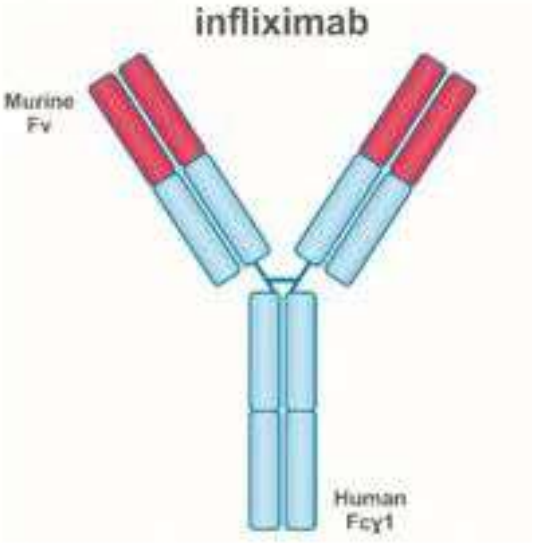
MONOCLONAL ANTIBODIES(MAB)

- Anti-TNF-α MONOCLONAL AB
- ADAlimumab, GOlimumab, CERTolizumab, INFLximab
- Clinical use

1) PSORIATIC
2) ANKYLOSING
3) IBD
4) RA

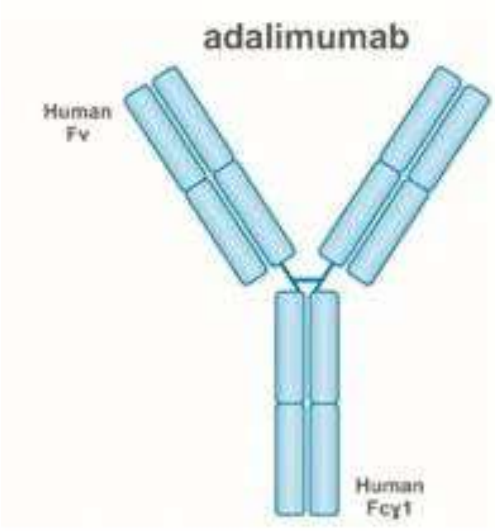
Infliximab

- Infliximab is a **C**himeric IgG1κ monoclonal antibody (mAb) directed against TNF-α.
- The variable regions of heavy and light chains are murine in origin, and the constant regions are human.
- It is given as an intravenous (IV) infusion.
- iv. 3 mg/kg at 0, 2 and 6 weeks, then every 8 weeks.



Adalimumab

- Adalimumab is a **H**uman IgG1κ monoclonal antibody directed against TNF-α.



- Binds and neutralizes soluble and membrane-bound tumor necrosis factor (TNF), so that it cannot interact with p55 and p75 cell-surface TNF receptors.

- The FDA has approved adalimumab-atto, adalimumab-adbm, adalimumab-adaz, adalimumab-bwwd as biosimilars and not as interchangeable drugs.
- Sc. 40 mg every other week

Golimumab

- Golimumab is a **H**uman IgG1κ mAb directed against TNF-α.
- Binds and inhibits soluble and transmembrane human TNFα.
- SC injection and is available in a prefilled syringe or an autoinjector.

(i) as an adjunct to methotrexate treatment in patients with moderate to severe active rheumatoid arthritis (RA)

(ii) in patients 2 years old and above with active psoriatic arthritis (PsA) (i

ii) as a single agent in patients with active ankylosing spondylitis (AS) or in combination with methotrexatea

(iv) as a single agent in patients with moderate to severe ulcerative colitis (UC) who require chronic steroids or have experienced intolerance or only a partial response to previous medications.

Certolizumab pegol

- Certolizumab pegol is a **R**ecombinant humanized anti-human TNF-α neutralizing antibody.
- **H**umanized Fab fragment of 50 kDa, from an IgG 1 isotype, fused to a 40 kDa **P**olyethylene glycol moiety replacing the Fc antibody region.
  The absence of the Fc region was ideated to prevent complement fixation and antibody-mediated cytotoxicity as well as to markedly increase its half-life
- It is given as a subcutaneous injection.

SIDE EFFECTS

- Toxicities associated with TNFi include Injection-site and Infusion reactions.
- Increased risks of bacterial infections, reactivation of latent tuberculosis, and certain fungal infections (eg, histoplasmosis, coccidioidomycosis) have been observed.
- Increased risk of malignancy in patients receiving TNFi. (Lymphoma and non-melanotic skin cancers) In rare cases, cytopenias have been associated with TNFi use.
- Patients should be screened for latent tuberculosis, hepatitis B, and HIV infection before beginning TNFi therapy.
- Safe in patients with chronic hepatitis C.
- Rarely, autoimmune syndromes (eg, a lupuslike illness) have been noted in patients receiving TNFi. A positive antinuclear antibody (ANA) test result, in the absence of clinical disease, may occur during treatment.

Interleukin-17A inhibitors

- Secukinumab and ixekizumab.
- Both are indicated for adults with active ankylosing spondylitis and for those with active non-radiographic axial spondyloarthritis with objective signs of inflammation.

- Secukinumab (Cosentyx), a **H**uman IgG**1** monoclonal a
- In 2020, approval was expanded to include non-radiogr
- Secukinumab (at a dose of 150 mg subcutaneously) .

Secukinumab

Ixekizumab

- Ixekizumab (Taltz), a humanized monoclonal IgG**4** antibody, also targets IL-17A & neutralizes the proinflammatory effects of IL-17A.
- In 2019, ixekizumab was approved by the FDA for adults with active AS.

Janus kinase inhibitors

- The JAK family contains four JAKs:
- JAK1, JAK2, JAK3 and tyrosine kinase 2 (TYK2).
- Two JAK inhibitors, Upadacitinib (Rinvoq) and Tofacitinib (Xeljanz), are approved by the FDA for treatment of active AS in adults who have an *inadequate response or are intolerant to one or more TNFi.*
- Both are available as Extended-release tablet

- Upadacitinib, a **JAK1**-selective inhibitor, was approved by the FD
- A small molecule that interferes with the JAK signaling pathways
- Patients who had an inadequate response (IR) or intolerance to 1

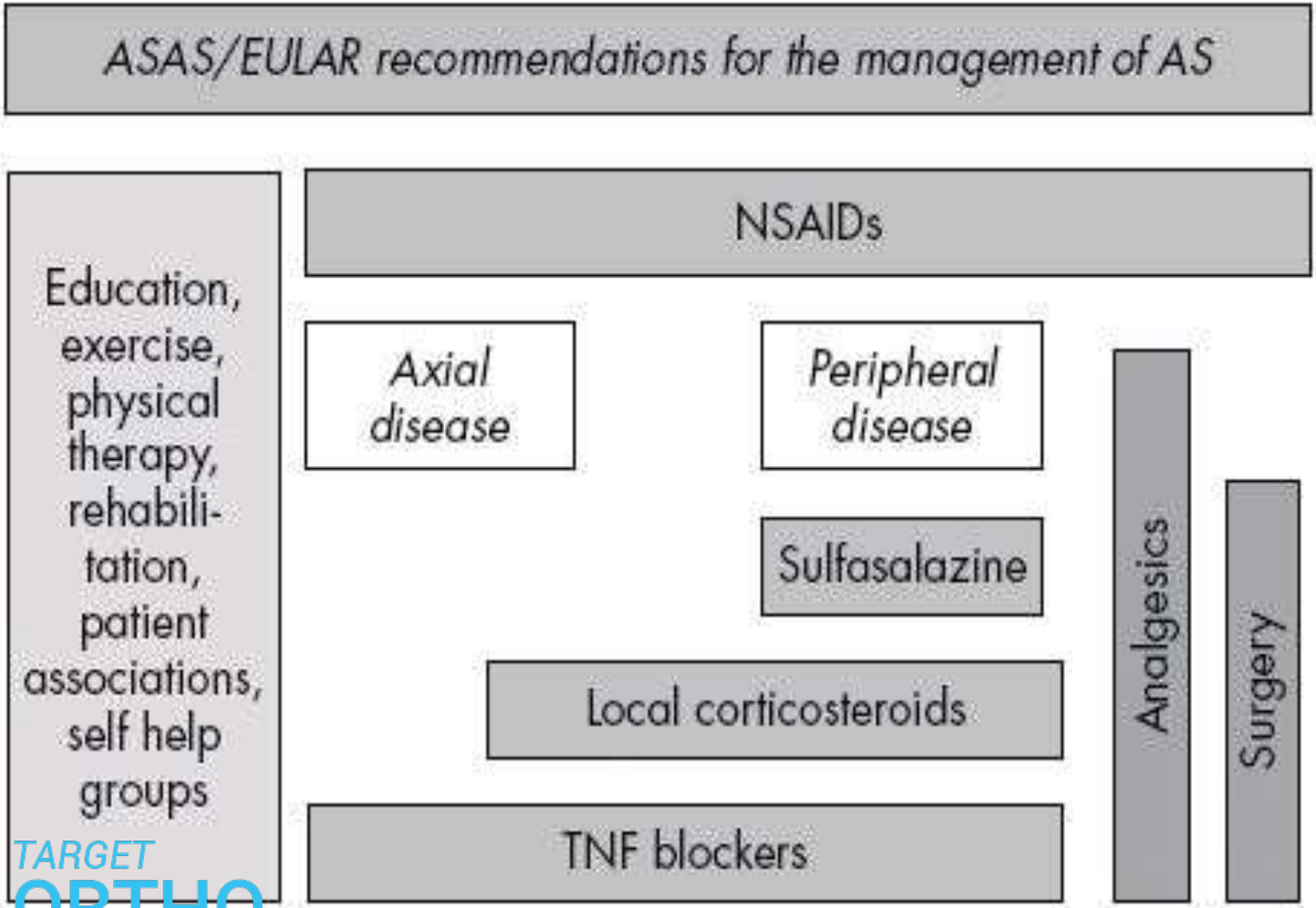
Upadacitinib

Tofacitinib

- Tofacitinib, which inhibits JAK**1** and JAK**3**, was approved by the FDA for use in AS in December 2021.
- A small molecule that is a partial and reversible Inhibitor of JAK.
- By inhibiting JAK, phosphorylation then activation of signal transducers and activators of transcription (STAT) is prevented.
- Inhibition results in a decreased inflammatory response. It is indicated for active AS in adults who have had an inadequate response or intolerance to at least 1 TNF blocker.

Treatment of Uveitis

- Generally, patients respond well to topical corticosteroids, mydriatics, and artificial tears, with resolution of the attack over 2-3 months.
- Treatment occasionally requires topical NSAIDs, retrobulbar corticosteroid injections, or immunosuppressive drugs.
- TNFi may be helpful in selected cases.
- Significant reduction in the recurrence rate of anterior uveitis in patients with AS who were treated with adalimumab.
- Adalimumab is FDA approved for treatment of noninfectious uveitis, including that associated with axial SpA.



Evaluation of Disease Activity and Treatment Response

1. ***ESR*** *and the C-reactive protein (****CRP****) level, to monitor the progression of the disease and the effectiveness of treatment.*
2. ***X-RAYS*** *of the sacroiliac (SI) joints, spine, or both may be used for long-term monitoring of structural damage, particularly new bone formation. (it should not be repeated more frequently than every second year).*
3. ***MRI short tau inversion recovery (STIR)*** *of the SI joints and/or the spine may be used to assess and monitor disease activity in axial spondyloarthropathy.*

Tools to measure AS disease activity

- Bath Ankylosing Spondylitis Disease Activity Index **(BASDAI)** - A questionnaire that assesses fatigue, pain (in the neck, back, and hip), peripheral joint pain and swelling, discomfort, and severity and duration of morning stiffness

- Bath Ankylosing Spondylitis Functional Index **(BASFI)** - A questionnaire of physical function that evaluates dressing, bending, mobility, standing, stairs, and full-day activities

- Bath Ankylosing Spondylitis Metrology Index **(BASMI)** - A physical evaluation of range of motion (ROM) of the cervical and lumbar spine

- Assessment in Ankylosing Spondylitis **(ASAS**) - The ASAS core set of domains (parameters) measures disease activity and includes patient global assessment of disease activity, patient assessment of back pain, BASFI, morning stiffness, synovitis and enthesitis score, ESR, CRP level, and fatigue

ASAS20

TABLE 12.4 – ASAS20 Response Criteria	
An improvement of ≥20% and absolute improvement of ≥10 units on a 0-to-100 scale in at least three of the following four domains:	
1.	Patient global assessment (by VAS global assessment)
2.	Pain assessment (average of VAS total and nocturnal pain scores)
3.	Function (represented by BASFI)
4.	Inflammation (the average of the BASDAI's last two VAS concerning morning stiffness: intensity and duration)
AND	Absence of deterioration in the potential remaining domain (deterioration is defined as 20% worsening)

Khan MA. *Ankylosing Spondylitis*. New York, NY: Oxford University Press; 2009.

ASAS5/6

- ASAS5/6 includes the four domains included in the ASAS20 plus spinal mobility (BASMI) and acute-phase reactants (CRP).
- An ASAS5/6 response is defined as improvement of at least 20% and an improvement of at least 1 unit in at least five of six domains, with no worsening of the remaining domain.

Surgical Correction and Stabilization

- Surgical interventions for AS include the following:

- Vertebral osteotomy
- Fracture stabilization
- Joint replacement

Vertebral osteotomy

- Patients with fusion of the cervical or upper thoracic spine may have significant impairment in line of sight, eating, and psychosocial well-being.
- These patients may benefit from Extension osteotomy of the cervical spine.
- This procedure is difficult and hazardous and should be performed only by surgeons specializing in spine surgery who have experience with the operation.
- The risk of major neurologic morbidity is significant; however, if the procedure is successful, it allows the patient to return to a more functional life.

Fracture stabilization

- Many patients with advanced disease have fusion of the spine.
- If these patients report any change in position or movement of the spine, they should be assumed to have a spinal fracture because such an injury is the only way for a fused spine to move.
- Patients should be treated cautiously until fracture has been ruled out.
- If spinal fracture is present, surgical stabilization may be necessary.

Joint replacement

- Patients with significant involvement of the hips may benefit from total hip arth
- These procedures may be very useful for reducing pain and improving functio
- Heterotopic bone formation may occur after total joint replacement, especially
- Heterotopic bone formation can be reduced by giving NSAIDs (eg, indometha

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