[هذا العمل اجتهاد شخصي لا يغني عن المصدر الأساسي للمقرر]

Rheumatology		
1	Rheumatoid arthritis	
2	SLE	
3	Spondylarthritis and seronegative arthritis	
4	Systemic sclerosis	
5	Inflammatory myositis	
6	Osteoarthritis	

Rheumatoid arthritis:

1. To identify the clinical **presentation** of inflammatory arthritis including joints distribution. and detailed inflammatory features.
2. To identify the **radiographic** features for **peripheral** arthritis mainly **X-ray**.
3. To be able to investigate the patient with appropriate **laboratory request** (antibodies and inflammatory markers) and **imaging**.
4. To be able to make a **differential diagnosis** for patients with features of Rheumatoid arthritis.
5. To be able to make a **treatment plan** including (NSAIDs -DMARDs – biological therapy).
6. To know the most common **side effects** and precautions of drugs and the appropriate. monitoring for the patients.

SLE:

1. To understand the clinical **presentation** of SLE and how to **diagnose** systemic lupus erythematosus.
2. Clinical manifestations include all **systematic features** and **complications.**
3. To learn the **treatment strategies** for **each system** involved in SLE.
4. Laboratory (**serology**) findings in systemic lupus erythematous.
5. To learn the use and **side effect** of the drug used in treating lupus patient (mainly Hydroxychloroquine, Cellcept (mycophenolate), Imuran (azathioprine) and cyclophosphamide).

Spondylarthritis and seronegative arthritis:

1. To understand all diseases under spondylarthritis (**mainly axial spondylarthritis- psoriatic arthritis and reactive arthritis**).
2. Differentiate between **inflammatory** back pain from **mechanical** back pain.
3. Know all **extra-articular manifestations** of spondylarthritis.
4. Learn **radiographic features** (mainly x-ray of spine and sacroiliac joints and the importance of MRI).
5. To establish a logical **differential diagnosis** for spondylarthritis.
6. Understand **laboratory findings** and **genetic screen** (mainly HLA-B27).

7. Understand the **treatment strategies** for axial and peripheral Spondylarthritis.
8. To be able to differentiate between **gout and pseudogout.**

Systemic sclerosis:
1. Identify patients presenting with **symptoms and signs** of systemic sclerosis.
2. Understand the **systemic involvement** of systemic sclerosis.
3. Understand the **key points** in the **management** mainly in **musculoskeletal** and **renal** involvement.

Inflammatory myositis:
1. Recall the **clinical manifestation** and symptoms of inflammatory myositis mainly **dermatomyositis** and **polymyositis**.
2. To be able to identify **systemic involvement**.
3. To list the **diagnostic modalities** to establish the diagnosis and management.

OA??

RA (Rheumatoid Arthritis)[1]

Inflammatory autoimmune disorder characterized by joint pain, swelling, and synovial destruction.
Etiology: chronic inflammatory autoimmune disorder of unknown etiology. Genetic disposition (HLA-DR4/DR1).

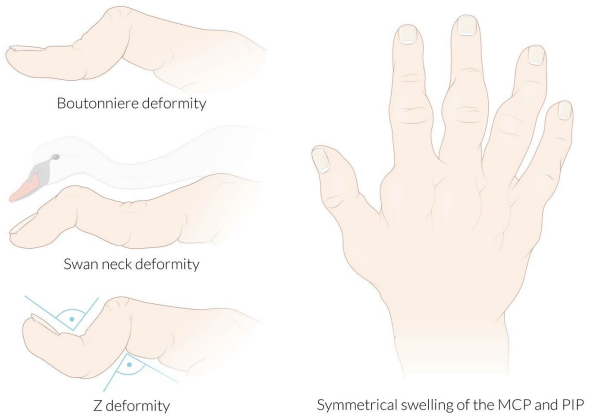
Clinical features

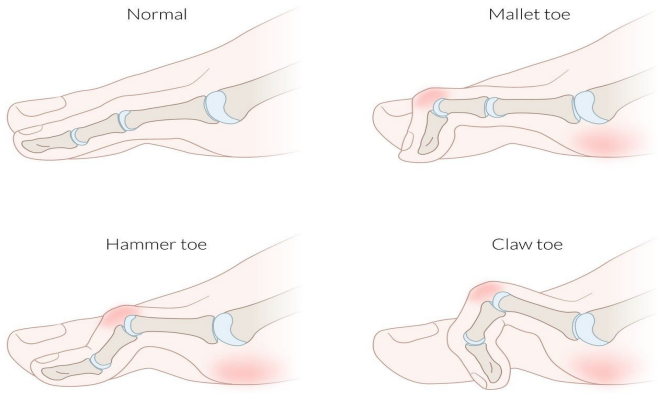
A. Articular:

1. Polyarthralgia: Symmetrical pain and swelling of affected joints (also at rest). Redness is uncommon. Frequently affected joints (MCP, PIP, wrist, knee. Joints of the axial skeleton are usually spared except for the cervical spine).
2. Morning stiffness > 30 min; often improves with activity.
3. Joint deformities:
   - **Rheumatoid hand** is characteristic, and can include the following deformities:
     - Deepening of the interosseous spaces of the dorsum of hand (↓ function and inactivity → atrophy → interosseous muscle wasting).
     - **Boutonniere**: PIP flexion & DIP hyperextension.
     - **Swan neck**: PIP hyperextension & DIP flexion. [2]
     - Ulnar deviation of the fingers.
     - Hitchhiker thumb deformity (**Z deformity** of the thumb): hyperextension of the interphalangeal joint with fixed flexion of the MCP joint.
   - Hammer toe, Atlanto-axial subluxation.

B. Extra-articular

- **Skin**: Rheumatoid nodules (common); non-tender, firm, subcutaneous swellings (2 mm–5 cm).
- **Lungs**: fibrosis, nodules, pleuritis, pleural effusions.
- **Eye**: keratoconjunctivitis sicca,[3] scleritis, episcleritis.
- **Heart**: pericarditis and myocarditis; higher risk of MI, stroke, and CHF.
- **Constitutional**: low fever, myalgia, malaise, night sweats.
- **Hematological**: anemia of chronic disease.
- **Other MSK**: Tenosynovitis and bursitis, Tarsal tunnel/ Carpal tunnel syndrome (entrapment neuropathy)[4].
- **Endocrine/Exocrine**: 2ry Sjögren syndrome.
- **Vascular**: peripheral vasculitis manifesting as livedo reticularis, Raynaud phenomenon, purpura, necrosing fingertips or peripheral neuropathy.





[1] **Pathophysiology:** Initially, non-specific inflammation affects the synovial tissue, which is later amplified by activation of T cells (autoimmune response) → with time, inflammatory joint effusion and synovial hypertrophy, as well as progressive destruction and deterioration of cartilage and bone: (1) Synovial lining hyperplasia. (2) Pannus formation along the synovial tissue → produce proteases → destroy cartilage extracellular matrix.
[2] Typically caused by contraction of the flexor tendon or tight surgical repair following tendon rupture; requires splinting or surgery
[3] "Dry eye disease" A condition caused by inadequate tear production and/or excessive evaporation of tears. Manifestations include conjunctivitis, dry eyes, blurred vision, and entropion or ectropion.
[4] Typical nocturnal paresthesia of volar hand & fingers I–III. Atrophy of thenar muscles → difficulty making a fist; inability to oppose thumb.

ACR criteria for RA (2010)
RA= score of **≥ 6 points** + confirmed presence of synovitis in at least one typical joint without an alternative, more probable diagnosis (e.g., trauma or degenerative joint conditions).

Points	**Joint** involvement (pain/swelling)	**Serology**	Acute phase **reactants**	**Duration** of symptoms*
0	≤ 1 large joints**	Negative RF and ACPA	Normal CRP & ESR	< 6 w
1	**2–10 large** joints		↑ **CRP** or **ESR**	**≥** 6 w
2	**1–3 small** joints	Low positive **RF** or **ACPA**		
3	**4–10 small** joints	High positive **RF** or **ACPA** (**> 3** times higher than normal)		
5	**> 10** (at least 1small)			
Key	*In the most chronically affected joint. **Large= shoulders, elbows, hips, knees, and ankles. Small= MCP and PIP; MTP, thumb interphalangeal joints, and wrists. The 1st CMC, 1st MTP, and DIP of hand and feet are not included here.			

Laboratory tests

A. **Non-specific** parameters: ↑ Inflammatory markers,[5] Anemia of chronic disease.
B. **Serology** (specific parameters): ACPA (anti-CCP) Specificity > 90%[6], Rheumatoid factor (RF) → IgM autoantibodies, Low specificity, Antinuclear antibodies (ANA) → not specific but imp to exclude DDx "SLE".
C. **Synovial fluid analysis** (joint aspiration), findings: Cloudy yellow, Sterile specimen with leukocytosis (WBC: 5,000–50,000/μL), ↑ Neutrophils, granulocytes, and ragocytes, ↑ Proteins, ↓ viscosity, Possibly RF.

Imaging [7] [8]

A. Conventional **x-ray** (Dorso-palmar of both hands), findings: Early → soft tissue swelling, demineralization (juxta-articular). Late → joint space narrowing, erosions of cartilage and bone, demineralization (generalized).
B. **MRI**: (+/- contrast), especially if c-spine involvement is suspected or in early stages.
C. **US**: joint effusion, formation of pannus.
D. Further diagnostic measures: contrast-enhanced US, scintigraphy.

[5] CRP, ESR correlate with inflammatory activity. ↑ Ferritin as an acute phase protein. Possibly leukocytosis, thrombocytosis.
[6] ACPA = Anti-citrullinated peptide antibodies - Anti-CCP = Anti-cyclic citrullinated peptide.
[7] Radiographic changes are typical for RA. But even in aggressive cases, it takes 6–24 months until erosions are radiologically evident. As a result, classification criteria for diagnosing early RA no longer include radiological joint findings. I.e., Even if radiographic findings are normal, RA is still possible!
[8] Before undergoing general anesthesia, airway and neck assessment is crucial in patients with rheumatoid arthritis. Atlanto-axial subluxation may be present, which increases the risk for spinal cord injury. Preoperative flexion-extension radiographs can help to evaluate the position of the cervical vertebra atlas (C1) with regard to the axis (C2).

Treatment

General measures: PT and OT, Physical activity, for acute episodes of inflammation → cryotherapy.

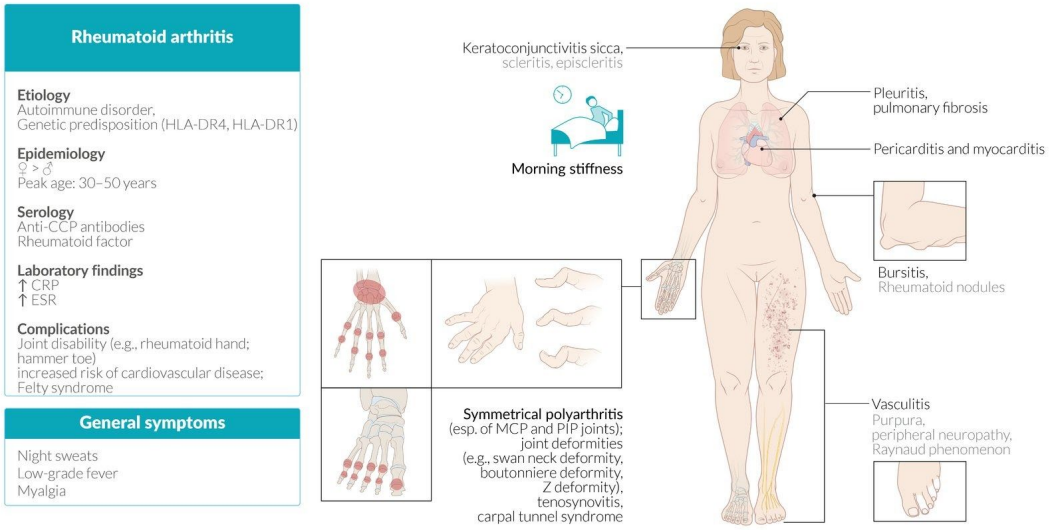
A. Acute anti-inflammatory therapy (Indication → acute attack)

1. **Glucocorticoids**: given until DMARDs onset of action or as long-term therapy for highly active RA. Intra-articular for rapid relief, and systemic[9].
2. **NSAIDs** and **COX-2 inhibitors**: symptomatic relief w/o improving prognosis.[10]

B. Long-term anti-inflammatory therapy with disease-modifying antirheumatic drugs (**DMARDs**)

- Induce immunosuppression, leading to potential remission of RA.
- Reduce mortality/morbidity by up to 30% (slow progression, preserve joint function, limit complications).
- Slow onset (≥ 6 weeks), so symptomatic treatment with glucocorticoids and NSAIDs is often required.

1. **Non-biologic agents**
   - Drug of choice: methotrexate (**MTX**) → First-line for moderate to severe RA (given once a week).[11]
     - SE: GI (stomatitis, nausea, diarrhea, bleeding), rash, hepatotoxicity (abnormal liver chemistry), interstitial pneumonitis and pulmonary fibrosis, bone marrow suppression , nephrotoxicity, increased risk of lymphoproliferative disorders, teratogenicity, alopecia (to minimize side effects, folic acid 24–48 hours after taking MTX).
   - Alternative drugs: Leflunomide, Hydroxychloroquine, Sulfasalazine (for use in pregnancy).
2. **Biologic therapy**
   - Indication: moderate or severe disease activity remaining after 3 months of DMARD therapy.
   - Should be combined with non-biologic DMARDs (MTX, sulfasalazine).
   - TNF α inhibitors: e.g., adalimumab, infliximab, etanercept.
   - Others: rituximab (anti-CD20), anakinra (interleukin-1 receptor antagonist, particularly for Still disease).



[9] Osteoporosis prophylaxis (optimization of sufficient calcium and vitamin D intake) is necessary if a daily dose of prednisolone or its equivalent > 7.5 mg over a period > 3 months. Systemic, Intra-articular injections of PRN (rapid relief).
[10] PPIs are recommended because combining glucocorticoids with NSAIDs substantially increases the risk of GI ulcers.
[11] Benefits: highly effective, relatively well-tolerated, low cost, possibly life-prolonging. Do not give NSAIDs on the same day as MTX, as they can worsen the side effects of MTX by inhibiting its renal excretion.

Condition	**OA** (most common)	**RA**	**Psoriatic arthritis**	**Gout**	**Pseudogout**
Specific groups	May be asymptomatic (majority will have radiological changes).	FHx	Hx/FHx of psoriasis. May be triggered by trauma or infections.	FHx, Often in alcoholics.	Mostly older pts (> 50).
Course	**Chronic**, progressive	**Chronic** w/ varied patterns: monocyclic, polycyclic,progressive.	**Chronic**, progressive	**Chronic** with acute attacks (rapid onset of symptoms)	
Clinical features	**No** constitutional Sx. Morning stiffness **<** 30 minutes. Pain/stiffness **worsens** with increased activity and relieved by rest. **Non-inflammatory**.	Constitutional Sx. Morning stiffness **>** 30 minutes. Pain/stiffness can be **relieved** by activity. Articular **inflammation** (swollen, warm).	Psoriatic skin **lesions** and nail changes. **Dactylitis** with "sausage digits". **Enthesitis**.	Articular **inflammation** (swollen, erythematous, warm). Eventually **tophi**.	Articular **inflammation** (swollen, erythematous, warm joints).
Symmetry	Usually **asymmetrical**	**Symmetrical**		**Asymmetrical**	
Pattern of disease	**Poly**arthritis: Predominantly weight-bearing joints(knee). Spares the wrist & MCPJ.	**Poly**arthritis: predominantly wrists, MCP and PIP.	**Poly**arthritis or **oligo**arthritis: Commonly DIPJ and/or spinal involvement. Sometimes large.	Usually **mono**arthritis: typically include the big toe (MTPJ), knee and thumb (MCPJ).	**Mono**arthritis (rarely oligoarthritis): commonly knees and wrist joints.

IM (Inflammatory Myopathies)

Chronic inflammation of skeletal muscles → progressive weakness → systemic muscle wasting diseases. IMs are classified according to clinicopathological features and include polymyositis (PM), dermatomyositis (DM), and inclusion-body myositis (IBM).

PM: inflammatory myopathy affecting the **P**roximal skeletal muscles.
DM: inflammatory myopathy that presents similarly to PM, with the addition of **skin** involvement.

Clinical features

A. General features (both PM and DM): Proximal muscle weakness and tenderness affecting both sides of the body (progresses within weeks to months).[12]

B. Cutaneous manifestations (DM):

1. Gottron papules: Prominent erythematous papules, symmetrically distributed on the extensor surface of the hands. Most often affects the MCP and interphalangeal joints.
2. Heliotrope rash: erythematous rash on the upper eyelids, sometimes accompanied by edema.
3. Midfacial erythema (affects the nasolabial folds “in contrast to SLE’s malar rash”).
4. Photosensitive poikiloderma:[13]
    a. Shawl sign: erythema of the upper back, posterior neck, and shoulders.
    b. V sign: erythema of the upper chest and neck.
    c. Holster sign: erythema of the lateral thighs.
5. Juvenile DM: Subcutaneous calcification (dystrophic calcinosis), AbdP, hematemesis, melena, lipodystrophy.

Diagnostic criteria

Diagnosis of PM and DM is based on clinical presentation, laboratory results, and pathology findings.

- PM is diagnosed if the following criteria are fulfilled:
    1. **Symmetric proximal muscle** weakness.
    2. Positive **laboratory** findings.
    3. **EMG** → suggestive of inflammatory myopathy.
    4. Typical **biopsy** findings.
    ★ DM is diagnosed if additional **cutaneous** manifestations are present.
- If **≥ 2** of the criteria are fulfilled, PM or DM is considered a possible diagnosis.

[12] Pelvic and shoulder girdle muscles r most commonly affected. Other muscles (neck flexors), may also be affected → Leads to difficulties combing hair, standing up, and climbing stairs. Dysphagia in approx. 30% because of esophageal muscle involvement.
[13] Hyperpigmentation or hypopigmentation, telangiectasia, and epidermal atrophy in areas exposed to the sun.

Labs:

- ↑ Muscle enzymes: ↑ **CK** and ↑ aldolase. Additional elevated enzymes (myoglobin, LDH, AST, ALT).
- Inflammatory markers: ↑ ESR, ↑ CRP, leukocytosis, γ-globulin in protein electrophoresis
- Antibodies: ANA, Myositis-specific antibodies (MSAs)[14].

Other procedures

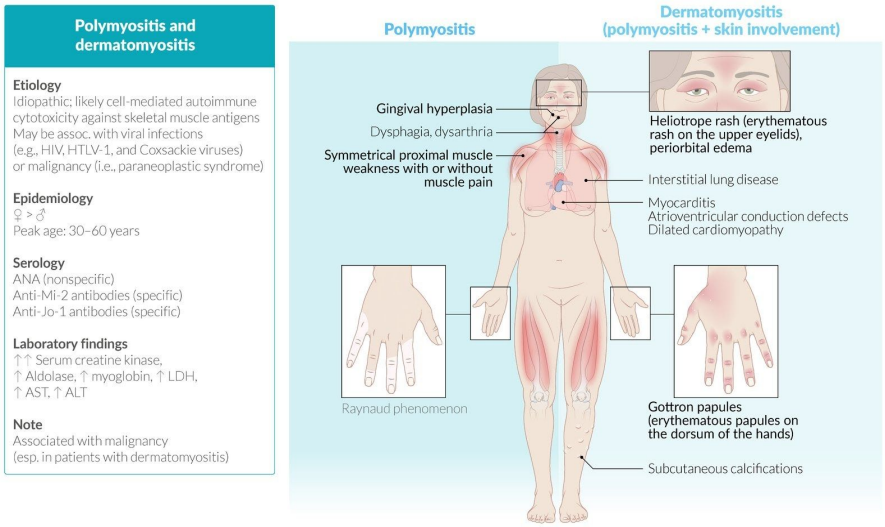
- Electromyography (**EMG**): abnormal in 90%, shows short-duration, low-amplitude units.
- Imaging: An MRI may be helpful in identifying inflammation and a potential biopsy site, although it is not always recommended.
- Muscle **biopsy** (muscle fiber necrosis, degeneration, and regeneration).[15]
- Skin biopsy (for suspected DM).

All patients diagnosed with DM should be tested for possible malignancies!

Rx:

- Drug of choice: corticosteroids (e.g., prednisolone).
- Alternative treatment:
  - indicated in patients who do not tolerate or do not respond to corticosteroids.
  - Immunosuppressants (e.g., methotrexate and cyclosporin), IVIG, plasmapheresis.

Complications: respiratory failure[16], Myocarditis, Esophageal disease[17], Dystrophic calcinosis (common in juvenile DM. Calcium deposits may be subcutaneous, intracutaneous, or intramuscular).



[14] **Anti-Jo-1 antibodies** (~ 5% DM, 30% PM): especially in patients with interstitial lung disease; responds poorly to treatment. Anti-Mi-2 antibodies (~ 10% of cases): more favorable prognosis. Anti-signal recognition particle antibodies (anti-SRP): associated with a severe treatment-resistant necrotizing myopathy; typically in patients with PM.

[15] **PM**: **Cell-mediated** inflammatory infiltrates that predominantly involve cytotoxic CD8+ T cells in the intrafascicular (within muscle fascicles) and endomysial (within the endothelial cell wall of endomysial capillaries) region. Immunohistochemistry → Overexpression of MHC-I on the sarcolemma. **DM**: **Antibody-mediated** inflammatory infiltrates that predominantly involve CD4+ T cells, plasmacytoid dendritic cells, and B lymphocytes in the perifascicular and perimysial region that lead to perifascicular atrophy.

[16] Due to respiratory muscle weakness; interstitial lung disease is an important complication, which arises from respiratory failure causing pneumonia.

[17] Weakness of the striated musculature in the upper ⅓ of the esophagus that often occurs in older pts and may lead to aspiration pneumonia.

SSc (Systemic Sclerosis)

Abnormal growth of connective tissue → leads to diffuse thickening and hardening of the skin and often the inner organs (a chronic disease).

Clinical features

A. Common symptoms

1. **Cutaneous findings**
   - Thickening and hardening of the skin (skin appears smooth and shiny).
   - Depigmentation of the skin with sparing of perifollicular pigmentation (salt-and-pepper appearance).
   - Sclerodactyly.[18] Multiple, painful ischemic digital ulcers.
   - Face: Loss of expression (mask-like facies), Shortened frenulum, Microstomia accompanied with characteristic perioral wrinkles.
2. **Vascular disease**: Raynaud's phenomenon, Thromboembolism.
3. Fatigue, weakness, Joint stiffness/pain.

B. Limited cutaneous systemic sclerosis

- In 90% of cases, Raynaud's phenomenon precedes the onset of other symptoms.
- Skin manifestations are usually restricted to the hands, fingers, and face.
- Extracutaneous organ involvement may occur.
- Often manifests as CREST syndrome:
  - **C** → Calcinosis cutis (small white calcium deposits on the pressure points of the extremities such as the elbows, knees, and fingertips).
  - **R** → Raynaud's phenomenon.
  - **E** → Esophageal hypomotility (esophageal dysmotility, gastroesophageal reflux, heartburn, dysphagia, which is caused by smooth muscle atrophy and fibrosis).
  - **S** → Sclerodactyly.
  - **T** → Telangiectasia.

C. Diffuse cutaneous systemic sclerosis

- Raynaud's phenomenon often coincides with or follows the onset of other symptoms.
- Skin manifestations typically spread proximally from the trunk to the elbow.
- Extracutaneous organ manifestations are common:
  - Arthralgia and myalgia → can result in contractures.
  - GI: Esophageal dysmotility → dysphagia and reflux, Small bowel dysmotility → bloating, gas, constipation, and cramping.
  - Pulmonary disease: PHTN and interstitial lung disease, increased risk of lung cancer.
  - Cardiac disease: fibrosis, myocarditis, pericarditis.
  - Renal disease: abnormal collagen deposition → thickening of renal arteriolar walls → decreased renal blood flow → reduced kidney function.[19]

[18] Red-blue discoloration of the fingers. Edema and fibrosis with waxy appearance of the skin and limited ROM. Atrophy and necrotic spots. Lesions on the proximal nail fold.

[19] Scleroderma renal crisis: Life-threatening complication with, e.g.: Oliguric renal failure, (Malignant) HTN, Encephalopathy, Microangiopathic hemolytic anemia. Occurs in 10–15% of diffuse SSc cases.

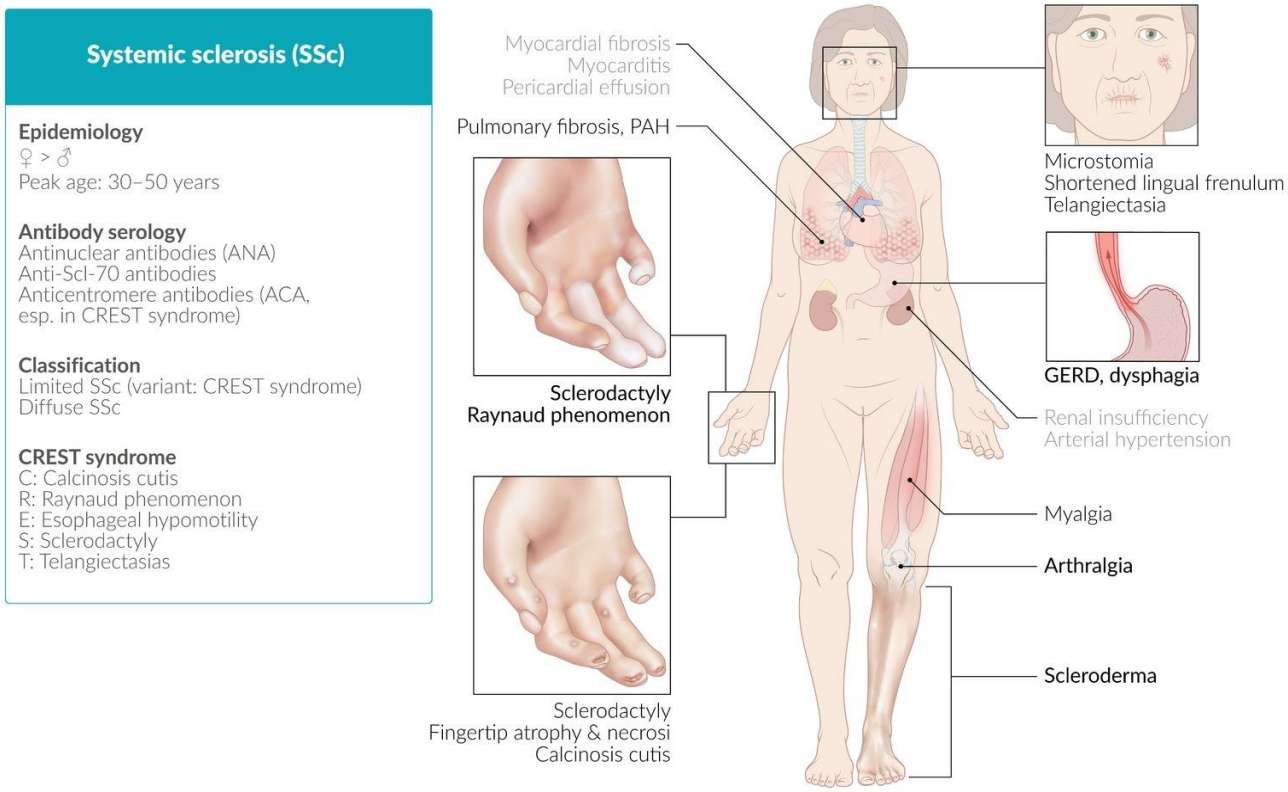
Dx:

- Auto-antibodies: ANA present in about 90% of cases.
  - Limited SSc: anticentromere antibodies (ACA)
  - Diffuse SSc: Anti-Scl-70 (anti-topoisomerase I antibody), Anti-RNA polymerase III.
- Serum protein electrophoresis (↑ γ-globulins), CBC w/ diff., CXR (detects possible pulmonary involvement).
- Other tests may be indicated based on organ-specific symptoms (e.g., signs of renal crisis).

Rx:

Treatment focuses on organ-specific, symptomatic therapy. In the case of diffuse cutaneous disease or severe organ involvement, immunosuppressive therapy is indicated.

- General measures: PT, Massage, Prevent dry skin (warm oil and paraffin baths, avoid soap), Phototherapy.
- Immunosuppressive therapy: e.g., methotrexate.
- Organ-specific therapy: e.g., PPIs in cases of GERD.



OA (Osteoarthritis)

A disabling joint disease characterized by a **noninflammatory degeneration** of the joint complex (articular cartilage, subchondral bone, and synovium) that occurs with old age or from overuse.[20]

Risk factors:
A. Modifiable: Obesity, excessive joint loading or overuse.
B. Nonmodifiable:
   a. Age (> 55), FHx, Hx of joint injury or trauma, gender (female).
   b. Anatomic factors causing asymmetrical joint stress (DDH → hip OA, genu varus/valgus → knee OA).
   c. Hemophilic hemarthroses and deposition diseases that stiffen cartilage.

Pathophysiology: Joint damage/stress → cartilage damage → ↓ proteoglycans → cartilage becomes friable, inelastic and starts to degrade → loss of joint space and bony surface → subchondral bone becomes thickened and sclerotic.

Clinical features
1. **Early**:
   a. Pain (on exertion, relieved with rest, in both complete flexion and extension).
   b. Crepitus on joint movement. Joint stiffness and restricted ROM.
   c. Radiating or referred pain (e.g., coxarthrosis may lead to knee pain).
2. Late: Constant pain (including at night) + Morning stiffness usually lasting < 30m, ROM is more severely restricted.
3. Hip[21] and knee[22] OA.
4. **Heberden's** nodes: Pain and nodular thickening on the dorsal sides of the DIP. In contrast to OA, RA doesn't affect DIP.
5. **Bouchard's** nodes: Pain and nodular thickening on the dorsal sides of the PIP.

Dx (Based on clinical and radiographic evidence of joint degeneration)**:** Radiological signs (**LOSS**) → **Loss** of joint space (Irregular narrowing), **Osteophytes** (also: bone spurs)[23], **Subchondral** sclerosis[24], **Subchondral** cysts[25].

Rx:
A. General: Weight loss, regular exercise, shoe inserts (e.g., buffer insoles) in, e.g., valgus deformity of the knee. targeted muscle growth, PT, and medical training therapy. Topical and heat therapy.
B. Pharmacotherapy: Peripheral analgesics (Acetaminophen, NSAIDs "ibuprofen"), opioid analgesics (tramadol).
C. Interventional therapy: In severe courses → intraarticular glucocorticoid injections (not a long-term treatment!).
D. Surgical therapy: if conservative and interventional measures fail.

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[20] It mainly affects the weight-bearing and high-use joints, such as the hip, knee, hands, and vertebrae. Despite the widespread view that OA is a condition caused exclusively by degenerative "wear and tear" of the joints, newer research indicates a significant heterogeneity of causation, including pre-existing peculiarities of joint anatomy, genetics, local inflammation, mechanical forces, and biochemical processes that are affected by proinflammatory mediators and proteases.
[21] **Pain** in the groin area and above the greater trochanter (+tenderness), **Increased contracture** in the flexor, external rotation, and adduction position → antalgic gait. **limited and painful internal rotation**. **Positive Thomas test** (for hip flexion contracture, in supine position): examiner passively flexes the hip joint opposite to the affected side to a maximum to compensate lumbar lordosis. Positive test → If flexion contracture is present, the ipsilateral leg will simultaneously flex independently as a reflex.
[22] Function-limiting knee **pain** (worse on walking distances), **swelling** which increases on activity, mechanical **instability**, **locking**, **catching** sensation. In case of patello-femoral OA: positive Patellar grind test (pain on movement of the patella) → The patient is asked to lie down in the supine position. The examiner pushes the patella distally with both thumbs and stabilizes it. The patient is asked to contract the quadriceps muscle. Pain indicates retropatellar OA (positive test).
[23] Bony projections that develop on joint surfaces as spurs or densifications. develop on the edges and thereby increase the joint surface.
[24] Dense area of bone (visible on x-ray) just below the cartilage, formed due to a compressive load on the joint.
[25] Fluid-filled cysts that develop at the surface of a joint due to local bone necrosis induced by the joint stress of osteoarthritis.

SLE (Systemic Lupus Erythematosus)

★ An autoimmune disorder leading to inflammation and tissue damage in multiple organs. Etiology is unknown.
Clinical features "typically characterized by phases of remission and relapse. It can affect any organ"

A. Most common:

1. Skin (> 70% of cases): **Malar rash** (butterfly rash) with sparing of the nasolabial folds, **Photosensitivity**, **Discoid** rash[26], Oral **ulcers**, Alopecia (nonscarring), Periungual telangiectasia.
2. Joints: **Arthritis** and **arthralgia** (> 90% of cases), Mostly nonerosive polyarthritis (normal x-ray).
3. **Fever** (> 50%), **fatigue** (> 80%), **weight loss**.

B. Other S&Sx: **MSK** (myalgia and lymphadenopathy), **Serositis** (pleuritis and pericarditis; effusions and chest pain may occur), **Kidney** (nephritis with proteinuria "lupus nephritis"), **Heart** (involvement of the myocardium, pericardium, valves, and coronary arteries; Libman-Sacks endocarditis "LSE"), **Lungs** (pneumonitis, interstitial lung disease, PHTN), **GI** (esophagitis, hepatitis, pancreatitis), **Vascular** (Raynaud phenomenon, vasculitis, thromboembolism), **Neurologic** (e.g., seizures, psychosis, personality changes, aseptic meningitis, polyneuropathy, MG), **Hematologic** (hemolytic anemia, thrombocytopenia, leukopenia), **Eyes** (keratoconjunctivitis sicca).

Diagnostics[27] - Approach:

A. **Suspect** SLE if **symptoms** in more than two of the organ systems listed in the ACR criteria for SLE (below).

B. **Screening** test: **ANA** titer (SLE is unlikely if the test is negative)

C. ↑ ANA titer → **confirm** diagnosis with tests that are highly specific for SLE:

a. Anti-dsDNA antibody testing: autoantibody against double-stranded DNA (dsDNA).[28]
b. Anti-Sm antibody testing → Autoantibody against Smith antigens (nonhistone nuclear proteins).

D. Other laboratory tests below may support the diagnosis:

a. CBC w/ diff: autoimmune hemolytic anemia, thrombocytopenia, leukopenia, lymphopenia.
b. ESR is frequently elevated, while CRP is often normal (if high, infection should be r/o).
c. ↓ C3 and C4 complement levels.
d. Urinalysis and urine microscopy: proteinuria and/or casts.
e. Additional antibody tests.[29]

[26] Erythematous raised patches with adherent keratotic scaling and follicular plugging.
[27] ANA testing has the highest sensitivity (95%) but low specificity. Anti-dsDNA & anti-Sm antibodies testing are the most specific.
[28] Positive in 70% of patients and highly specific. Levels correlate with disease activity. Associated with lupus nephritis.
[29] Antiphospholipid antibodies may be elevated. Anti-histone antibodies are elevated in drug-induced lupus erythematosus. Anti-Ro antibodies are elevated in the majority of cases of neonatal lupus erythematosus.

	ACR **diagnostic criteria** for **SLE** ★ Requirements: at least **4 of the 11** criteria must be met (specificity: 95%, sensitivity: 85%).
Dermatological	1. **Malar rash** (butterfly rash): flat or raised fixed erythema over both malar eminences; tends to spare nasolabial folds. 2. **Discoid rash**: erythematous raised patches w/ adherent keratotic scaling & follicular plugging. 3. **Photosensitivity**: due to an overly sensitive reaction to light. 4. Oral or nasopharyngeal **ulcers**: usually painless.
Internal organs	1. **Nonerosive arthritis**: involves at least two peripheral joints with swelling, tenderness, or effusion; rarely deforming (normal x-ray). often among the first manifestations. 2. **Serositis**: evidence of pleuritis and/or pericarditis.[30] 3. **Renal** disorder: Persistent proteinuria (> 0.5 g/day) OR Cellular casts (red cells, hemoglobin, granular, tubular, or mixed). 4. **Neurologic** disorder: Seizures OR psychosis; both in the absence of offending drugs or known metabolic derangements.
Laboratory tests	1. **Hematologic** disorders.[31] 2. **Immunological** findings.[32] 3. **ANA**: on immunofluorescence or an equivalent assay in the absence of medications associated with drug-induced lupus.

"**SOAP BRAIN MD**"

S = **S**erositis, **O** = **O**ral ulcers, **A** = **A**rthritis, **P** = **P**hotosensitivity, **B** = **B**lood disorders, **R** = **R**enal involvement, **A** = **A**ntinuclear antibody, **I** = **I**mmunologic phenomena, **N** = **N**eurologic disorder, **M** = **M**alar rash, **D** = **D**iscoid rash.

[30] **Pleuritis** → Hx of pleuritic chest pain, pleuritic rub during auscultation, or pleural effusion,
Pericarditis → evidence on ECG (e.g., diffuse ST elevations), a pericardial rub during auscultation, and/or pericardial effusion.
[31] **Autoimmune hemolytic anemia** with reticulocytes OR **Thrombocytopenia** < 100,000/mm3 in the absence of offending drugs OR **Leukopenia** < 4,000/mm3 on ≥ 2 occasions OR **Lymphopenia** < 1,500/mm3 on ≥ 2 occasions.
[32] Positive findings of **Anti-dsDNA** antibodies OR **Anti-Sm antibodies** OR **Antiphospholipid antibodies** on an abnormal serum level of IgG/IgM anticardiolipin antibodies.

Further diagnostics

- Lupus band test (LBT): direct immunofluorescence staining of immunoglobulin and complement component deposits (IgG, IgM, IgA und C3); found along the dermoepidermal junction in affected as well as unaffected skin.
- Kidney biopsy: if lupus nephritis is suspected(proteinuria, red blood cell casts, or acanthocytes in urinary sediment).
- Imaging: assessment of organ or joint involvement (e.g., x-ray for joint symptoms, US to evaluate renal complications).

Treatment "There is no cure; treat to control symptoms"

A. **General management**: Avoid exposure to UV light (sunlight → exacerbate cutaneous rashes), Smoking cessation (reduce risk of atherosclerotic vascular disease), Immunize patients before initiating immunosuppressants.

B. **Medical therapy**:
   a. **NSAIDs** are used to treat arthritis and pleurisy (naproxen).
   b. **Corticosteroid** creams are used to treat skin rash; antimalarial drugs (hydroxychloroquine) and oral corticosteroids may also be used for skin and arthritic symptoms.
   c. **Cytotoxic drugs** (azathioprine, cyclophosphamide) are used for **severe** symptoms (lupus nephritis, heart and lung involvement, hemolytic anemia, CNS involvement), along with corticosteroids.
   d. Mycophenolate is often used to treat lupus nephritis.

<table>
<tr><th></th><th>Mild Sx, no vital organs affected</th><th>Severe symptoms, no vital organs affected</th><th>Organ damage</th></tr>
<tr><td>Basic therapy</td><td colspan="3">Hydroxychloroquine (or chloroquine)[33]</td></tr>
<tr><td rowspan="2">Induction therapy[34]</td><td rowspan="2">Low-dose , short-term, oral glucocorticoids (prednisolone).</td><td>Medium-dose oral glucocorticoids</td><td>High-dose IV glucocorticoids</td></tr>
<tr><td colspan="2">Immunosuppressive agents (azathioprine[35], mycophenolate[36], cyclophosphamide[37])</td></tr>
</table>

[33] Visual disturbances: in cases of long-term use, regular ophthalmological exams are recommended → **Irreversible retinopathy** (key fundoscopic feature is Bull's eye maculopathy), Reversible corneal opacity, Blurred vision, Photophobia. GI (nausea with cramps "most common", anorexia, vomiting), Neurologic (sensorineural deafness, tinnitus, cranial nerve palsies, and myasthenia-like muscle weakness), Dermatologic (photosensitivity, pruritus, alopecia, bleaching of hair).
[34] Administered until remission is achieved. Combination with other immunosuppressive agents allows reduction of the glucocorticoid dose.
[35] SE: **Pancytopenia** (leukopenia, macrocytic anemia, thrombocytopenia), Acute pancreatitis, Hepatotoxicity, N/V, and dose-related diarrhea, Malignancies (e.g., cervical cancer, lymphoma, squamous cell carcinoma, melanoma "rare").
[36] SE: **Pancytopenia**, Infection (e.g., respiratory or urinary tract), Vomiting and diarrhea, Peripheral edema, Hyperglycemia, ↑ BUN, Hypercholesterolemia, HTN, Back pain, Cough.
[37] SE: include myelosuppression, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and hemorrhagic cystitis (risk reduced with prophylactic administration of mesna and aggressive hydration).

Complications

Lupus nephritis (LN)

Description: Most crucial prognostic factor in SLE, can be nephritic and/or nephrotic.

Pathophysiology: mesangial and/or subendothelial deposition of immune complexes (e.g., anti-dsDNA antibodies, anti-Sm antibodies) → expansion and thickening of mesangium, capillary walls and/or GBM.

Diagnosis

1. Urine tests: proteinuria, hematuria, cellular casts (red cells, hemoglobin, granular or tubular)
2. Kidney biopsy: determination of severity of disease:
    a. Classically, immune complex-mediated glomerulonephritis
    b. Diffuse proliferative glomerulonephritis (DPGN): characterized by increased glomerular cellularity in more than 50% of the glomeruli.
        i. Electron microscopy typically shows subendothelial deposits leading to capillary ("wire loop") thickening.
        ii. Most commonly seen in SLE and IgA nephropathy, but also other inflammatory, autoimmune, or infectious diseases

Rx: Depending on the severity of the disease, prednisone, cytostatic drugs (mycophenolate, cyclophosphamide), and general measures to protect the kidneys (e.g., blood pressure control) may be necessary.

Comorbid conditions: Accelerated atherosclerosis and cardiovascular complications (MI), PHTN, Pancytopenia (peripheral destruction of all cell line), Osteopenia/osteoporosis (prolonged use of glucocorticoids), Antiphospholipid syndrome[38], ↑ Risk of thrombosis (particularly in individuals with antiphospholipid syndrome) → avoid treatment with estrogens.

[38] Antiphospholipid antibody syndrome (lupus anticoagulant or anticardiolipin antibodies) is a hypercoagulable state associated with a group of antibodies that are directed against phospholipids or cardiolipins. It is unclear whether the antibodies are directly involved in the etiology of the clotting disorder associated with this syndrome. The nature of these antibodies causes the common lab abnormalities associated with the syndrome, i.e., elevated PTT and false-positive RPR or VDRL. Clinically, it presents with spontaneous abortions in otherwise healthy women or thromboembolism (PE, DVT) in other patients. Two first-trimester spontaneous abortions suggest antiphospholipid antibodies.

Seronegative spondyloarthropathies[39]

★ Include several chronic inflammatory arthritic diseases that affect the vertebral column. The most important diseases in this group are ankylosing spondylitis, reactive arthritis, and psoriatic arthritis.

Common features of seronegative spondyloarthropathies:

- Negative for rheumatoid factor (RF). Genetic association with HLA-B27. FHx is important.

> 🧠: Conditions commonly associated with HLA-B27 are **A-PAIR**: **A**nkylosing spondylitis, **P**soriasis, **A**cute anterior uveitis, **I**nflammatory bowel disease, **R**eactive arthritis.

- Generally more commonly affects men. Age of onset → typically between 20–40 years of age.
- Non-specific symptoms (fever, fatigue, weight loss).
- **Arthritis**:
  - Insidious, often unilateral onset. Particularly of the sacroiliac joints (especially for ankylosing spondylitis).
  - Asymmetrical peripheral oligoarthritis.
  - Stiffness and pain is worse in the morning (typically > 30 minutes) and improves with movement.
  - Often involves inflammatory enthesopathy[40] (e.g., achillodynia). Usually responds well to NSAID therapy.
- Extra-articular Sx: vary according to type, but involvement of the eye is common (iritis, iridocyclitis, uveitis).

Psoriatic arthritis

inflammation of joints (primarily on hands, feet, spine) that may occur with psoriasis.

Clinical features:

- Psoriasis and psoriatic arthritis may occur independently or together (usually psoriasis precedes). There are several types of psoriatic arthritis.[41]
- Other rheumatological features: Enthesitis, Tenosynovitis, Dactylitis (inflammation and swelling of fingers or toes “sausage digit”, to the entire digit not only the joins as in synovitis), Arthritis mutilans[42].

Diagnosis “no specific test, it’s a clinical Dx“:

- Recognition of **inflammatory joint symptoms** (prolonged morning stiffness >30 minutes, improvement with use, and recurrence with prolonged rest) is the essential first step. In a patient with **psoriasis**, morning first-step foot pain, and **joint** or **digit swelling** strongly suggest psoriatic arthritis.
- Hx/FHx (1st/2nd degree) of psoriasis, or Sx suggestive of psoriasis psoriasis (scalp/nail problems).
- Peripheral arthritis (swelling and tenderness of individual joints), monoarticular or oligoarticular pattern.
- X-ray: joint destruction, ankylosis. Fingers → pencil-in-cup deformity (advanced disease) - Spine → syndesmophytes, and in particular asymmetric paravertebral ossification.[43]
- ESR/CRP (high), RF (-ve).

Rx: Mild disease (NSAIDs), moderate-severe (DMARDs), PT.

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[39] Spondyloarthritis (aka spondyloarthropathy ”SpA”): A family of disorders including axial spondyloarthritis (ankylosing spondylitis (AS) and non radiographic axial spondyloarthritis (nr-axSpA)), and reactive arthritis and forms of arthritis associated with psoriasis and with IBD, and other conditions. SpA with predominantly axial involvement is designated as "axial spondyloarthritis" (axSpA), which comprises AS, and axSpA without definite radiographic changes of sacroiliitis (nr-axSpA). SpA with predominantly **peripheral involvement** is designated as "peripheral SpA," with Sx of predominantly or entirely peripheral rather than axial; these features include arthritis, which is predominantly of the lower limbs and/or asymmetric; enthesitis; and dactylitis.

[40] enthesitis: inflammation around the enthesis (site of insertion of ligaments, tendons, joint capsule, or fascia to the surface of the bone).

[41] Oligoarthritis (most common, 70%): typically with involvement of both the DIPs and PIPs. Spinal involvement (up to 40%).

[42] Destruction of the IP joints and resorption of the phalanges; causes the soft tissue of the fingers to collapse (“telescoping fingers” or “opera glass hand”). The deformity is called telescoping fingers as the affected finger can be lengthened on pulling it. Arthritis mutilans can occur secondary to any severe destructive arthritis (e.g., psoriatic arthritis, rheumatoid arthritis, gout).

[43] In contrast to syndesmophytes, paravertebral ossification doesn’t extend from vertebra to the next & doesn’t lead to movement restriction.

AS (Ankylosing Spondylitis)

A chronic inflammatory disease of the axial skeleton that leads to partial or even complete fusion and rigidity of the spine. Positive HLA-B27 and +ve FHx are strong risk factors.

Clinical features

A. Articular Sx

- Most common presenting symptoms: back and neck pain (**gradual** onset, **dull** pain that progresses slowly, independent of positioning, also appears at night associated with **morning stiffness** that improves with activity, and tenderness over the sacroiliac joints).
- Limited mobility of the spine (especially reduced forward lumbar flexion).
- Inflammatory enthesitis (e.g., of the Achilles tendon, iliac crests, tibial tuberosities): painful on palpation.
- Dactylitis. Arthritis outside the spine: hip, shoulder, and knee joint.

B. Extra-articular manifestations: Acute, unilateral **anterior uveitis** (Most common), GI Sx (associated with chronic IBD), prostatitis, constitutional Sx (fatigue, weakness, fever, weight loss), restrictive pulmonary disease (due to decreased mobility of the spine and thorax).

Diagnostics

★ Diagnostic approach

1. Hx[44] → PEx → and pelvic x-ray: If results are conclusive, no additional testing is required!
2. If inconclusive → HLA-B27 testing.
3. If still inconclusive → pelvic MRI.

A. Clinical tests: Spine mobility tests, examination of the hip (Mennell sign and FABER test).[45]

B. Labs: ↑ CRP/ESR, Auto-antibodies (e.g., RF, ANA → -ve), HLA-B27 positive in 90–95% of cases.

C. Imaging:

1. **X-ray** "changes are generally more evident in later disease"
   - Can help confirm a diagnosis or evaluate the severity of disease, but is not required for the diagnosis.
   - Sacroiliac joints: signs of sacroiliitis, including ankylosis of sacroiliac joints.
   - Spine:
     - Loss of lordosis with increasing abnormal straightening of the spine.
     - Sclerosis of the vertebral ligamentous apparatus.
     - Syndesmophytes resulting in a so-called '**bamboo spine**' in AP radiograph in the later stages.
     - Signs of spondyloarthritis, including ankylosis of intervertebral joints.
2. **MRI**: More sensitive than CT scan for detecting sacroiliitis. Best method for early detection.

Rx

- **PT**: Consistent and rigorous physical therapy.
- **Medical therapy**
  - First choice: NSAIDs (indomethacin).
  - Additional options: TNF-α inhibitors (etanercept). In case of peripheral arthritis → DMARDs (sulfasalazine). In cases with local intra-articular inflammation or enthesitis → temporary, intra-articular glucocorticoids.
- **Surgery**: in severe cases to improve quality of life.

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[44] Inflammatory back pain → including early morning back stiffness, improvement of stiffness with exercise, insidious onset, age at onset <40 years, and back pain lasting >3 months.

[45] **Mennell sign**: tenderness to percussion and pain on displacement of the sacroiliac joints. **FABER test**: FABER (Flexion, ABduction, and External Rotation) provokes pain in the ipsilateral hip.

	Syndesmophytes	Osteophytes
Definition	Ossification or calcification of the annulus fibrosus or a spinal ligament	Lipping of vertebral bodies (development of bony overgrowth)
Radiographic features	Symmetrical, vertical growth, directly from vertebral body to vertebral body. Full manifestation → "bamboo spine"[46]	Horizontal growth
Etiology	Inflammatory spine disease (e.g., AS)	Degenerative spine disease (diffuse idiopathic skeletal hyperostosis)

Reactive arthritis (ReA)

Formerly known as Reiter's syndrome, an **autoimmune** condition that occurs after a bacterial **infection** of the GI or urinary tract. It is categorized as a seronegative spondyloarthritis because of its association with HLA-B27.

Etiology: **Post-infectious autoimmune disorder** (Post-urethritis → after infection with Chlamydia "common" or N.gonorrhoeae - Post-enteritis → after infection with Shigella, Salmonella, or Campylobacter).

RF: male , HLA-B27 genotype and preceding chlamydial or GI infection.

Clinical features:

1. **MSK**: Polyarthritis (Acute, often asymmetrical with a migratory character, occurs predominantly in the lower extremities). Sacroiliitis, Enthesitis, Dactylitis.
2. **Extra-articular**: Conjunctivitis or iritis, Oral ulcers, Dermatologic manifestations (skin lesions of the glans resembling psoriasis (balanitis circinata); hyperkeratinization of the palms and soles "keratoderma blenorrhagicum").
3. **Sx from preceding infection**: Diarrhea, Urogenital tract Sx (dysuria, pelvic pain, urethritis, prostatitis).

> Classic triad → **conjunctivitis**, **urethritis**, and **arthritis** → Can't **see**, can't **pee**, can't **climb** a tree!

Diagnostics "clinical diagnosis that may be supported by diagnostic steps, but there is no confirmatory test"

1. **Labs**: ↑ ESR and CRP. Test for potentially positive HLA-B27.
2. Arthrocentesis: may be performed to r/o differentials (but not indicated for ReA). Findings from synovial fluid analysis include: ↑ WBC count (10,000-40,000/μL), Mostly polymorphonuclear leukocytes predominate, Gram stain and cultures (negative).

Rx[47]: for Sx relief "acute" → NSAIDs (Naproxen), corticosteroids (2nd line). If chronic/persistent → DMARDs.

[46] Bone bridges between adjacent vertebrae → fusion of adjacent vertebrae → block vertebra formation.
[47] The treatment of arthritis with anti-inflammatory and immunosuppressives can be divided into two stages: the treatment of acute reactive arthritis and the treatment of refractory (chronic) ReA, usually defined as disease of greater than six months' duration.

Gout "just know the difference b/w it and pseudogout i.e EXTRA"

More prevalent in men (Estrogen promotes renal uric acid excretion → Postmenopausal women are more likely to develop gout due to decreased estrogen levels).

Etiology

1. Gout: Urate crystals (deposition into joints), Hyperuricemia (predisposes to gout). Associations (DM, HTN, Hypercholesterolemia, hypertriglyceridemia, Anemia)
2. Hyperuricemia (production-excretion imbalance).[48]
   - **A.** Primary hyperuricemia.[49]
   - **B.** Secondary hyperuricemia
     a. Decreased uric acid excretion (most common)
        - Medications (pyrazinamide, aspirin, loop diuretics, thiazides, niacin).
        - Chronic renal insufficiency; lead nephropathy.
        - Ketoacidosis (due to starvation, DM) and lactic acidosis.

     b. Increased uric acid production
        - High cell turnover (e.g., tumor lysis syndrome, hemolytic anemia,[50] psoriasis, myeloproliferative neoplasms, chemotherapy, or radiation).
        - Enzyme defects (e.g., Lesch-Nyhan syndrome, phosphoribosyl pyrophosphate synthetase overactivity, von Gierke disease).
        - High-protein diet (high mead diet), Obesity.

     c. Combined decreased excretion and overproduction: high alcohol consumption.[51]

Pathophysiology

a. Uric acid has poor water solubility, even under physiological conditions.[52]
b. Crystalline arthritis.[53]
c. Chronic effects: repeated attacks → aggregations of urate crystals and giant cells (tophi)[54] → deformities and arthritis.

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[48] Uric acid is an end-product of purine metabolism that is renally excreted. Insufficient excretion or increased production of purines leads to hyperuricemia, possibly triggering a gout attack. May be primary or secondary.
[49] (1) Idiopathic extracellular supersaturation of uric acid. (2) No history of comorbidities or medications that affect uric acid formation or excretion. (3) Aggravated by poor dietary habits.
[50] Hemolysis of RBCs does not increase uric acid, as RBCs do not have nuclei (which means they have no purines). However, hemolysis also causes destruction of nucleated red blood cell precursor cells (reticulocytes), which results in hyperuricemia.
[51] Defective excretion is due to the formation of organic acids that compete with uric acid to be excreted. Overproduction is due to the high amount of purines contained in alcoholic beverages (esp. in beer).
[52] Factors that trigger urate crystal deposition include: ↑ Uric acid levels, Acidosis, Low temperature (e.g., cool peripheral joints).
[53] supersaturation of uric acid in extracellular fluid → intra articular uric crystal precipitation (coated by IgGs) → phagocytized by polymorphonuclear cells → release of inflammatory mediators and enzymes → local joint inflammation.
[54] Deposition of urate crystals in tissue, including bone (bone tophus) and soft tissue (cartilage, tendon sheaths, subcutis; known as soft tissue tophus). Manifests as hard, painless nodules that may appear yellow and chalky if close to the surface of the skin.

Clinical features

Asymptomatic stage: Hyperuricemia with no symptoms. Last up to 20 years or longer.

Acute gouty arthritis

- Triggers: anything that leads to hyperuricemia.
- Arthritis: usually monoarticular during first attacks.[55]
- Locations: Peripheral small joints in the lower extremities are especially affected.[56]

Intercritical stage: Asymptomatic. May also last up to several years.

Chronic gouty arthritis

- No longer common
- Progressive joint destruction.
- Tophi formation
  - Multiple painless hard nodules with possible joint deformities
  - Bone tophi: urate crystal deposition in bones (e.g., elbows, knees, extensor surfaces of forearms)
  - Soft tissue tophi: urate crystal deposition in the pinna of the external ear, subcutis, tendon sheaths, or synovial bursae.
- Renal manifestations with uric acid nephrolithiasis and uric acid nephropathy.

Diagnostics

- Arthrocentesis
  - Indications
    - New-onset acute gout attack (to relieve Sx and r/o pseudogout and septic arthritis).
    - If past suspected gout attacks were not confirmed via polarized light microscopy.
  - Polarized light microscopy: needle-shaped, negatively birefringent monosodium urate crystals.[57]
  - Synovial fluid: WBC > 2000/μL with > 50% neutrophils.
- Laboratory tests: ↑ WBC and ↑ ESR (typical in acute attacks) ↑ Serum uric acid levels.[58]
- Imaging: US,[59] MRI (Excellent measure to detect tophi formation. Method of choice to detect spinal involvement), CT (can detect bone erosions as well as tophi), X-ray[60].

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[55] Acute severe pain with overlying erythema, decreased ROM, swelling, and warmth; possible fever. More likely to occur at night, typically waking the patient. Sx peak after 12-24 hours; regression may take days to weeks. The recovering joint may present with desquamation of the overlying skin.

[56] Podagra: MTPJ inflammation (big toe is the most common site), Gonagra (inflammation of the knee), Chiragra (inflammation of finger joints, esp. MCPJ of the thumb), Others (ankle and tarsus, other toe joints, wrist, elbow). “The tissue temperature within them is physiologically lower → promotes uric acid deposition.”

[57] In contrast to pseudogout, which shows positively birefringent calcium pyrophosphate crystals

[58] However, it may be normal, raised, or low during an acute gouty attack. Therefore, measuring serum uric acid levels may not be useful in diagnosis.

[59] "Double-contour" sign representing hyperechoic monosodium urate crystals covering hyperechoic bone contour. Tophus (a mixture of hyperechoic and hypoechoic structures).

[60] Acute → no use, can’t detect early changes, Chronic → radiopaque soft tissue (Urate deposition in soft tissue), punched-out lytic bone lesions with spiky periosteal appositions.

Treatment

Acute gout attack

- NSAIDs (indomethacin, naproxen, ibuprofen).[61]

  ★ The use of aspirin in acute gout attacks is contraindicated as it inhibits uric acid excretion, thereby delaying the cessation of symptoms.

- Colchicine: inhibition of microtubule polymerization → inhibits phagocytosis of urate crystals, leukocyte activation and migration, and cell chemotaxis.[62]
- Oral glucocorticoids (prednisolone): Indications → no response or CI to NSAIDs and colchicine. Dose should be tapered gradually (over the course of 2 weeks).
- Intra-articular corticosteroids: Indicated particularly with single-joint involvement.
- Local ice therapy may help relieve pain. Rest the affected joint to avoid recurrence.

  ★ PPI should be given to patients being treated with both NSAIDs and glucocorticoids to avoid GI ulcers.

Chronic gout

General measures: Close management of DM and BP, Weight loss (if applicable), Purine-restricted diet (e.g., low-protein diet), Consuming dairy products, vitamin C, and coffee can lower levels of uric acids and therefore prevent gout, Sufficient/high fluid intake, Reduce alcohol consumption.

Medical therapy

- Indications: Recurrent (>2 per year), Uric acid nephropathy, Tophi development, Serum uric acid > 9 mg/dL.
- General approach:
  - Delay initiation of urate-lowering medication until ~ 2 weeks after an acute attack has resolved
  - Despite their therapeutic effect, urate-lowering medications may trigger or prolong an acute gout attack.
    - Urate-lowering drugs should be combined with colchicine during the initiation of therapy for prevention of an acute exacerbation.

[61] Indicated if can't tolerate oral glucocorticoids/colchicine. Initiate as soon as Sx occurs. Discontinue 2–3 days after Sx resolve.
[62] Indications → patients who cannot tolerate NSAIDs (CKD or GI ulcer) or oral glucocorticoids. Prophylaxis → prevents flares of acute or recurrent gouty attacks in patients beginning uricosuric agents (e.g., probenecid) or xanthine oxidase inhibitors (e.g., allopurinol). Side effects → diarrhea, nephrotoxicity, and myelosuppression.

	First-line: **xanthine oxidase inhibitors** (**allopurinol**)	Second-line: **uricosuric** (benzbromarone, probenecid))	Third-line: **recombinant uricase** (pegloticase)
Mechanism	Reversible inhibitor of xanthine oxidase → Hypoxanthine and xanthine will not be degraded into uric acid.	Inhibition of uric acid reabsorption along renal tubules → increased renal elimination.	Catalyzes the breakdown of uric acid to allantoin.
Notable side effects	Allergic skin reaction, Toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome.	Urolithiasis (uric acid stones), GI Sx, Rash.	Infusion reactions (multiple premedications are administered as a prophylactic measure, e.g., hydrocortisone and antihistamine).
Indications	**Standard** medication for chronic gout and/or hyperuricemia (> 9 mg/dL). Hyperuricemia prophylaxis (e.g., tumor lysis syndrome).	As an alternative to or in combination with allopurinol.	Patients who do not benefit from 1st/2nd medications. Used if rapid relief is desired (e.g., to quickly reduce tophus or improve quality of life).
CI	**Acute**, Previous hypersensitivity. In kidney disease: dose adjustment (febuxostat is an alternative).	Acute gout attack. Kidney disease (nephrolithiasis, impaired renal function)	**Acute** gout attack, G6PD deficiency.

- ★ The combination of allopurinol and azathioprine leads to increased bone marrow toxicity!
- ★ During the first 2 weeks of an acute gout attack, treatment with urate-lowering drugs (e.g., allopurinol) should not be initiated or altered → can lead to urate crystal mobilization, which worsens the symptoms!

Pseudogout (CPPD)[63]

- Short description: paroxysmal joint inflammation due to calcium pyrophosphate crystal deposition (calcium pyrophosphate dihydrate)
- Clinical presentation
  - Often asymptomatic
  - Acute (pseudogout attack): monoarthritis (rarely oligoarthritis), mostly affecting the knees and other large joints (e.g., hips, wrists, and ankles)
  - May become chronic (can affect multiple joints)
    - Osteoarthritis with CPPD (most common form of symptomatic CPPD): progressive joint degeneration with episodes of acute inflammatory arthritis typical of pseudogout attacks
- **Diagnosis**
  - Arthrocentesis should be performed, especially in acute cases.
    - Polarized light microscopy: detection of rhomboid-shaped, positively birefringent CPPD crystals
    - Synovial fluid findings: 10,000-50,000 WBCs/μL with > 90% neutrophils.
  - X-ray findings: cartilage calcification of the affected joint (chondrocalcinosis)
    - Fibrocartilage (meniscus, annulus fibrosus of intervertebral disc) and hyaline cartilage (joint cartilage) may be affected.
  - Test for hypercalcemia (esp. hyperparathyroidism).
  - Serum uric acid levels are normal.
- **Treatment**
  - Asymptomatic cases do not require treatment unless there is an underlying condition (e.g., hyperparathyroidism).
  - Symptomatic (similar to gout): NSAIDs (initial), Alternatives → colchicine or intra-articular corticosteroids.
  - Arthroscopic lavage may also be considered, Possible joint replacement.

[63] Ca pyrophosphate deposition disease: A form of inflammatory arthritis due to the deposition of Ca pyrophosphate dihydrate crystals in the hyaline or fibrocartilage.

To rearrange some of the points mentioned in the objectives

1. Differentiate between **inflammatory** back pain from **mechanical** back pain.
2. Know all **extra-articular manifestations** of spondylarthritis.
3. Learn **radiographic features** (mainly x-ray of spine and sacroiliac joints and the importance of MRI).
4. Understand the **treatment strategies** for axial and peripheral Spondylarthritis.

1. The history differentiates mechanical back pain from inflammatory back pain. OA (for example): Presents with mechanical pain typically becoming worse at the end of the day and after activity, with no morning symptoms. May occur after lifting or bending. Radiographs of the back may demonstrate degenerative disc disease or the presence of osteophytes.

2. Extra Articular manifestations:
Acute anterior uveitis: presents as acute unilateral pain, photophobia, and blurring of vision.
Inflammatory bowel disease: Ileal and colonic mucosal inflammation.
Psoriasis, CVS (increased risk), pulmonary (restrictive lung disease).

3. Sacroiliac joints and pelvis —
Radiography — Radiographic findings of the SI joints range from subtle joint-space narrowing and sclerosis to erosive change and may eventually result in bony ankylosis (fusion). Plain AP radiograph of the pelvis; the SI joint abnormalities can include erosions, ankylosis, changes in joint width, or sclerosis. **MRI** of sacroiliac joints — unlike radiography, can reveal **inflammatory changes**, fatty changes, and subtle structural abnormalities. Such findings are especially important in **nr-axSpA** because the radiographs in nr-axSpA, by definition, are normal or equivocal. Findings of active sacroiliitis have been defined by the ASAS; they include active inflammatory lesions of the SI joints, which appear as "bone marrow edema" (BME). However, MRI contrast use is not required for evaluation of the SI joints in patients with suspected axial SpA. It is rare for MRI of definite sacroiliitis to show only one lesion. BME in the SI joints is not entirely axSpA-specific. Structural abnormalities (eg, erosions, bony ankylosis, fat metaplasia, or sclerosis) may also be seen but can be nonspecific as well, as are other inflammatory lesions such as synovitis, enthesitis, or capsulitis, which may also be present.

4. GOALS AND GENERAL PRINCIPLES OF MANAGEMENT

- The primary goals of management for patients with axial spondyloarthritis (SpA) are to optimize short- and long-term health-related quality of life through the following:
- Relief Sx (pain, stiffness, and fatigue or to reduce them to the minimal possible level).
- Maintenance of function.
- Prevention of complications of spinal disease (prevent flexion contractures, especially dorsal kyphosis).
- Minimization of extraspinal and extraarticular manifestations and comorbidities (to reduce the impact of axial SpA-associated disorders such as uveitis and aortic valve insufficiency).
- Maintenance of effective psychosocial functioning – To preserve social participation, prevent job loss, and improve health status and function.

General principles of management and approach to therapy in axial SpA include:

- Care by rheumatologist, and care should be coordinated with appropriate clinical specialists, depending upon the clinical features, such as a dermatologist for psoriasis, a gastroenterologist for inflammatory bowel disease (IBD), and an ophthalmologist for uveitis.
- Disease activity should be regularly measured and therapy adjusted accordingly to improve outcome.
- Nonpharmacologic measures: patient education, PT and exercise, smoking cessation.
- Pharmacologic (axial and peripheral articular manifestations): one or more of the following: NSAIDs, non-NSAID analgesics, DMARDs (biologic "TNF[64]/IL-17 inhibitors" and nonbiologic "sulfasalazine, methotrexate").

Symptomatic axial SpA:

Initial **NSAIDs[65]**, if failed → we switch to a **second NSAID**, Failed ? → **add a TNF-alpha inhibitor.** Failed ? → **add** a second TNF inhibitor **<u>or</u>** a **switch** to an **IL-17 inhibitor.[66]**

Peripheral:

1. Arthritis

<u>Mild</u> → NSAIDs (trial of 2 different medications, for 2-4 weeks at least), mono/oligoarthritis (might benefit from intra-articular glucocorticoids).

<u>Severe</u> → NSAIDs/Intra-articular glucocorticoids, if fail → oral glucocorticoids (low-moderate daily dose as a bridge therapy) → then control the disease by DMARDs.

2. Enthesitis: Achilles/plantar fascia → NSAIDs, other tendons might benefit from peritendinous glucocorticoids injection. If failed → TNF inhibitor.

3. Dactylitis: NSAIDs → DMARDs.

Best wishes 💪😍
Adel Al Shihri ^-^

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[64] CI: Active infection, Latent (untreated) TB, Demyelinating disease (eg, MS, optic neuritis), Heart failure, Malignancy.
[65] Regardless of the NSAID used, the maximum dose is usually required, and the response should be assessed after a sustained dose on a daily basis for at least 2-4 weeks.
[66] if the 1st TNF inhibitor failed after initial response → then try another one. If there wasn't any response from the beginning then switch to IL-17 inhibitor.