RHEUMATOLOGY

UPDATED 2025

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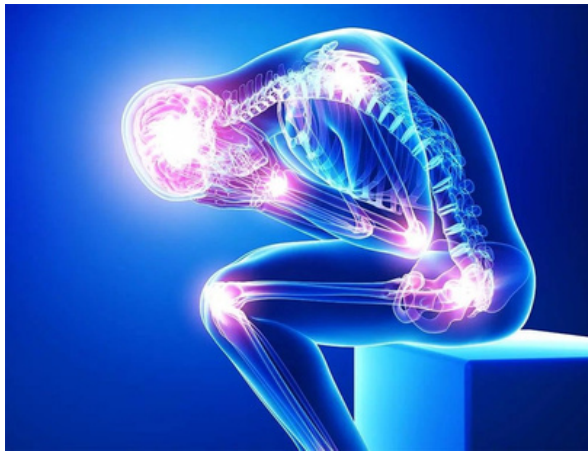
Introduction

☆ Rheumatology is a subspecialty of internal medicine and pediatrics that focuses on the diagnosis and treatment of autoimmune, inflammatory, and musculoskeletal diseases. These conditions primarily affect joints, muscles, bones, and connective tissues, often leading to pain, swelling, stiffness, and systemic complications.



Historical Background

- The term "rheumatology" originates from the Greek word "rheuma," meaning "that which flows," referring to the concept of fluid disturbances causing joint diseases.
- Advances in immunology have significantly contributed to the understanding of autoimmune rheumatic diseases.
- The development of disease-modifying anti-rheumatic drugs (DMARDs) and biologics has revolutionized treatment

Common Rheumatic Diseases

Rheumatology encompasses a wide range of disorders, including:

1. Autoimmune and Inflammatory Disorders

- Rheumatoid Arthritis (RA): Chronic autoimmune arthritis affecting multiple joints.
- Systemic Lupus Erythematosus (SLE): Multi-organ autoimmune disease.
- Sjögren's Syndrome: Autoimmune disorder affecting salivary and lacrimal glands.
- Scleroderma (Systemic Sclerosis): Connective tissue disorder causing skin and organ fibrosis.
- Polymyositis & Dermatomyositis: Inflammatory muscle diseases.
- Vasculitides: Inflammatory diseases of blood vessels, including ANCA-associated vasculitis (GPA, MPA) and large-vessel vasculitis (GCA, Takayasu).

2. Degenerative and Mechanical Disorders

- **Osteoarthritis (OA):** Progressive joint cartilage degeneration.

- **Crystal-induced Arthritis:**
  - **Gout:** Uric acid crystal deposition.
  - **Pseudogout (CPPD Disease):** Calcium pyrophosphate crystal deposition.

- **Fibromyalgia:** Widespread pain syndrome with central sensitization.

3. Pediatric Rheumatology

Juvenile Idiopathic Arthritis (JIA): Most common chronic arthritis in children.

Kawasaki Disease: Vasculitis affecting coronary arteries in children.

Henoch-Schönlein Purpura (HSP): IgA-mediated vasculitis common in pediatrics.

Pathophysiology of Rheumatic Diseases

Autoimmunity: Immune system attacks self-antigens, leading to chronic inflammation.

Inflammatory Mediators: TNF-α, IL-6, IL-1, and autoantibodies (e.g., RF, ANA, ANCA) play key roles.

Genetic & Environmental Factors: HLA associations (e.g., HLA-DR4 in RA, HLA-B27 in Ankylosing Spondylitis) and infections contribute to disease onset.

Aapproach patient with joint pain

A. Chief Complaint

- Symmetric joint pain (arathralgia : joint pain , arithritis joint pain + swelling + limitation of movement + redness + hotness)
- swelling, and morning stiffness lasting >1 hour.
- Fatigue, low-grade fever, weight loss.
- Difficulty performing daily activities (e.g., dressing, walking, gripping objects).
- Worsening joint symptoms with rest and improvement with activity.

B. History of Present Illness

- Onset: Gradual onset over weeks to months (RA, SLE, ...) vs. acute onset(septic arithritis, reactive arithritis).
- Duration: Symptoms persisting for at least 6 weeks.
- Pattern: Symmetric involvement of small joints (MCP, PIP, wrists, MTPs), sparing the DIP joints.
- Progression: Initially intermittent symptoms that become persistent and progressive.
- Morning Stiffness: Lasting >1 hour (significat indicat RA), improving with movement but worsening with prolonged rest(inflammation) or increasing with movement (meaning it mechanical as Osteoarthritis).
- Joint Distribution: Predominantly affecting hands, wrists, and feet, but can involve elbows, shoulders, knees, and cervical spine.

- Number of joint :
  A) Monoarticular :
    - Trauma
    - Septic arithritis
    - Crystal induced arithritis
    - TB
    - Haemoarethrosis

Note : Oligoarthritis and poly arthritis could be started as Mono

B) Oligoarithritis [2-3] :
  - Seronegative arithritis (asymmetrical)

C) Polyarithritis :
  - RA : symmetrical with morning stiffness for more than 1 hour.
  - SLE : symmetrical may be asymmetrical

- back symptoms (SI joint , Epiphyseal joint , disc plate)
  ☆ indicates seronegative arithritis.

- Systemic Symptoms and Constitutional symptoms :
  - Fatigue, malaise, weight loss (The most common risk of significant weight loss present in rheumatology is – lymphoma and TB spec. in old age.
  - Low-grade fever (suggests systemic inflammation , shuold exclud infection)
  - Rigor: shaking chills – transient passage of micro organism through blood [uiremia/bacteremia]
  - Chills: feeling of coldness
  - Dry mouth/eyes (suggesting secondary Sjögren's syndrome)
  - Paresthesia (suggestive of carpal tunnel syndrome due to synovial hypertrophy).
  - Shortness of breath (may indicate interstitial lung disease).
  - Arthritis and sweating = TB or Brucellosis

- Age of patients:
  - Rheumatic fever: childhood 5-15 .
  - SLE: menarche to menopause

Note: usually females affected with rheumatoid disease

- Rash : - Rash on forehead and chin – photosensitive rash painless ulcer and pleuratic chest pain SLE (50% have nephritis so we don't use NSAID in SLE)

- Past medical history : Autoimmune, Infection
- family history
- Social history

C) physical examination

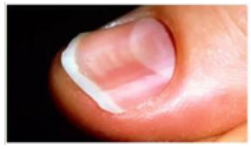
1. General Examination

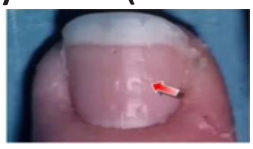
Vital signs: Low-grade fever, signs of systemic inflammation.

Appearance: Fatigue, pallor (anemia), weight loss.

2. Joint Examination

- Inspection:
  - Swelling, redness,
  - Nails changes : anemia (IDA : Koilonychia (nail spooning)) ,
- psoriasis in case of 3 pits , Vasculitis .

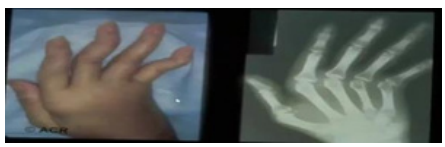


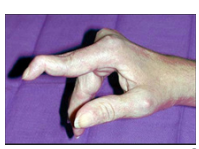


  - Skin : color , texture (thick as with scleroderma)

  - deformities: Swollen PIP joint , swan-neck deformity [hyperextension of the PIP joint with flexion of the DIP joint] , Ulnar deviation , Swollen (MCP) joint [in RA]

Kyphosis : anterior bending of spine
Lordosis : posterior bending of spine
Scoliosis : lateral bending of spine





swan-neck

  - Osteopenia (decreased bone density in x-ray)

- Palpation: signs of arthritis : swelling (you have to confirm what you see with inspection) , Hotness , Tenderness , effusion (fluid inside joint) , skin abnormalities (pinch the skin : thin (old age loss supportive connective tissue) or patient with steroid (cushioned skin) OR thick)

- To examine effusion : Bulge sign (milking method for mild effusion) Patellar tap , fluctuation →moderate to severe .

Note: TB is localized to the lower thoracic and upper lumbar regions, as seen in Pott's disease or brucellosis. Ankylosing spondylitis involves the entire spine and starts from the lower spine (SI joint)."

- Movement range : we examine range , types of movement and power .

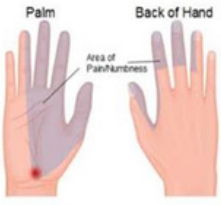
In cases of normal passive movement and abnormal active (thinke about periarticular)

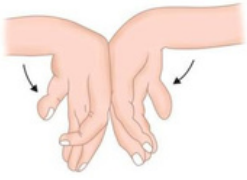
In both abnormal it's pathology of joint

- Special maneuvers **:**

1- Tinel's test : tapping on median nerve for carpal tunnel syndrome CTS **(** paresthesia on three lateral and 1/2 of fourth **)**

2- Phalen's test : Dorsal flexion of both wrist for one minute.





NOTES : commonest cause of CTS : DM . Other causes : Hypothyroidism , RA , acromegaly , cholles fracture , fracture of distal forearm (radius bent backward)
Physiological cause : Pregnancy

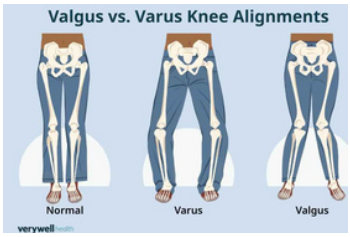
Raynaud's phenomenon mechanism according to colors :seen in SLE and scleroderma

White	Blue Deoxygenating ,	Red
Vasculo-occlusive , no adequate blood flow	depletion of o2	Painful , hyperactive vasodilation , hyperemia, local tissue acidosis

HIP : inspection not yielding it's a deep joint , palpate bone prominence : ASIS , Iliac crest , PSIS , greater trochanter .

→Burse mean Sac , Bursitis → inflammation of this sac as peritrochanteric bursitis

Deformities : Genu Varus : Bowing , Rickets , OA in old age . Genu valgus



- Laboratory Tests

Inflammatory Markers: ESR, CRP (elevated in active disease).

Autoantibodies:

Rheumatoid Factor (RF) (positive in ~70-80%).

Anti-Citrullinated Peptide Antibody (Anti-CCP) (more specific for RA).

Complete Blood Count (CBC): Anemia of chronic disease.Thrombocytosis in RA : platelets are acute phase reactant . Thrombocytopenia in SLE

Liver & Kidney Function Tests: Baseline before DMARD initiation.

Synovial Fluid Analysis: If joint effusion present (exclude infection, crystals).

D) Extra articular manifestations :

1. hair fall [100 h] – alopecia – common in females
2. facial rash (Malar rash : over cheeks , nose bridge , spares nasolabial area)
3. photosensitivity – when the patient exposed to light the rash will increase .
   (2+3 : criteria of SLE diagnosis)
4. oral ulcer (painful or painless)
5. eye symptoms : redness/dryness
6. pleurisy : sharp chest pain (knife like) , increase with respiratory cough , breathing .
7. pericardial pain : sharp , retrosternal , increase by lying flat and decrease by pitting up-ward.
   (6+7 : can occur with SLE)
8. renal symptoms : heavy proteinuria[frothy urine] , hypoalbunimia
   Glomerulonephritis: decrease oncotic pressure : edema , hematuria (RBC cast) , oliguria: less than 400 ml/24 h 4 , newly onset of hypertension or worsening HTN .
   Oliguria : more common and serious , Polyuria : uncommon except in case of loss concentrating ability in renal tubules . Note: normal protein in urine : less than 150mg / day .
   nephrotic syndrome amount of proteinuria is more than 350/24h
9. CNS : fits.seziures (as with hypertensive encephalopathy) , multiple infarct , headache .
   25 years old female presented with seizure (think of uremic seizure) or very advanced renal Failure
10. skin: any rash

*What type of crystals makes gout ?urate [uric acid] , and CPPD [calcium pyrophosphate dehydrate] make pseudogout

Pattern of joint involvement :

1– migratory : Pain moves from one joint to another, with previous joints improving as new joints become affected no period without pain (Rheumatic fever)

2– additive: if the first joint still inflamed and another joint involved (RA , SLE)

3– intermittent: it resemble migratory but it have pain free period – gout and pseudogout.

Hemophilia A - factor 8 def, Hemophilia B – factor 9 def, Hemophilia C – factor 11 def
NOTE : Hemophilia A doesn't cause joint disease , unless in case of joint bleeding and cause Hemarthrosis

RHEUMATOID ARTHRITIS

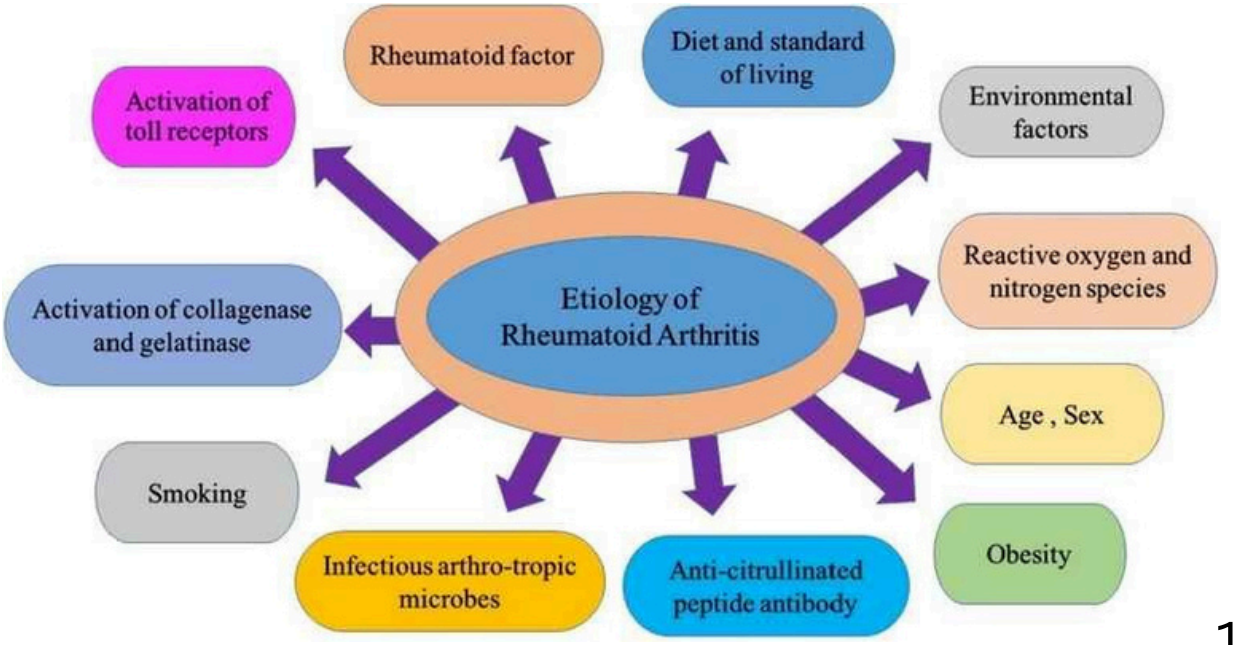
Most Rheumatic diseases are : chronic , inflammatory , systemic (not a mechanical (joint) disease that affects primarily the joints) , autoimmune , symmetrical , affect joint with variable extent with unknown etiology .
Most joints affected here are small (symmertical) joints : PIP , MCP , wrists , MTP , ankles knees

- Prevalence
  - 0.24% worldwide [1]
  - 1% in northern Europe and US [2]
- Sex: f > m (3:1) [3]
- Peak incidence: 30–50 years (as patient younger think of SLE) Older than 65 years and presented as RA : you have to rule out : chronic infection as TB + Malignancy manifested by para neoplastic syndrome

Etiology

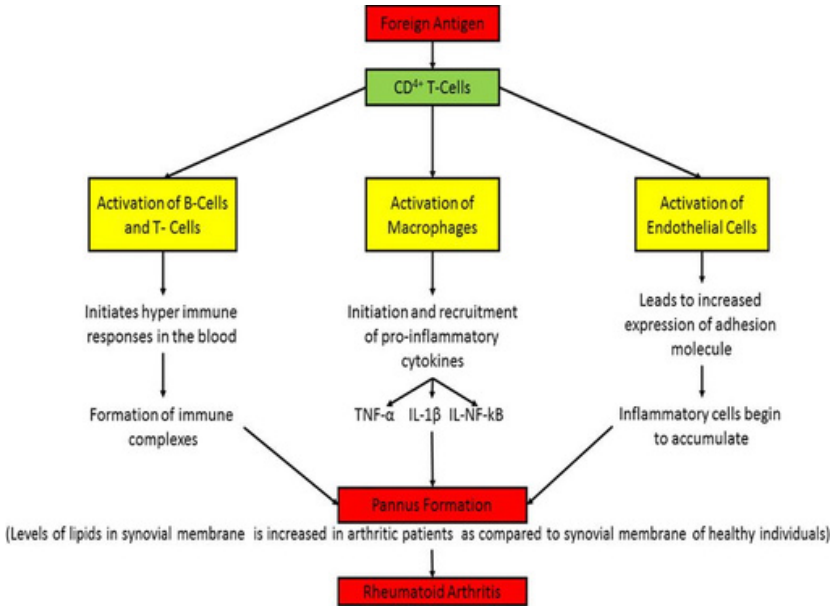
- Idiopathic inflammatory autoimmune disorder of unknown etiology
- Risk factors include:

Genetic disposition: associated with HLA-DR4 (MC) and **HLA**-DR1 (bad prognosis here the Anti CCP positive : worse disease)
Environmental factors (e.g., smoking)
Female sex hormones: Risk of RA is increased in premenopausal individuals and in the first year postpartum
Infection (e.g., periodontitis , EBV)
Obesity
Family history of RA



Pathophysiology

- Certain interstitial tissue proteins (e.g. intracellular filament protein vimentin, filaggrin, type II collagen) undergo a posttranslational modification that involves the conversion of arginine to citrulline (citrullination).
- Citrullinated proteins are recognized as foreign by the antigen-presenting cells that present them to $CD4_+$ T cells.
- Activation of $CD4_+$ T cells leads to the following sequences of events: [9]
  - IL-4 production → B-cell proliferation and differentiation → production of anticitrullinated peptide antibodies → type II hypersensitivity reaction and type III hypersensitivity reaction
  - Migration of $CD4_+$ T cells to synovial joints → secretion of cytokines (IFN-γ, IL-17) → recruitment of macrophages → secretion of cytokines (TNF-α, IL-1, IL-6) → (Osteoclast : bone destruction by RANK-RANK ligand → decrease OPG , Chondrocyte : cartilage destruction and apoptosis , Synoviocyte hypertrophy &inflammatory cell)
- Bouts of inflammation, angiogenesis, and proliferation → proliferative granulation tissue with mononuclear inflammatory cells → pannus and synovial hypertrophy → invasion, progressive destruction, and deterioration of cartilage and bone
- **Antibodies IgM against Fc portion of IgG (rheumatoid factor, RF) IgM is pentamere so is big molecule can accumulate cells and augment RA !**
  - RF excess triggers formation of new immune complexes and type III HSR. [NOTES: RF & Anti ccp mean (worse prognosis)]
    anti ccp is specific factor for RA
- The Importance of CCP : 1- Good for diagnosis 2- Prognosis 3- Help in prediction (REMEMPER → damage of joint start early in course)



Clinical Features :

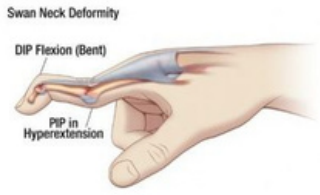
Articular manifestations (chronic, Symmetrical, additive pattern, fluctuation cours and not rimet alone without treatment except in rare cause)

- Polyarthralgia
  - Symmetrical pain and swelling of affected joints (also at rest)
  - Frequently affected joints
    - Metacarpophalangeal joints (MCP joints)
    - Proximal interphalangeal joints (PIP joints)
    - Wrist joints
    - Knee joints

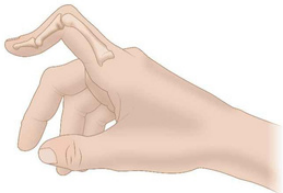
  - Rarely affected: distal interphalangeal joints (DIP joints), first carpometacarpal (CMC) joint, and the axial skeleton (except for the cervical spine)

- Morning stiffness (often > 30 min) that usually improves with activity

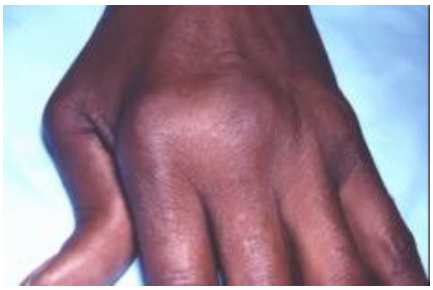
- Joint deformities
  - Rheumatoid hand is characteristic and typically manifests with one or more of the following deformities:
    - **Deepening of the interosseous spaces of the dorsum of hand**
    - **Swan neck deformity: PIP hyperextension and DIP flexion**

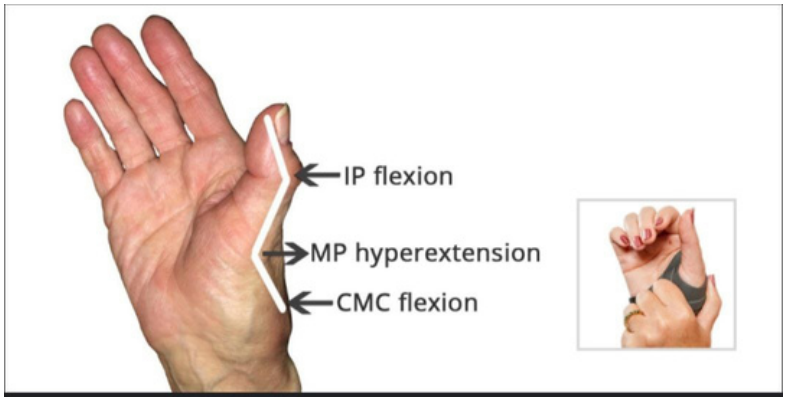


    - **Boutonniere deformity: PIP flexion and DIP hyperextension.**

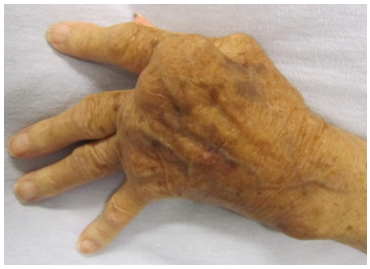


- **Hitchhiker thumb deformity (Z deformity of the thumb): flexion of the interphalangeal joint with fixed hyperextension of the MCP joint**

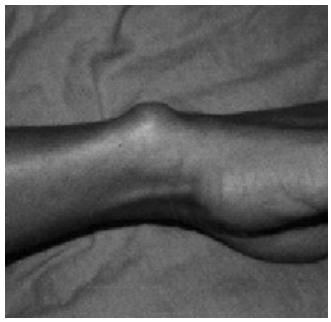




- **Ulnar deviation of the fingers**

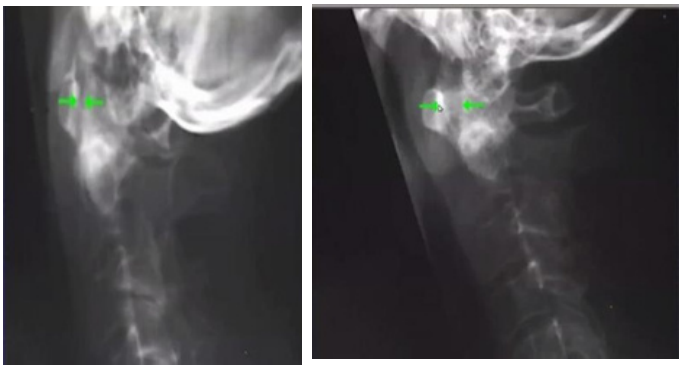


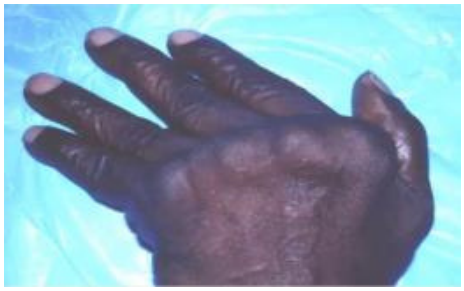
- **Piano key sign: dorsal subluxation of the ulna**



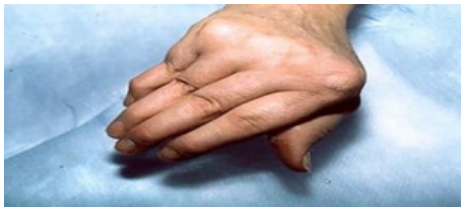
- **Hammer toe or claw toe**
- **Atlantoaxial subluxation** (→ Neck sub laxation in C1 & C2 (patient come with electric like pain in back when he looking down) can compress the pyramidal tract leading to quadriparesis.

Any patient presented with RA we have to do cervical spine x ray to check for C1 ,C2 subluxation.

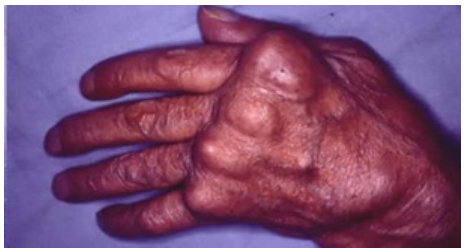




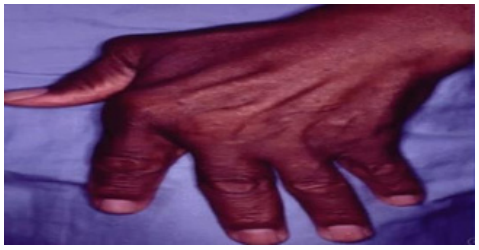
→ Ulnar deviation , Swollen MCP in the 2nd , 3rd ,4th and 5th fingers. Swan-neck deformity in the 3rd finger. Finger clubbing ; indicates lung fibrosis in RA. Step sign ,confirmed by palpation (subluxation) .



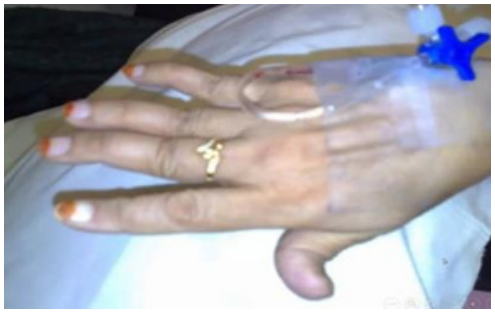
→Swan-neck deformity in the in the 3rd ,4th and 5th fingers Ulnar deviation , Swollen MCP , Tobacco stained fingers , Hyper keratotic lesion



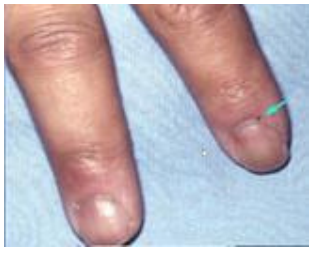
→ Volar subluxation of MCP joint (step sign) & clubbing !!! why ? lung fibrosis of RA .



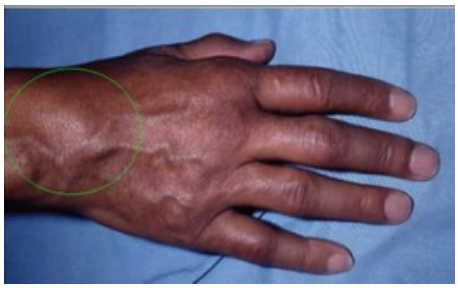
Ulnar deviation , Muscle wasting(dorsal interossus muscle) , Z deformity



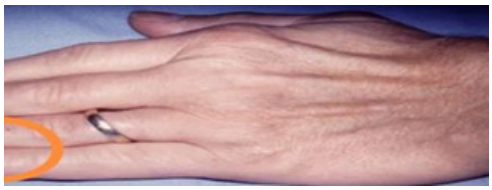
→Swan-neck deformity , Muscle wasting , Finger clubbing



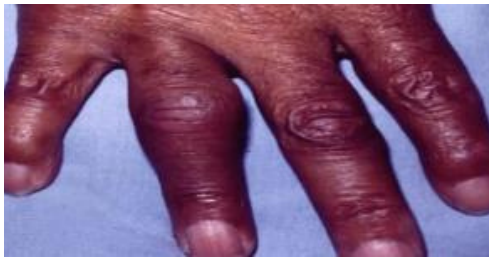
→ digital infarction / vasculities



→Swelling in the wrist joint , Swelling in the PIP of 2nd, 3rd ,4th and 5th fingers, Swelling in the MCP of 2nd and 3rd fingers. Early case patient



→Swollen wrist.Muscle wasting. Pinpoint lesions ; probably Vasculitis



PIP joint swelling 4th & swan neck 5th

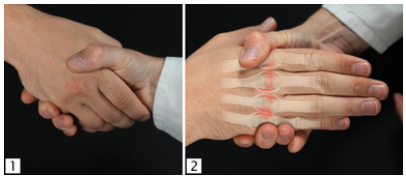
x-ray of bone show joint erosion >> destruction >> deformity (70% of joints erosions occur in first 2 years of disease so early treatment and diagnosis very important) , Most have fluctuation course (exacerbation + remission), active disease 10-20% through its course .

NOTE : Morning stiffness (FOR MORE THAN ONE HOUR): - since it's an inflammatory process
- due to edema inside the joints and the intra articular pressure is high .

NOTE : if you see that joint symptoms persist for more than month most likely

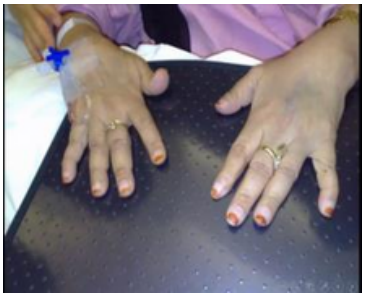
you're not dealing with Rheumatic fever ! And so : The old criteria for diagnosis require persistent symptom for six weeks at least ; to exclude viral and reversible arthritis .

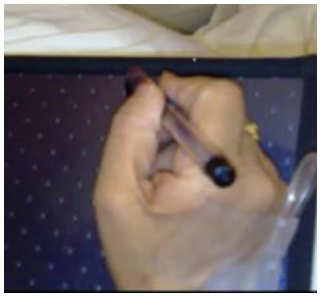
- **Physical examination: compression test (Gaenslen squeeze test)**
  - **Painful compression of hands (or feet) at the level of the MCP**
  - **Painful handshake is an early sign of arthritis**

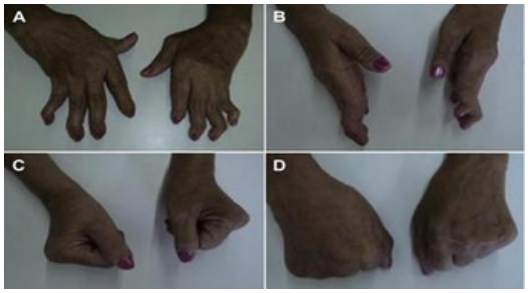


- **→Pregnancy : RA :70% improve due to placental steroids, and the methotrexate is stopped before 3 month . most DMARD can be stopped , HCC and azathioprine are relatively safe (in case of symptomatic pregnant) SLE : mostly worse more and more**

→NOTE : when you see deformity look for reversibility , if reversible then the disease NOT in the joint , but could be periartcular (ligaments , capsules , muscles , nerves)
So : Fixed deformity → disease in joint , as RA
Not Fixed / reversible → periartcular (ex : SLE & rheumatic fever)







You can see here a reversible sawn neck deformities , it's mostly SLE Not RA

NOTES

→ DIP joints not affected , its go with OA + psoriasis → RA affect both small and large joints , but if small joints aren't affected then the diagnosis of RA should be questioned !!

→ Large joints are the least joints affected (central joints : Hip , shoulder) → They begin distal to proximal (progressive) :PIP → MCP →wrist→ elbow → and less likely shoulder and so on .

→ Symmetrical , if Asymmetrical it go against RA

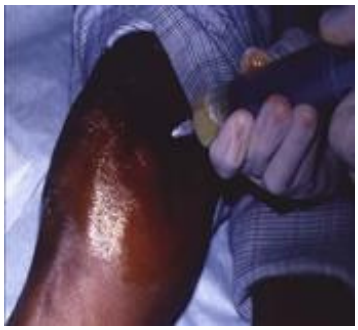
Asymmetrical involve : the sero negative arthritis (ankylosing spondylitis , Reactive arthritis , (IBD) Related arthritis , psoriasis which behave away from the group) and they affect Large joints , except psoriasis : affect small joints .

Rheumatic fever	Rheumatoid arthritis
Large / major joints	Small joints
On the joint itself (olecranon process)	On the extensor aspect of the forearm
Migratory	Additive
☒ No morning stiffness	✓ morning stiffness
Smaller nodules with shorter duration	Larger nodules with longer duration

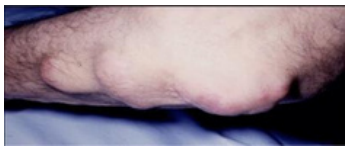
[RA nodules] : large , on extensor aspect of forearm , long duration (months to years) .

→ joint aspiration , usually we don't do it in RA (not routinely) , but we do it when I have MONO ARTHRITIS as (gout , septic arthritis (pus from joint), haemarthrosis)
RA fluid is turbid (inflammatory). Normal fluid : light yellow clear , viscus , transparent , translucent .

In RA we do aspiration if one of joint painful more than other joints



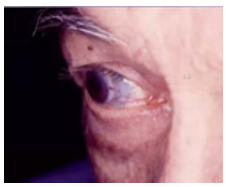
Eextraarticular :



- **Constitutional symptoms**
- **Rheumatoid nodules**
  - **Skin**
    - **Nontender, firm, subcutaneous swellings (2 mm–5 cm)**
    - **Commonly occur in areas exposed to higher pressure, e.g., extensor side of the forearm, bony prominences**
  - **Lungs**
    - **Typically bilateral and peripheral**
    - **Rheumatoid pulmonary nodules may be accompanied by fibrosis and pneumoconiosis (Caplan syndrome).**
- **Lungs**
  - **Pleuritis, pleural effusions**
  - **Interstitial lung disease (e.g., organizing pneumonia)**

- **Eye: keratoconjunctivitis sicca, scleritis, and episcleritis**

→ scleromalacia : thinning in sclera (dangerous sign ! it can cause rapture of globe and loss of vision) blue in color due to exposure of the choroidal veins; due to Scleritis which could rupture and lead to blindness.



- **Endocrine and exocrine glands: secondary Sjogren syndrome**

eumatoid arthritis

- **Hematological :**
  - **anemia**
  - **Neutropenia**
  - **splenomegaly**
  - **lymphoma**

☆ Felty syndrome: a triad of RA, splenomegaly and neutropenia

Thrombocytopenia (Thrombocytosis: inflammation)

- **Musculoskeletal**
  - **Tenosynovitis and bursitis**
  - **Carpal tunnel syndrome**
    - **Typical nocturnal paresthesia of volar hand, thumb, index and middle fingers**
    - **Atrophy of thenar muscles → difficulty making a fist and inability to oppose the thumb**
  - **Tarsal tunnel syndrome**
- **Heart**
  - **Pericarditis and myocarditis**
  - **Increased risk of myocardial infarction, stroke, CHF, and atrial fibrillation**

- **Vascular**
  - **Peripheral vasculitis, manifests as livedo reticularis**
  - **Raynaud phenomenon**
  - **Purpura**
  - **Vasculitic ulcers**
  - **Necrosing fingertips**
  - **Peripheral neuropathy**

Poor prognosis of RA :

1- Poly articular joint disease.
2- Persistent active disease.
3- Extra – articular manifestation
4- anti RF and CCP
5- elderly
6- HLA 8
7- Cardiovascular disease and infections are the most common causes of death
8- smoking
9- male sex

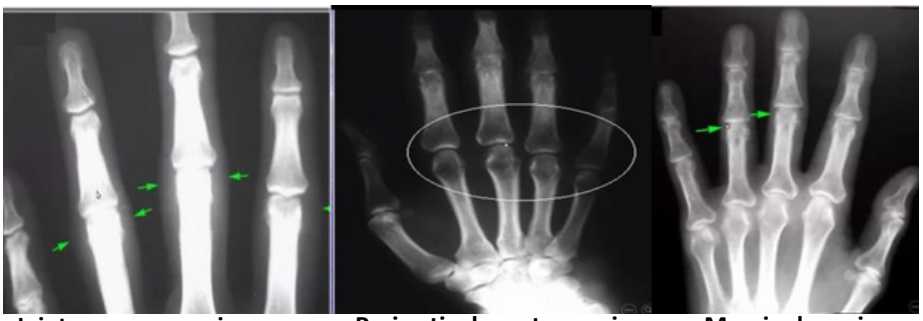
Imaging :

Early: soft tissue swelling, osteopenia (juxtaarticular)
Late: joint space narrowing, marginal erosions of cartilage and bone, osteopenia (generalized), subchondral cysts

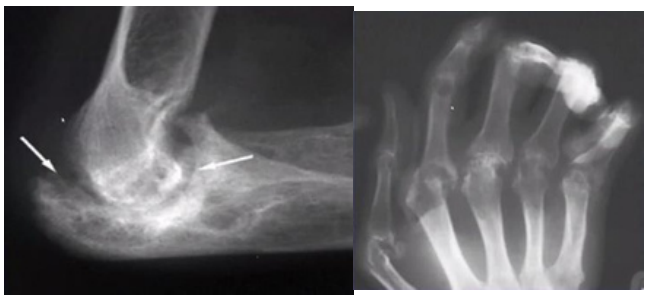
If you see X-ray of hand you can see :
(X ray is usually valid for 6-12 months)

- ➔ Soft tissue swelling
- ➔ Osteopenia
- ➔ Joint space narrowing
- ➔ Joint erosion (very important)

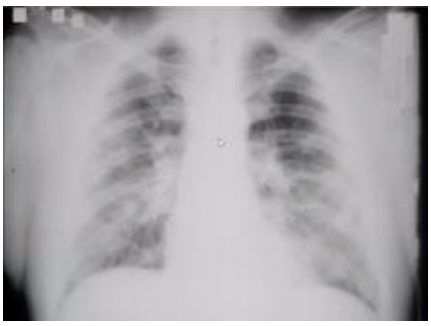
Typical RA findings on x-rays may be subtle or absent upon diagnosis in many patients with early RA; therefore, ultrasound or MRI may be more informative, as they have higher sensitivity for detecting early signs of inflammation and erosion.



Joint space narrowing | Peri-articular osteopenia | Marginal erosion



Bone destruction and osteophytes



→ chest x- ray show interstitial lung disease (bilateral reticular nodular shadow) sarcoidosis

Diagnosis :

Old

Criterion	Definition
A patient is classified as RA if 4/7 criteria are satisfied. Criteria 1-4 must have been present for ≥6 weeks	
1. Morning stiffness	Morning stiffness in and around the joints, lasting at least an hour before maximal improvement
2. Arthritis of ≥3 joints areas	≥3 joints areas simultaneously have had synovitis observed ay a physician
3. Arthritis of hand joints	At least 1 area swollen in a wrist, MCP or PIP joint
4. Symmetric arthritis	Simultaneous involvement of the same joint areas on both sides of the body
5. Rheumatoid nodules	Subcutaneous nodules, over bony prominences, extensor surfaces or juxta-articular regions
6. Serum rheumatoid factor (RF)	Positive RF
7. Radiographic changes	Radiographic changes typical of RA in posteroanterior hand and wrist radiographs

1987 ACR Classification criteria for RA[3]

New

Target population: Patients who (i) have at least one joint with clinical synovitis, and (ii) the synovitis not better explained by another disease	Score
Add score of categories A-D, score of ≥6/10 needed to classify patient as having definite RA	
A. Joint involvement (tender/swollen)	
1 large joint	0
2-10 large joints	1
1-3 small joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)	5
B. Serology	
Negative RF /ACPA	0
Low-positive RF/low positive ACPA	2
High positive RF/high-positive ACPA	3
C. Acute phase reactants	
Normal CRP&ESR	0
Abnormal CRP/ESR	1
D. Duration of symptoms	
<6 weeks	0
≥6 weeks	1

2010 ACR/EULAR Classification criteria for RA[5]

THE Difference between old and new criteria : (this points not found in new criteria) : Morning stiffness, The symmetry, The Nodules , X-ray findings

In old criteria [7] , 1987 :

→ Symptom must last for 6 weeks at least
→ Patient must exhibit four of them
→ you can diagnosed here by history only !
→ anti CCP (No) !? ما كان مكتشف وقتها

NOTE : subcutaneous nodules present also in Rheumatic fever ! (see the Jones criteria for rheumatic fever)

In new criteria [4] , 2010 :

•to be diagnosed with RA in new criteria you need score of more or equal to 6/10 .
→ACPA : anti citrulinated peptide antibody , the same with other name : (anti ccp)
→RF (rheumatoid factor) : antibody against FC portion of another antibody .
•Acute phase reactant : positive * CRP , ESR (fibrinogen) , platelet , ferritin + and negative albumin

Advantages of new criteria it is following score system
And allow you to make an early diagnosis (how) as it not require the duration just to be more than 6 weeks .

New criteria for early diagnosis , in case of late diagnosis : deformities and erosions +ve RF in 2/3 of patients . also +ve anti-CPP up to 2/3 patients Patient came with both hands involved and other small joint : 3 points of criteria are checked !! 2+3+4 points

Approach

- **The diagnosis of RA is clinical. Consider RA in patients with arthralgia, joint stiffness, and synovitis lasting ≥ 6 weeks .**
- **Consider alternative diagnoses in patients with atypical presentations (see "Differential diagnoses").**

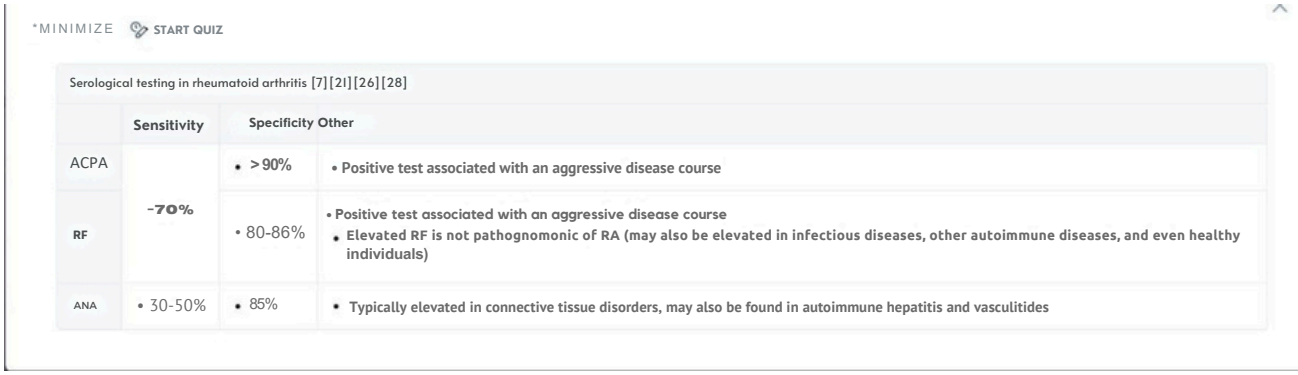
- **Perform diagnostic studies to further support the diagnosis and help establish disease severity.**
  - **Routine laboratory tests.**
  - **X-ray as the initial imaging study**
- **Consult rheumatology, particularly if the diagnosis is uncertain and when choosing a treatment regimen.**

Laboratory studies

Routine studies

- **Nonspecific parameters** ↑ Inflammatory markers
  - ↑ CRP and ↑ ESR
  - Other acute phase reactants may also be elevated (e.g., ferritin).
- CBC: anemia of chronic disease, thrombocytosis
- TFTs: to rule out an autoimmune thyroid disease, which is common in patients with RA
- Serology: ↑ ANAs in 30–50% of patients with RA [21]

- **Specific parameters** (serological studies) [7][26]
  - **Anticitrullinated peptide antibodies** (ACPA), e.g., anticyclic citrullinated peptide (anti-CCP) [27]
  - **Rheumatoid factor** (RF): **IgM autoantibodies** against the Fc region of IgG antibodies [21]
  - Serological studies may be negative (i.e., seronegative RA)



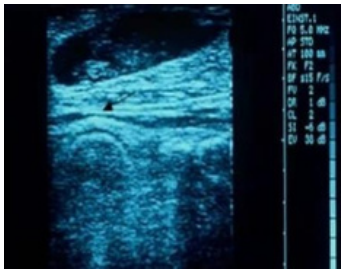
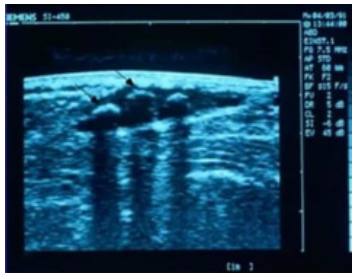
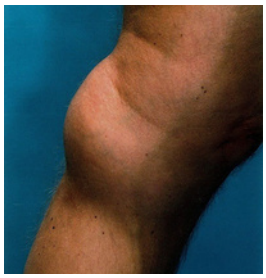
Additional studies

Additional studies should be considered on an individual basis.

- **Synovial fluid analysis**: not routinely recommended
  - Indications
    - Suspicion of septic arthritis
    - Atypical presentation, to rule out differential diagnoses (e.g., gout)
  - Findings are nonspecific
    - Cloudy, yellow appearance
    - Sterile specimen with leukocytosis **(WBC count 5000–50,000/mcL)**
    - ↑ Neutrophils, granulocytes, and ragocytes
    - ↑ Protein level
    - Possibly RF

Complications

- **BAKER cyst : knees (arthritis with effusion) fluid in the posterior popliteal region sitting with completely flexion might lead to its rupture; fluid will diffuse to the calf muscle leading to acute inflammation that simulates DVT**

Treatment

Approach

- **Initiate acute antiinflammatory treatment with** glucocorticoids **and NSAIDs for disease flares.**
- **Long-term treatment**
  - **Initiate treatment with** conventional DMARD **monotherapy.**
  - **Consider short-term concomitant antiinflammatory treatment.**
- **Initiate nonpharmacological management.**
- **Consider surgical treatment in specific cases (e.g., patients with severe joint deformities).**

Pharmacological :

☆ Acute antiinflammatory treatment

Temporary (< 3 months) symptomatic treatment with glucocorticoids and/or NSAIDs is indicated for disease flares (i.e., episodes of increased disease activity and symptom worsening).

- **Glucocorticoids** (Oral , IV , Intaarticular)
  - **Systemic prednisone DOSAGE**
    - **Short-term (i.e., < 3 months) therapy at the lowest effective dose is preferred.**
    - **Longer-term therapy: Only use in patients with highly active RA who do not respond to maximum doses of DMARDs.**
    - Used in : 1 -Acute disease (exacerbation)
      2- Interval (6 weeks) until methotrexate act (bridging)
      3- If there is vasculities
  - **Intraarticular injections (e.g., with triamcinolone acetonide) can be considered by specialists alongside treatment with DMARDs in patients with predominant symptoms in ≥ 1 medium or large joint.**
- **NSAIDs and selective COX-2 inhibitors: relieve symptoms and pain control, but do not improve the prognosis**
  - **Ibuprofen**
  - **Diclofenac**
  - **Celecoxib (selective COX2 : no GI symptom + don't affect platelet , they end by – COXIB) , increased risk of thrombosis**

Glucocorticoids should be used at the lowest effective dose and only for short periods of time to reduce the risk of their many adverse effects (e.g., hypertension, osteoporosis, infections)

☆ Long-term pharmacological treatment

Initiation of treatment

- **All patients (regardless of baseline disease activity or disease duration): monotherapy with a conventional DMARD**
- **Consider short-term concomitant use of acute antiinflammatory therapy (i.e., glucocorticoids and/or NSAIDs) for symptom control until the onset of action of DMARDs (e.g., ≥ 6 weeks).**

DMARDS (most important)

Drug class	Agent	Important considerations
Conventional DMARDs	• Methotrexate (MTX) DOSAGE : first-line treatment in patients with moderate to high disease activity [30][35]	• Adverse effects [25][30][35] ◦ Stomatitis ◦ Pancytopenia ◦ ↑ AST, ALT ◦ Teratogenicity ◦ Pneumonitis • To minimize adverse effects, administer folic acid. DOSAGE . [30] • Avoid administering NSAIDs on the same day as MTX.
	• Hydroxychloroquine DOSAGE : Consider in patients with low disease activity. [30]	• Adverse effects [7] ◦ Hyperpigmentation ◦ Retinopathy [25][30] ◦ Severe rash
	• Sulfasalazine DOSAGE : Consider in patients with low disease activity if MTX is contraindicated, e.g., during pregnancy. [30]	• Adverse effects [7][30] ◦ Diarrhea ◦ Agranulocytosis ◦ Cutaneous hypersensitivity reactions
	• Leflunomide DOSAGE : Consider if all other conventional DMARDs are contraindicated. [30] ◦ Mechanism of action: reversibly inhibits dihydroorotate dehydrogenase → impaired pyrimidine synthesis → inhibition of T-cell proliferation ◦ Other indications: psoriatic arthritis	• Adverse effects ◦ High blood pressure ◦ ↑ AST, ALT ◦ Teratogenicity ◦ GI symptoms (e.g., nausea, diarrhea)
Targeted DMARDs (JAK inhibitors)	• Tofacitinib DOSAGE or baricitinib DOSAGE : second-line treatment	• Adverse effects ◦ Severe infections ◦ TB reactivation ◦ Anemia [30]

Methotrexate monotherapy is strongly recommended over all other synthetic and biologic DMARDs in patients with moderate to high disease activity.

☆ DMARDS shouldn't be stopped even if the patient in remission

- **Methotrexate is the best initial drug**
  - **modify outcome , slowly act , long term effect , considerable SE (need close monitoring (CBC , LFT , urine analysis , examine eyes))**
  - **monitoring of MTX by liver function test (risk of hepatitis), bone marrow (risk bone suppression).**
  - **SE of MTX : Bone marrow suppression , Hepatitis , folate deficiency , interstitial disease as pneumonitis ,GI ulceration from oral to anus , Teratogenicity .**

Final NOTE : methotrexate times of action is 6 weeks and we use corticosteroid in this interval to gain an action and it's not safe in pregnancy as it can end the pregnancy or cause birth defect .

Biologic DMARDs

- **Indication**: persistent moderate or severe disease activity after 3 months of conventional DMARD therapy
- **Agents**
  - **TNF-α inhibitors**: e.g., adalimumab , infliximab (IV), etanercept(sc)
  - Others: rituximab, anakinra, tocilizumab
  - Abatacept : prevent interaction between T cells and APC.
  - Rituximab : block CD20

Disadvantages: very expensive , Infections , TB reactivation , Hepatitis B reactivation

- **Gold injection : not used now (nephrotoxicity)**

- **Surgery : Joint replacement : in advanced and deforming RA , Synovectomy , Excision and fusion .**

➔ We can use combination therapies : Combination DMARD , DMARD + anti TNFalpha.

NON PHAMACOLOGICAL THERAPY

- **Patient education, Exercise, Rest**
- **Heat or cold packs for pain management.**
- **We treat the morbidity , CVD , Stop smoking , treat HTN , DM , Dyslipidemia and so on .**
- **Assessment of activity (DAS28 Disease activity score) :**
  - **Tender joints**
  - **swollen**
  - **ESR , +/- CRP**
  - **patient global health(0-10) zero is the best**

CHRONIC ARTHRITIS

Primarily , 40% of patients are RA

Seronegative spondyloarthropathies

Seronegative spondyloarthropathies 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 include the **absence of rheumatoid factor (RF)** and a strong genetic association with **HLA-B27.** Spondyloarthropathies disproportionately affect men, with symptom onset generally occurring before the age of 45. The cardinal sign is slowly progressive pain in the lower back and sacroiliac joints (especially at night). **Asymmetrical oligoarthritis and enthesopathy are also common**. The diseases differ in the involvement of other organs, such as the eyes, the genitourinary tract (particularly in reactive arthritis) or the skin(particularly in psoriatic arthritis). Seronegative spondyloarthropathies usually respond well to NSAID therapy.

Types of seronegative spondyloarthropathies

- Ankylosing spondylitis
- Reactive arthritis
- Psoriatic arthritis
- Spondyloarthritis associated with inflammatory bowel disease

Common features

- **Associations** [1]
  - Negative for rheumatoid factor /anti CCP
  - Genetic association with **HLA-B27**
- **Epidemiology**
  - Generally more commonly affect men
  - Age of onset: typically between 20–40 years of age

A-PAIR of conditions is commonly associated with HLA-B27: **A**nkylosing spondylitis, **P**soriasis, **A**cute anterior uveitis, **I**nflammatory bowel disease, **R**eactive arthritis.

CHRONIC ARTHRITIS

Primarily , 40% of patients are RA

Seronegative spondyloarthropathies

Common features

- **Clinical features** [1]
  - Arthritis
    - Particularly of the sacroiliac joints (especially for ankylosing spondylitis)
    - Asymmetrical peripheral oligoarthritis **except** for **PSORIATIC ARTHRITIS** which is involving the small joints (Distal interphalangeal joint) , Poly-arthritis(4 or more) and symmetrical (bilateral) involvement.
    - Stiffness and pain is worse in the **morning** (typically > 30 minutes) and improves with movement
  - Enthesitis or insertional tendinopathy (e.g., achillodynia)
  - Dactylitis: fingers have a **sausage-like appearance**
  - Extra-articular manifestations vary according to type, but involvement of the eye is common (e.g., iritis, iridocyclitis, uveitis) Lung (fibrosis) , Heart , Skin (psoriatic plaques).

HLA-B27 associations

- HLA-B27 is strongly associated with seronegative spondyloarthropathies and other autoimmune conditions:
  - Ankylosing spondylitis
  - Psoriatic arthritis
  - Acute anterior uveitis
  - IBD-associated ankylosing spondylitis
  - Reactive arthritis

Treatment :

If it's peripheral arthritis : treat it as RA
If it's axial (SI joint) : don't use DMARD or Methotreaxate , we use biological agents directly .

Ankylosing Spondylitis

- Three times more common in male than in female patients.
- Bilateral sacroiliitis is a prerequisite for making the diagnosis.
- Onset is in adolescence or young adulthood.
- It is characterized by “fusion” of the spine in an ascending manner (from lumbar to cervical spine).

Clinical Features

- Low back pain and stiffness (secondary to sacroiliitis)—limited motion in lumbar spine/ Neck pain and limited motion in cervical spine—occurs later in course of disease
- Enthesitis—inflammation at tendinous insertions into bone (Achilles tendon and supraspinatus tendon)
- Constitutional symptoms—fatigue, low-grade fever, weight loss
- Chest pain and diminished chest expansion—due to thoracic spine involvement
- Shoulder and hip pain—most commonly the peripheral joints are affected
- **Extra-articular manifestations**:
  - a. Eye involvement (most common)—acute anterior uveitis or iridocyclitis
  - b. Other extra-articular features are rare, but may involve the following systems: Cardiac (AV heart block and aortic insufficiency), renal, pulmonary, and nervous systems
- Restrictive pulmonary disease:
  - Due to decreased mobility of the thoracic spine and costovertebral joints
  - Secondary to apical pulmonary fibrosis or more widespread interstitial lung disease

Quick HIT

In ankylosing spondylitis, low back pain and stiffness are characteristically worse in the morning and better as the day progresses. They **improve with activity** and a hot shower and worsen with rest or inactivity.

Diagnosis

- Imaging studies of lumbar spine and pelvis (plain film, MRI, or CT) reveal sacroiliitis—sclerotic changes in the sacroiliac area. Eventually, the vertebral columns fuse, producing “bamboo spine”
- Elevated ESR in up to 75% of patients (due to inflammation)— nonspecific
- HLA-B27 is not necessary for diagnosis. Present in 8% of general population

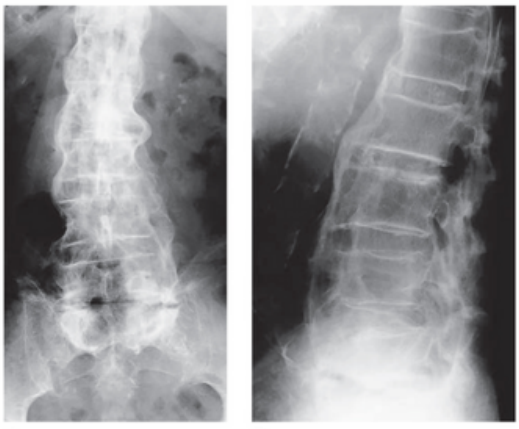


FIGURE 6-8 Anteroposterior (A) and lateral (B) radiographs of the lumbar spine in a patient with ankylosing spondylitis. This patient presented to the emergency department with increasing back pain after a motor vehicle collision. Careful review of the radiographs shows a cleft in the fusion mass at L5–S1. A bone scan confirmed increased activity at this level, which is indicative of a new fracture.

Treatment

- NSAIDs (indomethacin) for symptomatic relief
- If insufficient response, anti-TNF medications (etanercept, infliximab). For those with a contraindication to anti-TNF medications, an anti–IL-17 monoclonal antibody (e.g., secukinumab, ixekizumab) can be used
- Physical therapy (maintaining good posture, extension exercises)
- Surgery may be necessary in some patients with severe spinal deformity

Reactive Arthritis

- Reactive arthritis is asymmetric inflammatory oligoarthritis of lower extremities (upper extremities less common) (see Table 6-7). The arthritis is preceded by an infectious process that is remote from the site of arthritis (1 to 4 weeks prior), usually after enteric or urogenital infections.
- The triad of postinfectious arthritis, conjunctivitis, and urethritis was previously known as **Reiter syndrome**.
- It occurs mostly in HLA-B27–positive individuals.
- The organisms usually associated with reactive arthritis include those that cause GI or GU infections: Salmonella, Shigella, Campylobacter, Chlamydia, Yersinia.

She Cherishes Cooking Yummy Salmon: *Shigella*, *Chlamydia*, *Campylobacter*, *Yersinia*, and *Salmonella* are the most common causes for reactive arthritis.

Quick HIT

Reactive arthritis is a clinical diagnosis. If any patient has acute asymmetric arthritis that progresses sequentially from one joint to another, reactive arthritis should be in the differential diagnosis.

TABLE 6-7 Causes of Joint Pain

Polyarticular Joint Pain	Monoarticular Joint Pain
RA	Osteoarthritis
SLE	Gout
Viral arthritis	Pseudogout
Reiter syndrome	Trauma
Rheumatic fever	Septic arthritis
Lyme disease	Hemarthrosis
Gonococcal arthritis	
Drug-induced arthritis	

Quick HIT

The term **undifferentiated spondyloarthropathy** is used when a patient has features of reactive arthritis but there is no evidence of previous infection (in the GI or genitourinary tract) and the classic findings are absent.

Diagnosis

- Reactive arthritis is primarily a clinical diagnosis.
- Laboratory studies and imaging typically show nonspecific signs of inflammation.
- Further studies may be necessary to:
  - Identify underlying infections (e.g., via stool culture, urethral swabs)
  - Exclude differential diagnoses of reactive arthritis (e.g., rheumatoid factor, arthrocentesis and synovial fluid analysis)

Classic triad of reactive arthritis (seen in approximately one-third of affected individuals): "can't see (conjunctivitis), can't pee (urethritis), can't climb a tree (arthritis)". [8]

Treatment

- Acute reactive arthritis
  - Management is primarily supportive as reactive arthritis is typically self-limiting.
  - Identify and treat underlying infections, e.g., genitourinary chlamydia.
  - Refer patients to rheumatology and physiotherapy.
  - **NSAIDs**: first-line treatment for all symptomatic patients.
  - Glucocorticoids: indicated in patients with inadequate response or contraindications to NSAIDs
- Chronic reactive arthritis (i.e., persistence of symptoms > 6 months) or severe disease: DMARDs (e.g., sulfasalazine) may be required.

Psoriatic Arthritis

- Develops in 10% to 30% of patients with psoriasis.
- It is typically gradual in onset. Patients usually have skin disease for months to years before arthritis develops.
- Usually asymmetric and polyarticular. Characteristic dactylitis ("sausage digits") and nail pitting may also be present.
- Upper extremities most often involved; smaller joints more common than large joints.
- Initial treatment is NSAIDs, but persistent arthritis may require methotrexate or anti-TNF agents. Steroids are typically not used.

Accompanying features [10]

- Enthesitis, e.g., of the calcaneal tendon or the plantar fascia [10]
- Dactylitis: inflammation and swelling of the fingers and/or toes ("sausage digits") [10]
- Tenosynovitis
- Nail involvement (e.g., pitting, onycholysis) [2][10]
- Uveitis [10]

In PsA, patterns of joint involvement can change over time and vary widely between patients. Oligoarthritis tends to be more common at onset, while polyarthritis may develop in later stages. [10]

26.62 The CASPAR criteria for psoriatic arthritis

Inflammatory articular disease (joint, spine or enthesis) with ≥ 3 points from the following (1 point each unless stated):

- Current psoriasis (scores 2 points)
- History of psoriasis in first- or second-degree relative
- Psoriatic nail dystrophy
- Negative IgM rheumatoid factor[1]
- Current dactylitis
- History of dactylitis
- Juxta-articular new bone[2]

Treatment [11][13]

Pharmacological treatment [11][13]

- **Disease-modifying antirheumatic drugs** (DMARDs): mainstay of treatment for most patients with PsA.
- **NSAIDs**, e.g., naproxen, indomethacin:
  - May be trialed as initial treatment in patients with very mild disease (limited evidence of efficacy)
  - Can also be prescribed for symptomatic relief
- **Intraarticular glucocorticoids**: used for symptomatic relief

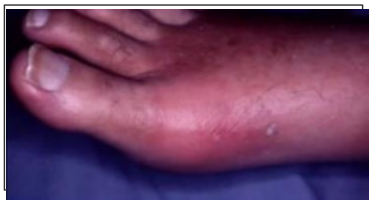
Supportive management [13]

- Encourage lifestyle modifications.
  - Smoking cessation
  - Low-impact physical activity
  - Maintaining a healthy weight
- Recommend physical therapy and occupational therapy.

Crystal Induced Arthritis

Definition

A type of inflammatory arthropathy caused by crystal deposition within or around joints and characterized by pain and swelling of the affected joints. Gout, caused by articular deposition of monosodium urate crystals, is the most common type, followed by calcium pyrophosphate deposition disease and basic calcium phosphate crystal deposition disease.



Types

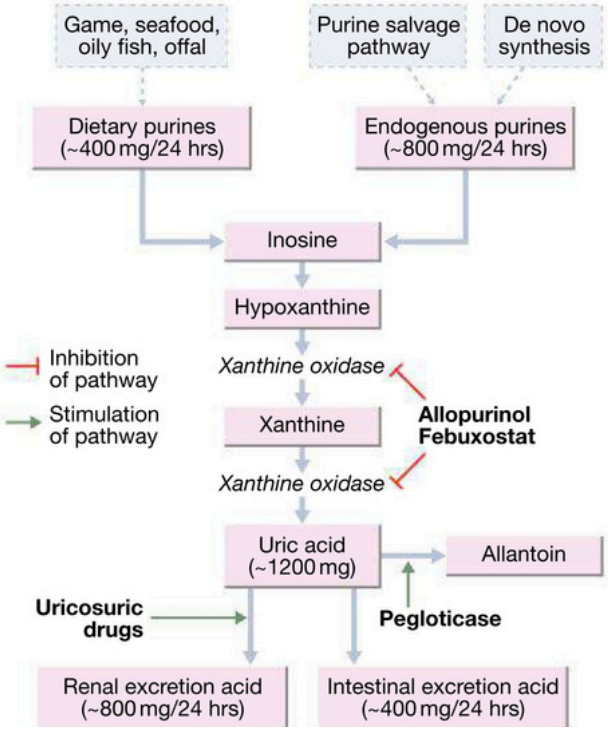
Three types of crystals can induce "crystal induced arthritis"

1- Mono-sodium urate causing **gout**

2- Calcium pyrophosphate causes **pseudogout**

3- Hydroxy-appetite crystals

Basics (للاستزادة في الفهم، غير مطلوب)



Purins (as adenine and guanine)converted into hypoxanthin. hypoxanthine converted by XO (xanthine oxidase, which play important pharmacological role) into xanthin, and then XO convert xanthin into uric acid, which is the defintive cause of gout.

Gout

- Gout is an inflammatory crystal arthropathy caused by the precipitation and deposition of uric acid crystals in synovial fluid and tissues.
- It is typically associated with hyperuricemia, but can also occur if uric acid levels are normal.

• Uric acid

-An end-product of purine metabolism that is excreted by the kidne

-Has somewhat poor water solubility

-Predisposes to gout

So one of complications of gout and hyperuricemia is tubular nephropathy, and one of causes of accumulation of uric acid related to low excretion by lowering kidney function, by both medecations or kidney functiona abnormalities

Etiology

Definitive cause is: **hyperuricemia**, which devided as:

1. **Primary hyperuricemia:** mainly idiopathic (may be triggered by poor dietary habits)
2. **Secondary hyperurecemia:** mainly due to to insufficient excretion or increased production of purines

Secondary hyperurecemia

Due to:

1. Decreased uric acid excretion: most common cause

- Medications (e.g., pyrazinamide, aspirin, loop diuretics, thiazides, niacin)
- Chronic renal insufficiency, lead nephropathy
- Ketoacidosis (due to, e.g., starvation, diabetes mellitus) and lactic acidosis
- postmenopause:

Estrogen promotes renal uric acid excretion. Postmenopausal women have decreased estrogen levels and are therefore more likely to develop gout.

2. Increased uric acid production

- High cell turnover →

Lysis of cell = DNA breakdown = more purines

eg:
- Tumor lysis syndrome
- Hemolytic anemia
- Psoriasis
- Myeloproliferative neoplasms
- Chemotherapy, radiation

- Obesity:

(Higher BMI correlates with higher uric acid levels, regardless of dietary habits)

- Hypercholesterolemia, hypertriglyceridemia
- Diet rich in protein and especially purine (e.g., red meat, seafood) [Calcium-poor diets may also contribute to hyperuricemia]
- Hypertension
- Sleep apnea:

(Hyperuricemia occurs as a result of respiratory acidosis and hypoxia secondary to sleep apnea)

- Enzyme defects →

Eg:
- Lesch-Nyhan syndrome
- Phosphoribosyl pyrophosphate synthetase overactivity
- Von Gierke disease

- Hemolytic anemia →

Hemolysis of RBCs does not increase uric acid levels, 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.

3.Combined decreased excretion and overproduction: high alcohol consumption

- Organic acids from alcohol metabolism compete with uric acid to be excreted by the kidneys.
- Many alcoholic beverages contain a high level of purines.

Imagine drugs associated with gout: AS a Guy painfully walking THe NIce PYRamid LOOP trail: aspirin, thiazides, niacin, pyrazinamide, loop diuretics.

Triggers of urate crystal deposition

- ↑ Uric acid levels (due to insufficient excretion or increased production of purines)
- Acidosis
- Low temperature (e.g., cool peripheral joints)

How attacks occur? breife pathophysiology

Crystalline arthritis: supersaturation of uric acid in extracellular fluid → intraarticular uric crystal precipitation (coated by IgGs) → phagocytosis by polymorphonuclear cells → release of inflammatory mediators and enzymes → local joint inflammation

Chronic effects: repeated attacks → aggregations of urate crystals and giant cells (tophi) → deformities and arthritis

26.42 The main causes of hyperuricaemia and gout

Diminished renal excretion	
• Increased renal tubular reabsorption*	• Drugs: Thiazide and loop diuretics, Low-dose aspirin, Ciclosporin
• Renal failure	• Pyrazinamide
• Lead toxicity	• Cancer chemotherapy
• Lactic acidosis	• ACE inhibitors
• Alcohol	
Increased intake	
• Game	• Offal
• Shellfish	• Red meat
Increased production	
• Myeloproliferative and lymphoproliferative disease	• Inherited disorders: Lesch–Nyhan syndrome (HPRT mutations), Phosphoribosyl pyrophosphate synthetase 1 mutations
• Psoriasis	
• High fructose intake	
• Glycogen storage disease	

*Usually genetically determined (see text).
(ACE = angiotensin-converting enzyme; HPRT = hypoxanthine guanine phosphoribosyl transferase)

Epidemiology

- Sex: m > f (3:1) / (5:1 – davidson)
- Age of onset: 2 peaks of incidence (at 30–39 years and at 60 years of age).
- Prevalence: 8 million people in the US.

Notes:

(زيادة توسع للي بحب، من Davidson)

Crystalloid arthropathy:

symptoms occur by 2 causes:

1. Inflammatory cause:

- The inflammatory potential of crystals resides in their physical irregularity and high negative surface charge, which can induce inflammation and damage cell membranes.
- They can reside in cartilage or tendon for years without causing inflammation or symptoms and it is only when they are released that they trigger inflammation.
- This may occur spontaneously but can also result from local trauma, rapid changes in the concentration of the components that form crystals, or in association with an acute phase response triggered by intercurrent illness or surgery
- In the longer term, a reduction in concentrations of the solutes that form crystals causes dissolution of crystals and remission of the arthritis.

2. Mechanical cause:

Crystals may also cause mechanical damage to tissues and act as wear particles at the joint surface.

Uric acid and Gout:

- About one-third of the body uric acid pool is derived from dietary sources and two-thirds from endogenous purine metabolism.
- Elimination of uric acid occur by the kidneys (two-thirds) and gut (one-third).
- The risk of developing gout increases with age and with serum uric acid (SUA) levels.
- SUA levels are higher in men, increase with age and are positively associated with body weight.
- Although hyperuricaemia is a strong risk factor for gout, only a minority of hyperuricaemic individuals actually develop gout.

Clinical features

The classical presentation is with an acute monoarthritis (joint pain affect single joint), which affects the first MTP (metatarsophalangeal, most coomon site, important for differentiation) joint in over 50% of cases.

Typical features include: مهم جدا

- rapid onset, reaching maximum severity in 2–6 hours, worse in the early morning.
- severe pain, often described as the 'worst pain ever'.
- extreme tenderness, so the patient is unable to wear a sock or to let bedding rest on the joint.
- marked swelling with overlying red, shiny skin.
- self-limiting over 5–14 days, with complete resolution.

Clinical presentation of gout divided into 4 stages as described here:

1 Asymptomatic stage	2 Acute gouty arthritis	3 Intercritical stage
- Hyperuricemia with no symptoms -May last ⩾ 10 years	- Have signs of gout and pain which described above. for specific information see next picture here from amboss.	- Stage between 2 attacks. - Asymptomatic. - May last up to several years

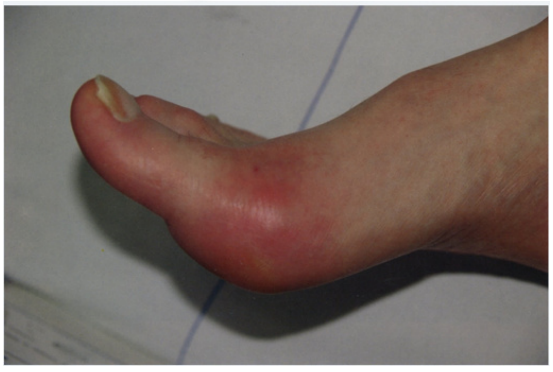
4 Chronic gouty arthritis

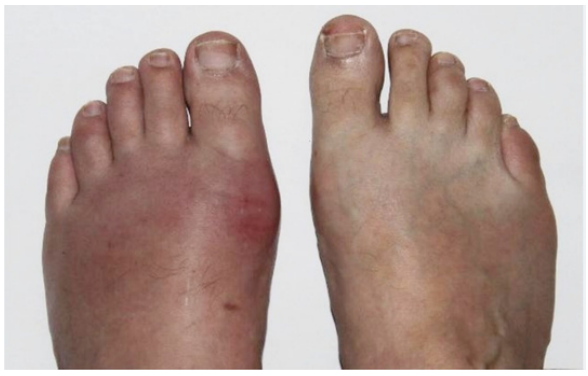
- Uncommon in these times (Appears in cases of inadequate treatment over a long period of time (i.e. after several years of attacks).
- Progressive joint destruction (Due to recurring gout attacks and deposition of urate crystals next to joints. They typically develop several years after the onset of disease.)
- Tophi formation (Due to urate crystal deposition in and around the joints)
- Renal manifestations with uric acid nephrolithiasis and uric acid nephropathy

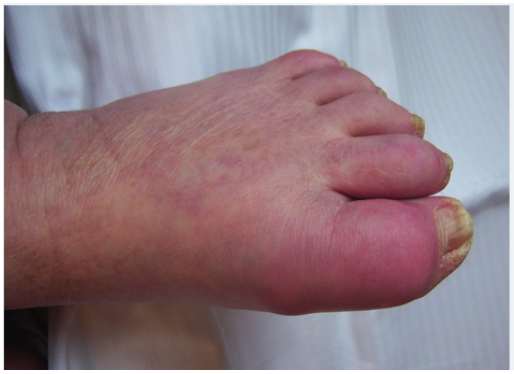
Acute gout:

- Triggers
  - Sudden increase in uric acid, e.g.,: consuming a large amount of purine-rich foods or alcohol (see risk factors for gout)
  - Trauma, surgery
  - Diuresis
  - Dehydration
- Most common manifestation
  - Acute severe pain with overlying erythema, decreased range of motion, swelling, warmth
  - Possibly fever
  - Symptoms are more likely to occur at night, typically waking the patient.
  - Symptoms peak after 12-24 hours and regress over days to weeks. [10]
  - Desquamation of the skin overlying the joint may be seen during the recovery from an acute gout flare.
- Location
  - Usually monoarthritis during first attacks
  - In < 20% of cases, patients present with polyarthritis during first attacks.
  - Asymmetrical distribution is common if more than one joint is affected
  - Peripheral small joints in the lower extremities are especially affected.
  - Podagra: metatarsophalangeal joint (MTP joint) inflammation of the big toe (the most common site)
  - Gonagra: inflammation of the knee
  - Chiragra: inflammation of finger joints, especially metacarpophalangeal joint of the thumb
  - Others: ankle, tarsus, other toe joints, wrist, elbow

Podagra



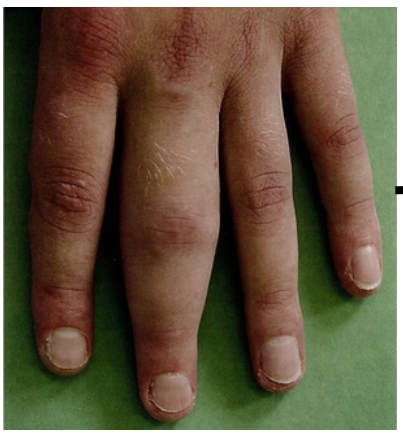




Erythema and swelling can be seen in the area of the first metatarsophalangeal joint (MTPJ) of this patient's left foot.

First MTPJ inflammation (podagra) is a characteristic presentation of acute gouty arthritis.

Chiragra



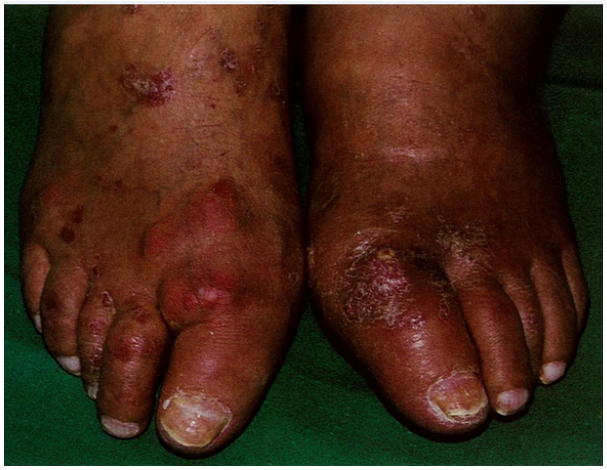
Severe swelling of the proximal interphalangeal joint of the left middle finger

Tophi

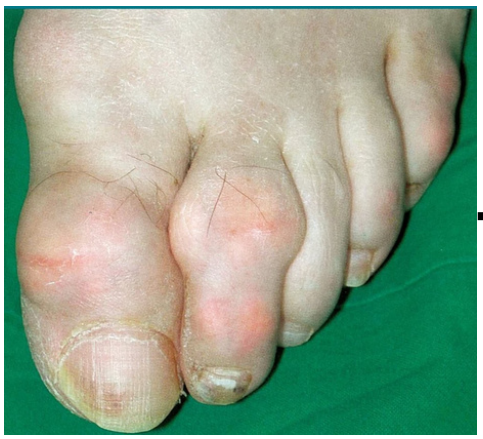
- Multiple painless hard nodules with possible joint deformities.
- May appear yellow or white because of overlying attenuated skin.
- Ulceration and discharge (chalky white substance) may occur

May be as:

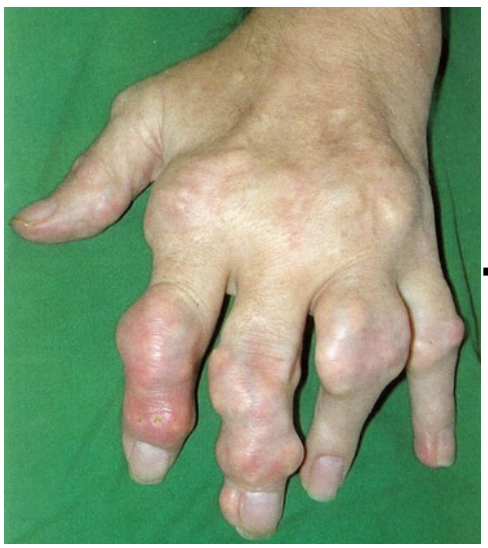
1.Bone Tophi: urate crystal deposition in bones (e.g., elbows, knees, extensor surfaces of forearms)



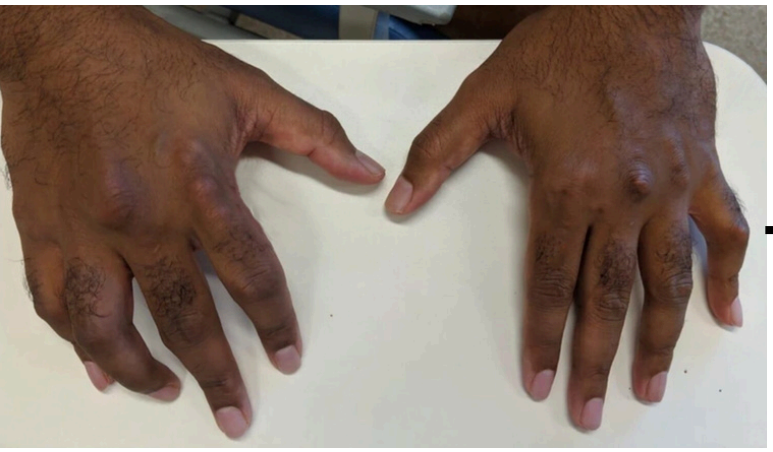
Multiple gouty tophi can be seen bilaterally in the region of the metatarsophalangeal joint of the big toe.
In this patient, the tophi developed secondary to increased uric acid production in psoriasis.



White chalky, nodules in the first and second toes (left)

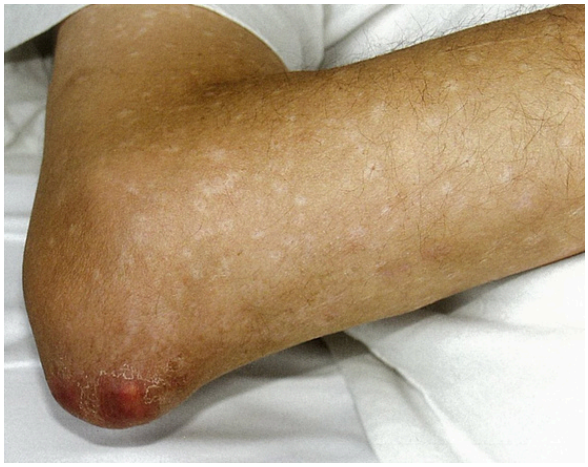


Tophi (monosodium urate crystal deposition in bones and soft tissues) are visible distributed irregularly in the fingers and metacarpus of this patient's left hand.



The dorsum of both hands shows multiple gouty tophi in the area of the metacarpophalangeal joints (MCP).
The proximal interphalangeal joints (PIP) appear swollen.

2.Soft tissue tophi: urate crystal deposition in the pinna of the external ear, subcutis, tendon sheaths (e.g., at the Achilles tendon), or synovial bursae (e.g., olecranon bursa)

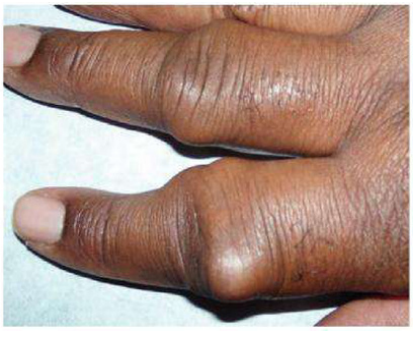


Painless, hard, soft, white chalky nodules in the bursa of the right elbow in a patient with gout.

Notes:

(زيادة توسع للي بحب، من Davidson)

- As the attack subsides, **pruritus and desquamation** of overlying skin are common.
- **Simultaneous polyarticular attacks are unusual.**
- The presentation of gout in old age may be atypical, with chronic symptoms rather than acute attacks (mainly associated with OA, long term diuritic therapy use)
- **Tophi have a white colour** (next picture), differentiating them from rheumatoid nodules.
- Occasionally, tophi may develop in the absence of previous acute attacks, especially in patients on thiazide therapy who have coexisting OA.



Tophi over the proximal interphalangeal joints of the hands

Dignosis

Parts of diagnostic approach:

1. Clinical diagnosis
2. Arthrocentesis and synovial fluid analysis:
   the gold standard for diagnosing gout
3. Laboratory studies:
   Serum uric acid level, CBC and inflammatory markers, Urinary uric acid measurement.
4. Imaging:
   Ultrasound, X-ray, Dual-energy CT

1. Clinical diagnosis of acute gout → without synovial fluid analysis

A clinical diagnosis of acute gout can be considered in patients who fulfill all of the following parameters:

- Typical clinical presentation.
- Low suspicion for septic arthritis.
- Monoarthritis.

The diagnostic rule for acute gout can improve diagnostic accuracy for patients with acute monoarthritis

The diagnostic rule for acute gout has not been validated for patients with oligoarthritis or polyarthritis. Although other clinical decision rules have been developed, this one is the most widely accepted.

Diagnostic rule for acute gout [17][18]

	Criterion	Number of points
Patient characteristics	Male	2
	≥ 1 of the following: hypertension, angina, MI, CHF, TIA, stroke, PVD	1.5
	History of previous arthritis attack	2
Features of current attack	Onset within 24 hours	0.5
	Joint erythema	1
	Affects 1st metatarsophalangeal joint	2.5
	Serum uric acid level > 5.88 mg/dL (0.35 mmol/L)	3.5

Interpretation

- ≤ 4 points: relatively low likelihood of gout; consider differential diagnoses of gout.
- > 4 but < 8 points: intermediate likelihood of gout; consider synovial fluid analysis, if feasible
- ⩾ 8 points: relatively high likelihood of gout; see "Treatment" section

2. Arthrocentesis and synovial fluid analysis

Synovial fluid analysis is the gold standard for diagnosing gout

Indications:

- Uncertain clinical diagnosis ⟶
- Higher probability of septic arthritis

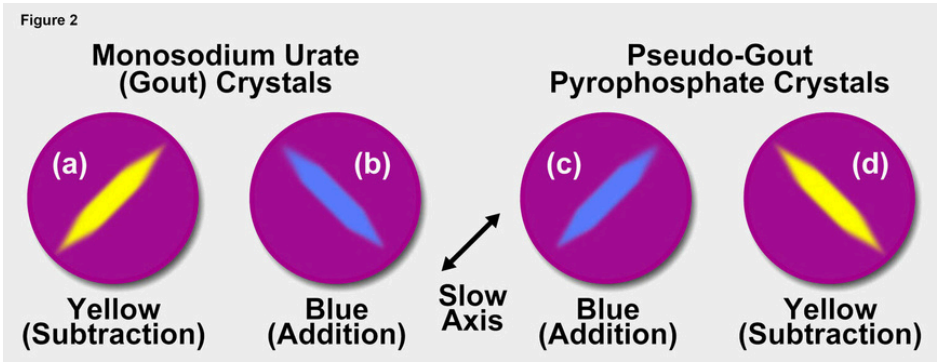
E.g., atypical presentation, lack of response to empiric treatment

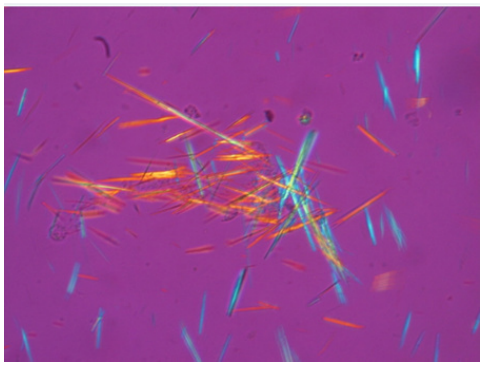
Characteristic findings:

- Polarized light microscopy:

needle-shaped monosodium urate crystals that are negatively birefringent

- Crystals appear yellow when their optical axis is oriented parallel to the polarizer.
- Crystals appear blue when their axis is perpendicular to the polarizer.





- Synovial fluid cell count:

WBC > 2000/µL with > 50% neutrophils (see "Interpretation of synovial fluid analysis")

- Gram stain:

negative; useful for ruling out septic arthritis

3. Laboratory studies

- Serum uric acid level:

The normal range of serum uric acid levels varies according to age and sex. The normal range of serum uric acid levels for an adult male is 3.7–8.0 mg/dL and for an adult female is 2.7–6.1 mg/dL.

- Acute gout flare: often elevated (hyperuricemia), may also be normal or low.
- Intercritical stage or chronic gout:

Baseline levels are useful to determine the need for urate-lowering therapy. A normal or low level has a very low negative likelihood ratio for (but does not rule out) a diagnosis of gout.

Notes

- There is no universally accepted serum uric acid level for diagnosing hyperuricemia. Hyperuricemia is typically diagnosed when serum uric acid levels are > 8.0 mg/dL in men or > 6.1 mg/dL in women.
- Consider CPPD as a differential diagnosis in patients with normal serum uric acid levels.
- Serum uric acid levels are not always elevated in acute gouty arthritis.

– CBC and inflammatory markers:

WBC and ESR are typically elevated in an acute gout attack.

– Urinary uric acid measurement

4. Imaging:

Imaging is indicated if synovial fluid analysis is unsuccessful or cannot be performed, and the diagnosis remains uncertain. It can be used to identify supportive findings of gout but cannot rule out septic arthritis

– Ultrasound:

- Signs of acute joint inflammation.
- Bone erosions.
- Signs of urate crystal deposition:

1- Double contour sign:

a hyperechoic band of crystals covering the surface of the hypoechoic articular cartilage, which is over the hyperechoic bone contour

2- Tophi

Arthrocentesis and synovial fluid analysis is recommended if septic arthritis is suspected.

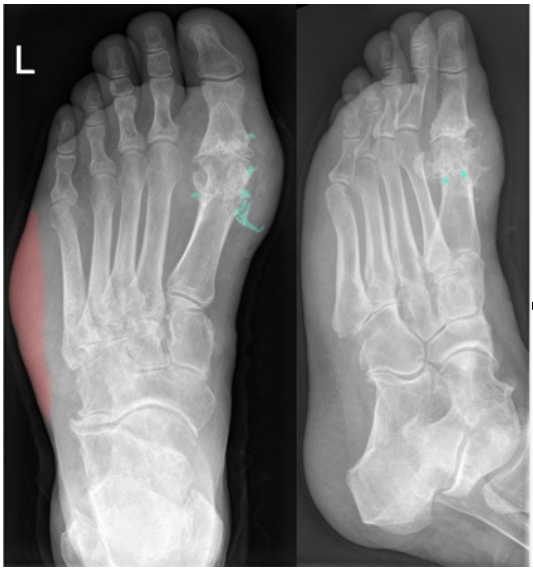
– X-ray:

Acute gout:

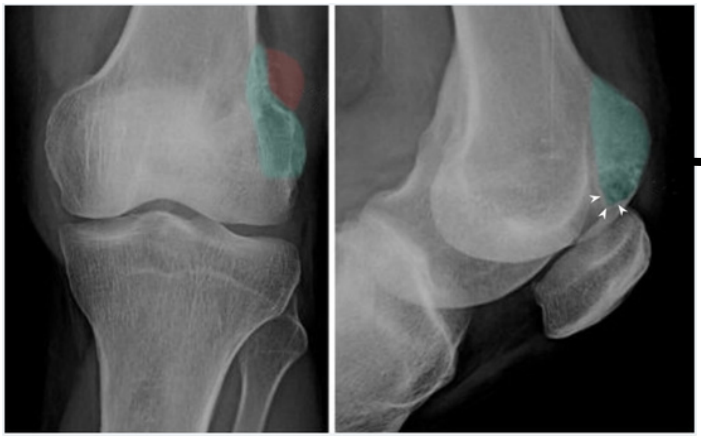
typically normal; useful for ruling out a fracture in patients with posttraumatic joint inflammation

Chronic gout:

• Punched-out lytic bone lesions with spiky periosteal appositions (overhanging edges), known as "rat-bite erosions".
• Radiopaque in surrounding soft tissue. → Due to calcified urate crystal deposition
• Joint space is preserved until late stages.



X-ray of a left foot (AP and lateral views)
Joint space narrowing of the first metatarsophalangeal joint with multiple spiky periosteal appositions (green overlay). Both the first metatarsal bone and the first proximal phalanx also show the characteristic "punched-out" lesions (green arrowheads). There is marked soft tissue swelling on the lateral border of the foot (red overlay).



X-ray knee (left: AP view; right: lateral view) of a patient with a history of gout

An eccentric lesion involves the lateral femoral condyle (green overlay) and adjacent soft tissues (red overlay). A sclerotic margin is seen along part of the lesion (arrowheads).

- Dual-energy CT (DECT):

- A modified CT technique in which urate crystals are color-coded, allowing for easier identification.
- can detect crystals within deeper anatomical structures (e.g., the spine) and extra-articular sites.

Notes

- The sensitivity of ultrasound for urate crystals is lower in early disease.
- Ultrasound or DECT are preferred imaging modalities to detect MSU crystal deposition within affected joints.

Differential Diagnosis:

– Septic arthritis:

presentation of septic arthritis is with acute or subacute monoarthritis and fever, so may confused with gout.

Clinical presentation

- The joint is usually swollen, hot and red, with pain at rest and on movement.
- Although any joint can be affected, lower limb joints, such as the knee and hip, are most commonly targeted

Etiology

- **Staphylococcus aureus**:
• Most common in adults and children > 2 years
• Frequently found in patients with arthritis following invasive joint procedures
- **K. kingae**:
most common in infants and children ⩽ 2 years
- Streptococci.
- Gram-negative rods esp. E. coli and P. aeruginosa .
Immunosuppressed state, trauma, elderly, IV drug use
- N. gonorrheae:
Most common in sexually active young adults (♀ > ♂)
- S. epidermidis.
- **H. influenzae:**
Was the most common cause in children but is now uncommon due to Haemophilusvaccination
- M. tuberculosis and atypical mycobacteria:
Rare but important causes of chronic indolent septicarthritis
- B. burgdorferi (Lyme disease)

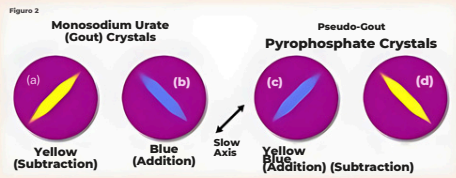
– Pseudo gout (CPPA):

discussed at end of this topic as separate topic.

– Osteoarthritis (OA):

discussed at end of this topic as separate topic.

Gout vs Septic arthritis

	Gout	Septic Arthritis
Clinical Epidemiology	● Inflammatory arthritis (mono- or polyarticular) due to uric acid crystal deposition within joints or tissues ● Most common inflammatory arthritis in men • Obesity, alcohol, dietary purines, chronic renal insufficiency are risk factors	•Acute arthritis due to an infection, commonly bacterial; from hematogenous seeding • Predisposing factors include: older age, previous joint pathology, skin infection, diabetes mellitus • Intravenous drug use (IVDU) assoc with unusual organisms (pseudomonas) & joint involvement (sternoclavicular)
Symptoms	- Episodic acute joint pain (maximum pain within 24 hours). - 90% monoarticular | 50% involves the 1st MTP joint in the foot. - Can be precipitated by surgery, trauma, alcohol use, systemic infection. -50% have recurrent attacks within one year. - May be associated with tophi (chalky deposits of urate crystals in soft tissues)	- Abrupt onset of joint pain & swelling are present in the majority of patients - The knee is the site of involvement in 50% of cases - Fever only present in - 57% - Signs of inflammation and pain with both active and passive ROM
Joint Fluid Analysis	 - Crystals in joint fluid are diagnostic - May have high WBC counts (> 50, 000 WBC/mm3) similar to septic arthritis	- Staphyloccus aureus (most common in all age and risk groups) - Commonly associated with high WBC counts (> 50, 000 WBC/mm3); > 100,000 WBC/mm3 virtually diagnostic
Lab Studies	- Hyperuricemia (gout) | commonly > 9 mg/dl - Uric acid levels commonly normal during an acute attack	↑ WBC count & acute phase reactants (sedimentation rate and C-reactive protein) are common
Radiographic Findings	- Common negative aside from soft tissue swelling - Note chondrocalcinosis (calcium in the articular cartilage) is pathognomic for pseudogout	Common negative aside from soft tissue swelling

treatment & management of gout

treatment will described as:

1. General measures → These apply to chronic gout management and prevention of an acute gout flare.

2. Acute gout

3 Chronic gout

1. General mesures:

- **Limit alcohol consumption**
- **Limit intake of purines (e.g., red meat and shellfish)**
- **Limit high-fructose corn syrup (e.g., sugary foods, juices, and non-diet sodas)**
- **Weight loss if patient is overweight**

2. Acute gout:

approach containing:

- **Nonpharmacological measures**: rest and ice the affected joint.
- **Pharmacotherapy**: Initiate within 24 hours of onset.

Pharmacotherapy:

- **First-line agents:** glucocorticoids, NSAIDs, or colchicine (described in detail below).
- Consider initiating urate-lowering therapy in select patients.
- If a patient is on long-term urate-lowering therapy, it should be continued during the treatment of an acute gout flare.
- Avoid combining NSAIDs with systemic glucocorticoids. If prescribed together, add a proton pump inhibitor to reduce the risk of gastrointestinal ulcers.

1.Glucocorticoid

A type of corticosteroid hormone produced naturally in the adrenal glands. Synthesized versions are used therapeutically to treat allergic, neoplastic, and autoimmune conditions, among other conditions. Commonly used agents include prednisolone, hydrocortisone, dexamethasone, and beclometasone.

Administration:

1. Systemic administration:

-Oral (e.g., prednisone or prednisolone)

-Parenteral or intramuscular (e.g., methylprednisolone) if NPO.

2. Intraarticular administration:

Consider if there are 1–2 joints that are accessible and a trained provider is available.

Note: Glucocorticoids are preferable if there are contraindications (e.g., CKD), intolerance, or inadequate response to colchicine or NSAIDs.

2.NSAIDs:

- Naproxen or an alternative (e.g., indomethacin, ibuprofen).
- Treat for shortest duration necessary to resolve symptoms (often at least 3–5 days).

3.Colchicine:

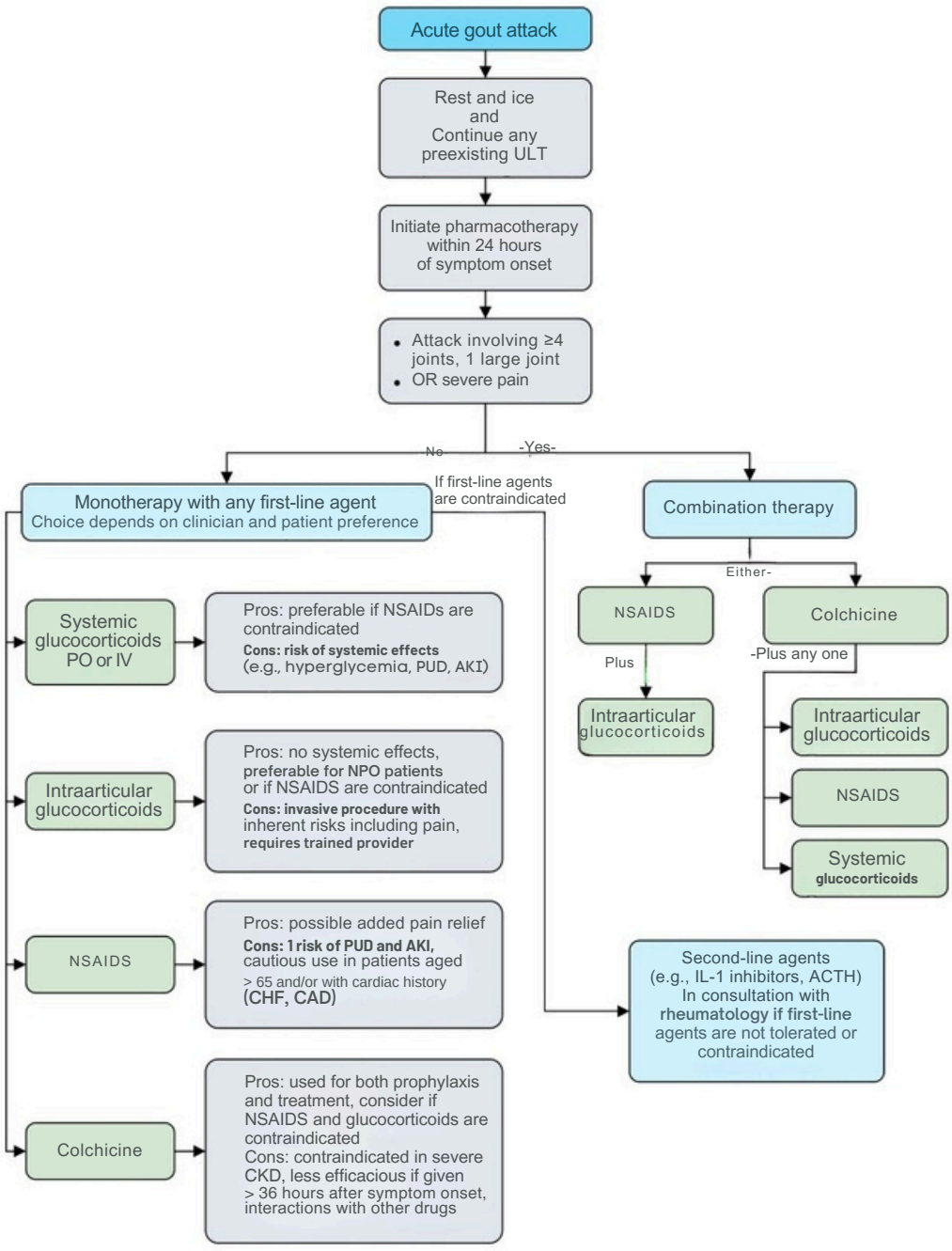
Mechanism of action: binds and stabilizes tubulin subunits → inhibits microtubule polymerization → inhibits phagocytosis of urate crystals, neutrophil activation, migration, and degranulation

Adverse effects:

- Gastrointestinal symptoms, e.g., diarrhea, nausea, vomiting, and abdominal pain, are the most common.
- Rhabdomyolysis , myopathy
- Polyneuropathy
- Cardiac toxicity, arrhythmias
- Nephrotoxicity
- Myelosuppression

CNS symptoms (e.g., fatigue, headache)

Colchicine is unlikely to be effective when initiated > 24–36 hours after symptom onset. Colchicine is preferable in patients who cannot tolerate NSAIDs or systemic glucocorticoids (e.g., patients with gastrointestinal ulcers)



3. Chronic gout:

Approach

1. Urate-lowering therapy (ULT) is recommended for chronic gout.

First-line: xanthine-oxidase inhibitors (allopurinol)

Second-line: uricosurics (probenecid)

Third-line: recombinant uricase (pegloticase)

2. Administer anti-inflammatory prophylaxis before initiating ULT as ULT may trigger, prolong, or worsen an acute gout flare

1. Initial anti-inflammatory prophylaxis:

- Indication: pre-treatment in patients planned for ULT therapy
- Important consideration: should be initiated 1 week before starting ULT therapy
- Options:
  - Colchicine
  - NSAIDs (e.g., naproxen)
  - Glucocorticoids (e.g., prednisone)

{ Administering XOIs or uricosuric agents during an acute gout flare may worsen symptoms by mobilizing urate crystals. Anti-inflammatory prophylaxis with colchicine, NSAIDs, or glucocorticoids must be administered before initiating ULT. }

2. Urate-lowering therapy (ULT):

Indication:

1. Absolute indications

- Damage due to chronic gout seen on imaging
- Tophi development
- Frequent gout attacks (≥ 2 per year)

2. Relative indications

- if < 2 gout attacks per year
- First episode of acute gout flare in patients with any of the following risk factors:
  - CKD ≥ stage 3
  - Serum uric acid > 9 mg/dL
  - History of urolithiasis

26.44 Indications for urate-lowering drugs

- Recurrent attacks of acute gout
- Evidence of bone or joint damage
- Tophi
- Renal impairment
- Nephrolithiasis
- Chemotherapy-related hyperuricemia

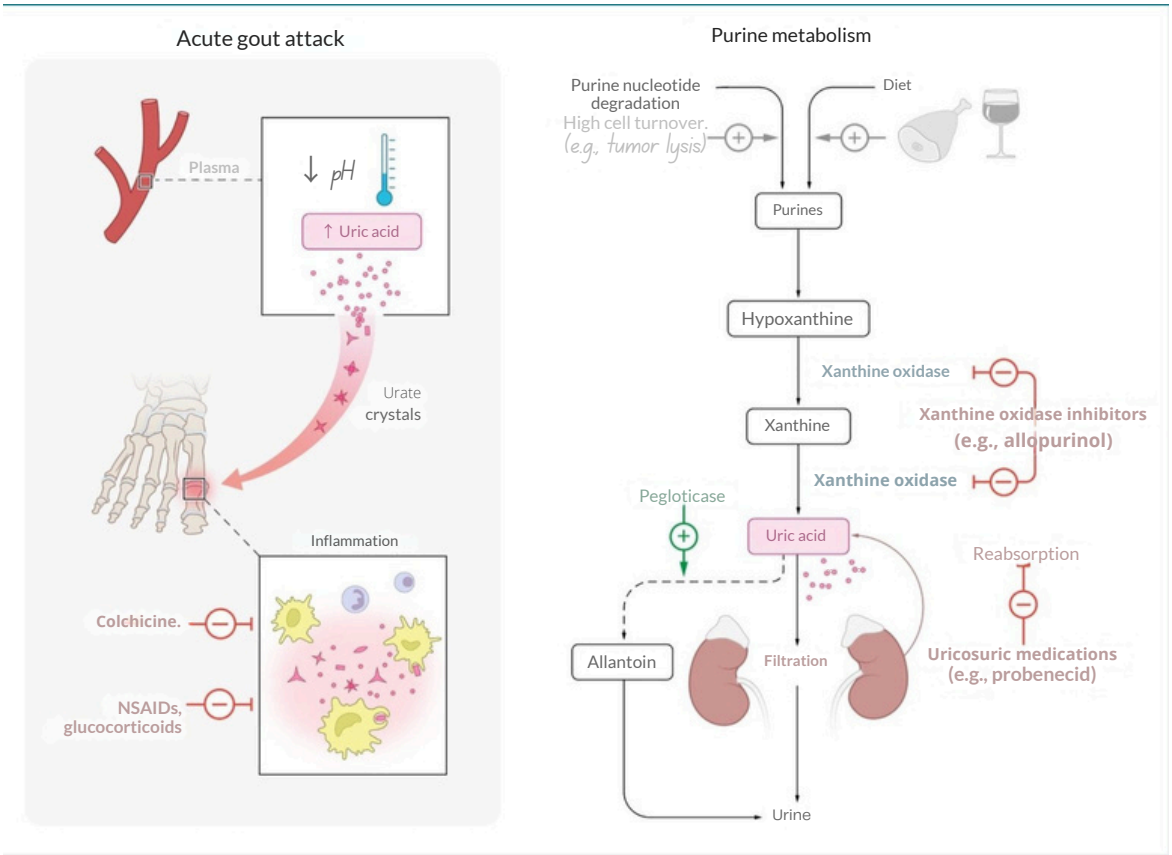
Contraindications:

1. Common to all ULT agents

- Acute gout flare (in the absence of the above-mentioned risk factors)
- Asymptomatic hyperuricemia

2. Specific contraindications

- Allopurinol: Previous hypersensitivity reaction.
- Probenecid: nephrolithiasis & Moderate to severe CKD (nephropathy)
- Pegloticase: G6PD deficiency



Notes about treatment:

- The long-term therapeutic aim is to prevent attacks occurring by bringing SUA below the level at which monosodium urate monohydrate crystals form. A therapeutic target of < 300 μmol/L (5 mg/dL) is recommended.
- Acute flares of gout often follow initiation of urate-lowering therapy. The patient should be warned about this and told to continue therapy, even if an attack occurs. The risk of flares can be reduced by prophylaxis with oral colchicine (0.5–1 mg daily) or an NSAID for the first few months.
- The combination of allopurinol and azathioprine leads to increased bone marrow toxicity.
- there are important gout therapy drug interactions (مش حنحطهم بالدوسية للتخفيف)

Complications of Gout:

- Nephrolithiasis: uric acid stones
- Uric acid nephropathy
    - Acute uric acid nephropathy
        - Can occur in tumor lysis syndrome
        - Causes tubular obstruction → acute renal failure
    - Chronic uric acid nephropathy: a form of chronic tubulointerstitial nephropathy with monosodium urate crystal deposition in the stroma of the kidney, which causes inflammation
        - Clinical features
            - Hypertension
            - In rare cases, progressive renal failure

Summary
(From Amboss)

Gout is an inflammatory crystal arthropathy caused by the precipitation and deposition of uric acid crystals in synovial fluid and tissues. Decreased renal excretion and/or increased production of uric acid leads to hyperuricemia, which is commonly asymptomatic but also predisposes to gout.

Acute gout flares typically manifest with a severely painful big toe (podagra) and occur most often in men following triggers such as alcohol consumption.

Diagnosis is based on clinical presentation and, ideally, by the demonstration of negatively birefringent monosodium urate (MSU) crystals on synovial fluid analysis.

Acute attacks are treated with corticosteroids, NSAIDs (e.g., naproxen, indomethacin), or colchicine. The management of chronic gout includes lifestyle modifications and urate-lowering medications (e.g., allopurinol) to control hyperuricemia.

Acute calcium pyrophosphate crystal deposition (CPPD) disease, sometimes referred to as pseudogout, is another crystal arthropathy that resembles an acute gout flare and is managed similarly. It is covered in detail in a separate article.

Calcium pyrophosphate deposition (CPPD) disease

inflammatory arthritis seen primarily in individuals over age 60. [Epidemiology]

It results from the deposition of calcium pyrophosphate dihydrate (CPP) crystals within articular cartilage. [Crystal type]

While it is typically idiopathic, it may also be caused by joint damage, various metabolic abnormalities, or a genetic predisposition. [Etiology]

CPPD disease can be asymptomatic or manifest with acute or chronic symptoms.
Pseudogout refers to acute CPP crystal arthritis, which typically presents as sporadic flares of monoarticular synovitis affecting a large joint and can last for much longer than a typical gout flare.
Chronic CPP crystal arthritis has many clinical phenotypes, the most common of which resembles severe osteoarthritis. [Clinical picture & DDx]

Identification of CPP crystals on synovial fluid analysis or on imaging in a patient with typical symptoms confirms the diagnosis. [Dx]

Treatment is primarily symptomatic and consists of antiinflammatory medications (including intraarticular and systemic glucocorticoids, colchicine, and NSAIDs). There is currently no specific treatment targeted at CPP crystals. [Treatment]

CPPD will share here briefly for differentiation with Gout and OA, focusing on clinical considirations

Gout vs Pseudogout

Gout		Pseudogout
Male gender, impaired renal function, obesity, metabolic syndrome, dietary (red meat, alcohol, seafood), diuretics (thiazides), tumour lysis syndrome	Risk factors	Elderly, hyperparathyroidism, haemochromatosis, hypophosphataemia, osteoarthritis
Acute monoarthropathy typically in MTP of first toe (podagra)	Acute presentation	Acute monoarthropathy typically of knee
Monosodium urate	Crystal	Calcium pyrophosphate
Negatively birefringent needle crystal	Polarised light	Weakly positive birefringent rhomboid crystal
Well-defined 'punched-out' periarticular erosions	X-ray findings	Chondrocalcinosis
• 1st line: NSAID • 2nd line: Colchicine* • Prophylaxis: Allopurinol (do not start during an acute attack)	Treatment	• 1st line: NSAID • 2nd line: Colchicine*

*Use in patients with CKD/HF where NSAIDs are contraindicated
*Stop when diarrhoea develops

PROJECT

Quick HIT

Presentation of pseudogout is similar to gout, but typically occurs in larger joints (knee).

Osteoarthritis (OA)

Osteoarthritis is a disabling joint disease characterized by degeneration of the joint complex (articular cartilage, subchondral bone, and synovium) that can have various causes, most notably advanced age and overuse. [Description]
It mainly affects weight-bearing joints and joints that are heavily used, such as the hip, knee, hands, and vertebrae. [Joint affected]

[Etiology]:
Despite the widespread view that osteoarthritis is a condition caused exclusively by degenerative "wear and tear" of the joints, newer research indicates that there are various causes, including preexisting joint abnormalities, genetics, local inflammation, mechanical forces, and biochemical processes that are promoted by proinflammatory mediators and proteases.

[Risk Factors]:
Major risk factors for osteoarthritis include advanced age, obesity, previous injuries, and asymmetrically stressed joints.

[Clinical picture]:
In early-stage osteoarthritis, patients typically report a reduced range of motion, joint stiffness, and pain that is aggravated with heavy use. As the disease advances, persistent pain may also be present during the night and/or at rest.

[Diagnosis]:
The diagnosis is predominantly based on clinical features and supported by radiological findings, as classic radiographic features of osteoarthritis do not always correlate with the patient's clinical symptoms or appearance.

[Mangagement]:
if lifestyle changes (e.g., moderate exercise, weight loss) fail to improve symptoms, pharmacotherapy is typically used for the management of active osteoarthritis. If these measures do not improve the patient's quality of life, surgical procedures such as arthroplasty may be necessary.

For more clinical details about clinical fetures and Dx or treatment of OA:

Clinical findings:

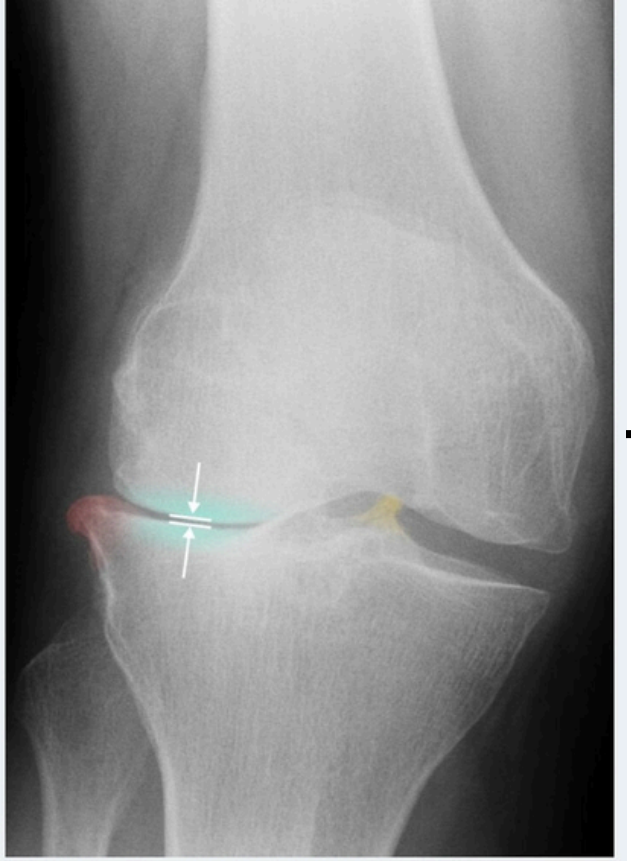
- Pain during or after exertion (e.g., at the end of the day) that is relieved with rest
- Pain in both complete flexion and extension-
- Crepitus on joint movement
- Joint stiffness and restricted range of motion
- Morning joint stiffness usually lasting < 30 minutes
- Possible formation of varus deformity if the knee is affected
- Joints are usually asymmetrically involved, as opposed to rheumatoid arthritis.
- Findings in late-stage disease: constant pain (including at night) and a more severely restricted range of motion than during the early stages

Diagnosis:

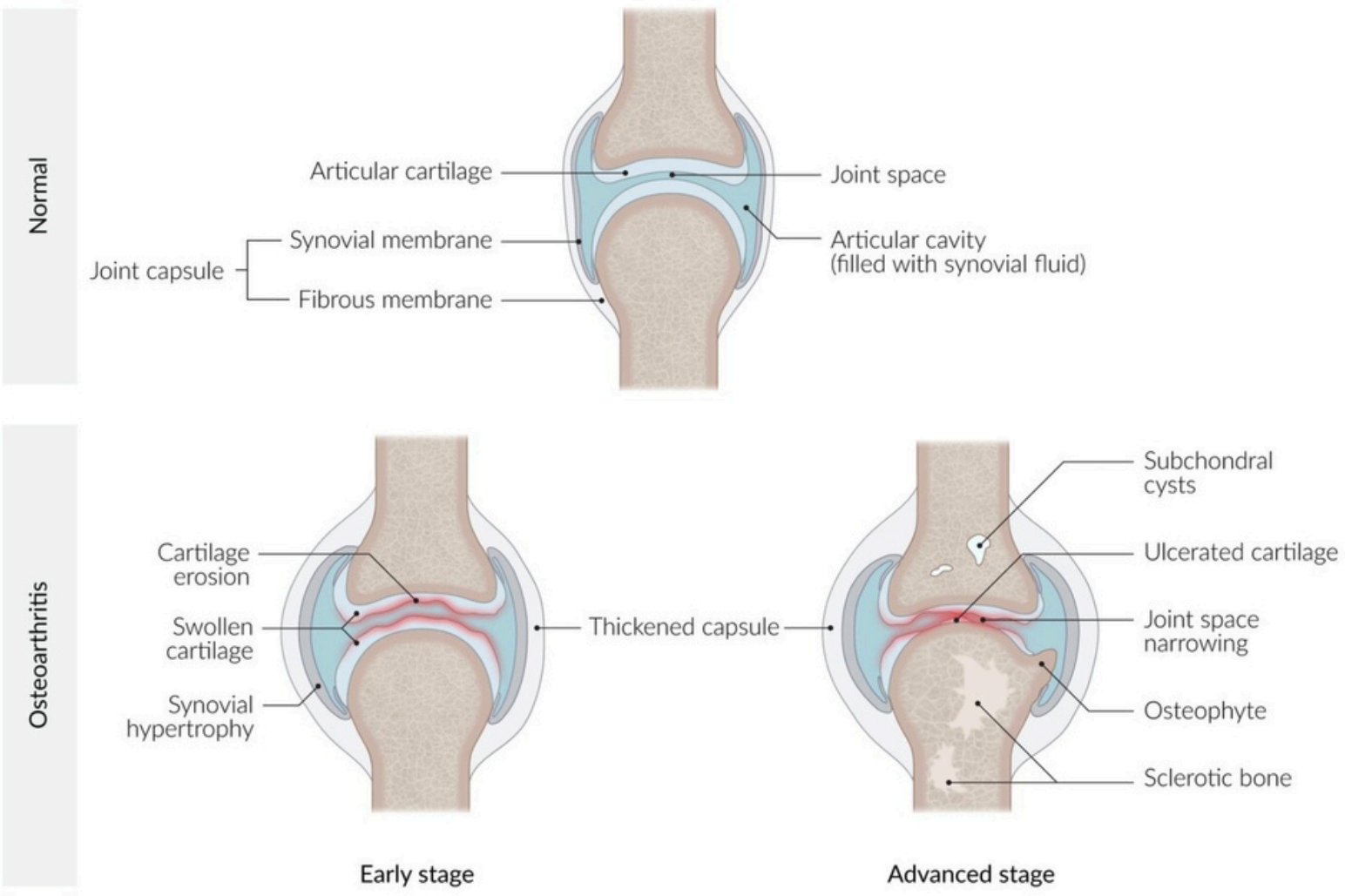
Osteoarthritis is often diagnosed based on the patient's history and the presence of typical clinical features. Radiographic signs often do not correlate with the patient's reported symptoms or clinical findings; therefore, imaging is usually used to support the diagnosis.

First-line modality: plain radiography of affected joints:

- Irregular joint space narrowing
- Subchondral sclerosis: a dense area of bone (visible on x-ray) just below the cartilage zone of a joint that forms as a result of a compressive load on the joint
- Osteophytes (bone spurs): spurs or densifications that develop on the edges of the joint, increasing its surface area
- Subchondral cyst: a fluid-filled cyst that develops on the surface of a joint due to local bone necrosis induced by the joint stress caused by osteoarthritis



Marked lateral compartment narrowing (indicated by white lines and arrows) is accompanied by subchondral sclerosis (green overlay) and osteophyte formation (red overlay). Tibial spine osteophytes (example indicated by yellow overlay) are also visible.



Treatment & management:

Approach has 3 considerations:

1. Nonpharmacological management:

as exercise (recommended for all patients) and weight loss (for overweight and obese patients).

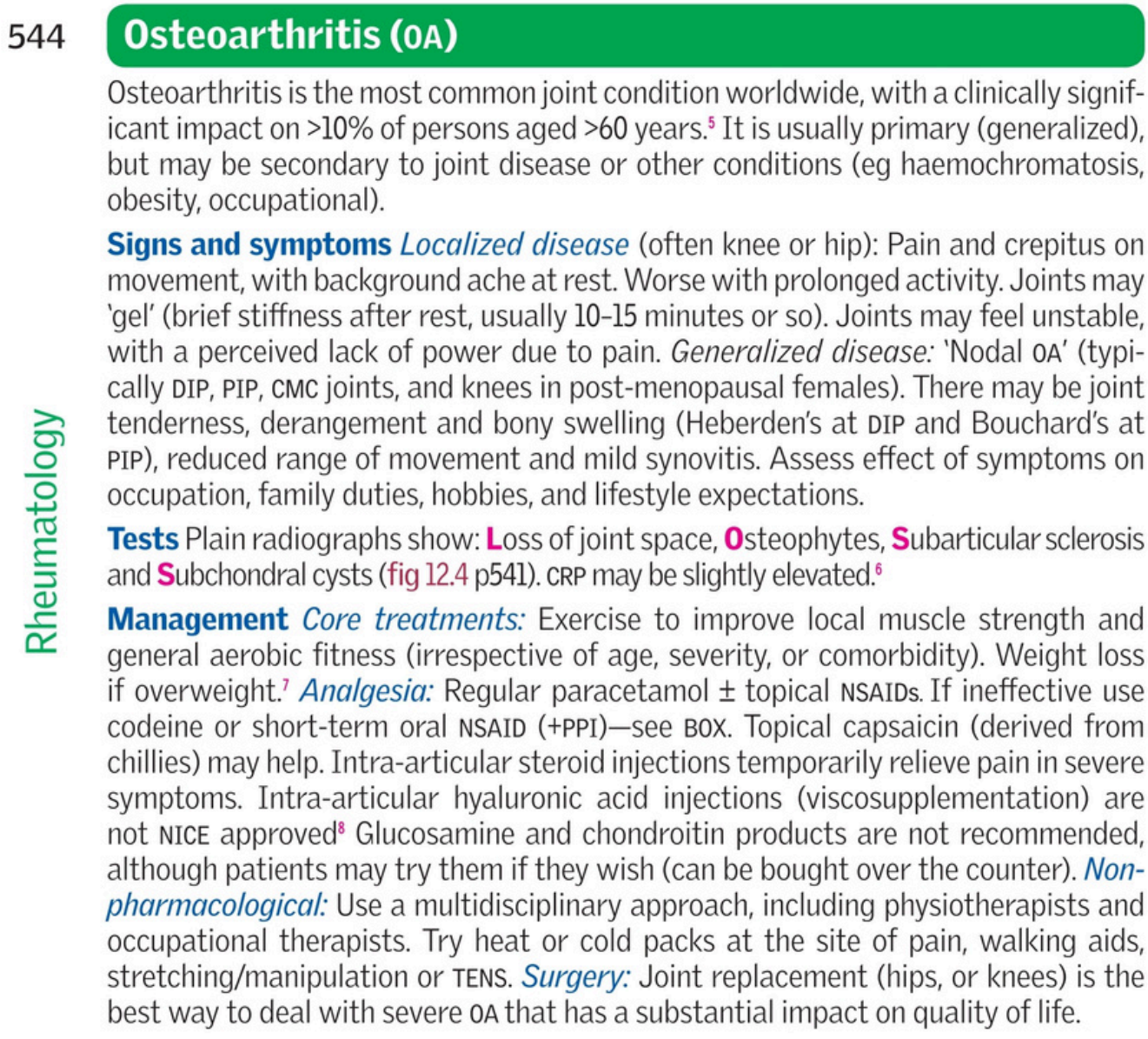
2. Pharmacotherapy:

- First line: e.g., topical or oral NSAIDs.
- Second line: e.g., acetaminophen or intraarticular glucocorticoid injections

3. Surgical management:

complete or partial joint replacement (arthroplasty) using an endoprosthesis

👇 oxford للاستزادة من كتاب



544 Osteoarthritis (OA)

Osteoarthritis is the most common joint condition worldwide, with a clinically significant impact on >10% of persons aged >60 years.[5] It is usually primary (generalized), but may be secondary to joint disease or other conditions (eg haemochromatosis, obesity, occupational).

Signs and symptoms *Localized disease* (often knee or hip): Pain and crepitus on movement, with background ache at rest. Worse with prolonged activity. Joints may 'gel' (brief stiffness after rest, usually 10–15 minutes or so). Joints may feel unstable, with a perceived lack of power due to pain. *Generalized disease:* 'Nodal OA' (typically DIP, PIP, CMC joints, and knees in post-menopausal females). There may be joint tenderness, derangement and bony swelling (Heberden's at DIP and Bouchard's at PIP), reduced range of movement and mild synovitis. Assess effect of symptoms on occupation, family duties, hobbies, and lifestyle expectations.

Tests Plain radiographs show: **L**oss of joint space, **O**steophytes, **S**ubarticular sclerosis and **S**ubchondral cysts (fig 12.4 p541). CRP may be slightly elevated.[6]

Management *Core treatments:* Exercise to improve local muscle strength and general aerobic fitness (irrespective of age, severity, or comorbidity). Weight loss if overweight.[7] *Analgesia:* Regular paracetamol ± topical NSAIDs. If ineffective use codeine or short-term oral NSAID (+PPI)—see BOX. Topical capsaicin (derived from chillies) may help. Intra-articular steroid injections temporarily relieve pain in severe symptoms. Intra-articular hyaluronic acid injections (viscosupplementation) are not NICE approved[8] Glucosamine and chondroitin products are not recommended, although patients may try them if they wish (can be bought over the counter). *Non-pharmacological:* Use a multidisciplinary approach, including physiotherapists and occupational therapists. Try heat or cold packs at the site of pain, walking aids, stretching/manipulation or TENS. *Surgery:* Joint replacement (hips, or knees) is the best way to deal with severe OA that has a substantial impact on quality of life.

Rheumatology

Comparison table: Gout vs Osteoarthritis

	Gout	Osteoarthritis
Overview	Redness and pain in the joint at the base of the big toe.	Impacts the tissue covering the ends of the bones in a joint.
Prevalence	Varies between populations.	68% of women and 58% of men over the age of 65.
Gender	More common in men and in women after menopause.	Before 50 more men than women, after 50 more women than men.
Symptoms	Joint pain usually around the big toe, joint discomfort, inflammation and redness, extreme tenderness, limited range of motion, development of tophi possible.	Joints painful (without swelling), affects joints asymmetrically, bigger joints such as hips & knees.
Causes	Occurs when urate crystals accumulate in your joints causing the inflammation.	Occurs when the cartilage that cushions the ends of bones in your joints gradually deteriorates.
Affected body parts	Joint of the big toe most commonly affected. Ankle, heel, knee, wrist, fingers, and elbow are also affected.	Finger joints closest to the fingernails or the thumbs, weight-bearing joints.
Complications	Recurrent or advanced gout, kidney stones.	Severe joint pain and stiffness, some people are no longer able to work.
Diagnosis	Imaging tests, drawing fluid from the swollen joint for analysis, blood tests.	X-ray, pain assessment, presence of deformity, evidence of muscle wasting, local inflammation.
Treatment	• Ice and elevate the joint. • Healthy diet low in purines (avoid alcohol, limit intake of meat). • Regular exercise. • NSAIDs, corticosteroids, colchicine (a painkiller), medications that target uric acid production or excretion.	• Gentle exercise – stretching, yoga, and tai chi. • Physical or occupational therapy. • NSAIDs (short term use), acetaminophen, analgesics.
Speed of onset	Sudden onset, often during the night.	Slow, over years.

Systemic Lupus Erythematous

Systemic :involve multi Systems.
Lupus: wolf like ugly looking rash
Erythematous : redness

Elevated with raised patches → discoid malar rash.
benign rash → **butterfly rash(malar rash)**

It's chronic multisystemic inflammatory disease , characterized by auto antibodies directed against self Ag , immune complex formation and immune Dysregulation resulting in damage any organ . T cells abnormality can induce b cells and result in variable auto antibodies

There are several kinds of lupus

1- ***Systemic lupus erythematosus (SLE)***
2- ***Discoid lupus erythematosus:*** is a chronic skin disorder in which a red, raised rash appears on the face, scalp, or elsewhere. may cause **scarring**
3- ***Subacute cutaneous lupus erythematosus:*** appear on sun exposed parts. **Not scarring**
4- ***Drug-induced lupus:*** presented atypically with systemic features and serositis (associated with anti-histone antibodies) and they typically go away completely when the drug is stopped. **The kidneys and brain are rarely involved.**
5- ***Neonatal lupus:*** rare disease in newborn babies of women with SLE, Sjogren's syndrome

Epidemiology:

- Sex: f > m (10:1) [1]
- Peak incidence and prevalence [1][2]
  - Age of onset
    - Women: 15–44 years
    - Men: no particular age
  - Race: highest in populations of African descen

Etiology :

The exact etiology is unknown, but several predisposing factors have been identified.

- **Genetic predisposition HLA-DR2 and HLA-DR3 are commonly present in individuals with SLE.**
- **Genetic deficiency of classical pathway complement proteins (C1q, C2, C4) in approx. 10% of affected individuals**

- **Hormonal factors: Hyperestrogenic states (e.g., due to oral contraceptive use, postmenopausal hormonal therapy, endometriosis) are associated with an increased risk of SLE.**
  - **Environmental factors Cigarette smoking and silica exposure increase the risk of developing SLE.**
  - **UV light and EBV infection may trigger disease flares, but there is insufficient evidence on whether they cause SLE.**
  - **Drugs such as procainamide or hydralazine**

TABLE 6-2 HLA Associations With Rheumatic Diseases

Disease	Associated HLA
SLE	HLA-DR2 and HLA-DR3
Sjögren syndrome	HLA-DR3
RA	HLA-DR4
Ankylosing spondylitis, Reiter syndrome, psoriatic arthritis	HLA-B27

Risk Factor :

1) female : -hormone (that's why increased in reproductive age from menarche to menopause * 16 -55 years in 65%] ,20 before 16 years , 15% after 65 years .

2) genetic : HLA DR2 , HLA DR3

3) kleinfelter : XXY male , 2 X chromosomes

4) UVR

5) infection esp. viruses

6)smoking -diet not affect lupus

7) pregnancy and ocp drugs (details later on)

8) lupus is a familial condition (mother to daughter) 1: 250 , As a twins : concordance rate of lupus if on twin get lupus 25-70% .

-Survival : 90% 10 years.

→ Antibodies spectrum correlates with SLE presentation→ variety clinical presentation

Clinical feature :

SLE is a systemic disease characterized by phases of remission and relapse. Some individuals only experience mild symptoms, while others experience severe symptoms and rapid disease progression. SLE can affect any organ.

constutional symptoms : general fatigu and fever and weakness.

1-skin :

Photosensitivity: skin rash as a result of unusual reaction to sunlight

malar rash over checks and bridge the nose :

*Malar rash(butterfly rash)

go w/o scar , benign lesion , little edema ,no raised edge , no hypo or hyper pigmentation no dermal atrophy .

***Discoid lesion can leave scar , treat it as a vital organ , raised edge , hypo or hyper pigmentation , dermal atrophy .**

2-Alopecia , patchy or diffuse alopecia and thin, friable hair may occur during acute SLE flares or as a medication side effect. (Permanent alopecia can occur)

3-Oral ulcer : (40%) usually painless and can occur on the hard palate, tongue, buccal mucosa, and gingival surfaces. Painless , 2-3 days will heal , superficial lesion .

4- Arthritis and arthralgia:
Non-erosive, symmetric; involving 2 or more small or large peripheral jointsIn contrast to rheumatoid arthritis, SLE has less morning stiffness and synovial thickening and usually does not lead to joint erosions or destruction
(< 10% of people with SLE will develop deformities of the hands and feet)

- Osteoporosis:
Risk factors: corticosteroids, smoking, early menopause, +ve family history

- Avascular necrosis:
Risk factors: steroids, hyperlipidemia, Raynaud's phenomenon, antiphospholipid antibodies, alcoholism.

5-Raynoud phenomenon : vascular response to cold or emotion

→White (vasospasm) then blue (deoxygenation) then red (local tissue acidosis will cause reactive vasodilatation) painful stage . this occure in 2,3,5 fingure thumb rarely (secondary Raynoud) . IF IT UNILATERAL MOST LIKELY SCLERODERMA.

6-Patechie Thrombocytopenia , vasculitis

7-Livedo reticularis (net like dilated blood vessels)

Ddx: 1. SLE 2. Vasculitis 3. Anti-phospholipids syndrome 4.Mixed CT disease

8-Renal finding →the most common cause of mortality and morbidity and affect 50% of the cases.
Common: an immune complex-mediated glomerulonephritis
Others: large-vessel vasculitis, interstitial nephritis, and renal tubular acidosis

-Glomerulonephritis:

I: Minimal change GN	- Mild **proteinuria**
II: Mesangioprolferative GN	- **Asymptomatic** hematuria or proteinuria - complete cure with **corticosteroid**
III: Focal proliferative GN	- Responds to treatment with **high doses** of corticosteroids
IV: Diffuse proliferative GN	- Treated with corticosteroids and immunosuppressive.
V: Membranous GN	- Characterized by **extreme edema** and **protein** loss
VI: Sclerosing GN	- Significant renal insufficiency (**RF**) in most cases - Not responding to medical therapy

used for prognosis .

→oliguria – proteinuria – edema – HTN - hematuria (RBC cast) so we have to do urine analysis for SLE patients .

9-Fever (so you have to exclude infection)

10-Serositis : pleurisy (stabbing , local. , increase with inspiration .) , phenomena , pleural effusion

11-Seizure (it happen because of renal(nephritic) , increase BP , so patient get HTN encephalopathy . (always in patient with seziure in SLE measure BP)

12-Hemolytic anemia and anemia of chronic disease:

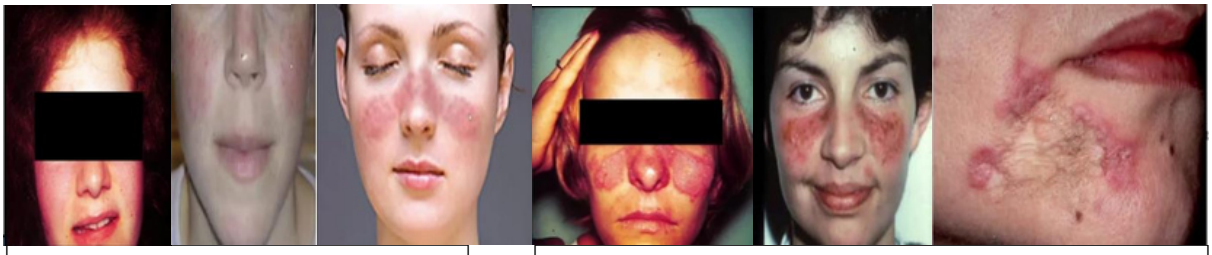
increase reticulocyte , diagnosed also by coombs test [+ve]) . leukopenia (decrease lymphocyte)

13-Aseptic endocarditis: (Libman-Sacks Endocarditis : immune complex non infected cause)

14-Psychosis , frequency 20-40 % , difficult to diagnose and treat , second to nephritis as most common cause of morbidity and mortality , can occur at any time even at first presentation .

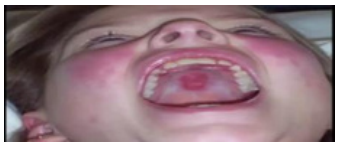
DDx: steroid overdose (rare).

15-lupus started with fatigue , fever , Weight Loss and affect other systems .

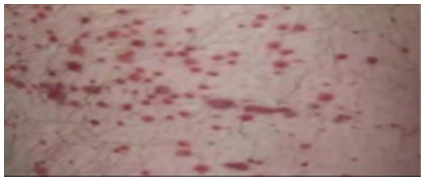


SIMPLE MALAR RASH

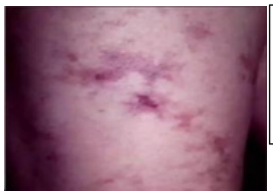
DISCOID MALAR RASH (scales with raised, edges that will heal with hypo or hyperpigmentation, resulting in dermal atrophy , follicular plugging and SCAR FORMATION



Malar rash with Lupus ulcer in the palate(painless , heals within few days)



RASH , Elevated rash ,Painful , Distributed over the lower limbs indicates Vasculitis.
Non –raised rash , Painless , Diffuse indicates Platelets' disorders.



Livedo Reticularis: Network of dilated blood vessels present in :SLE, Vasculitis, Mixed CT diseases, Anti-phospholipid syndromes.

Diagnosis :

- SLE is a clinical diagnosis**.**
- Diagnostic studies support the diagnosis and serve as markers of disease activity and/or organ damage.

Laboratory studies :

The following studies are commonly part of a minimum diagnostic workup if SLE is clinically suspected:

- **Antinuclear antibodies** (ANAs)Positive titers of ≥ 1:80 have 98% sensitivity for SLE (entry criterion for the 2019 EULAR/ACR classification criteria for SLE).If negative, consider differential diagnoses and/or follow-up with the patient regularly.
- **Antigen-specific ANAs:** Request only if ANAs are positive **:**
  - Anti-dsDNA antibodies
    - ✓ Autoantibodies against double-stranded DNA.
    - ✓ Positive in 60–70% of patients.
    - ✓ Highly specific for SLE.
    - ✓ Levels correlate with disease activity (especially lupus nephritis activity).
  - Anti-Sm antibodies
    - ✓ Autoantibodies against Smith antigens .
    - ✓ Positive in < 30% of patients, but highly specific for SLE .
- **Antiphospholipid antibodies:** Screen all patients for antiphospholipid syndrome.
- **Laboratory markers of disease activity and/or organ damage in SLE**
  - o Complement levels: ↓ C3 and/or ↓ C4 in patients with active disease .
  - o Inflammatory markers :
    - ✓ ESR: may be elevated in patients with active disease.
    - ✓ CRP: often normal (may be elevated in patients with serositis, arthritis,or. infections).
  - o CBC: may show leukopenia, thrombocytopenia, and/or autoimmune hemolytic anemia or anemia of chronic disease .
  - o CMP: may show ↑ BUN and/or creatinine, and/or electrolyte abnormalities .
  - o Urinalysis and urine microscopy: may show proteinuria, hematuria, and/or urinary casts .

NOTE : RPR and VDRL are usually used to test for syphilis but may also be positive in SLE.

- **Antihistone Abs (in 70%)** : are present in >95% of cases of drugin duced lupus. If negative, drug-induced lupus can be excluded
- **Ro (SS-A) and La (SS-B)** are found in 15% to 35%. Associated with:

Sjögren syndrome, Subacute cutaneous SLE , Neonatal lupus (with congenital heart block), Complement deficiency (C2 and C4), ANA-negative lupus

Diagnosis by SLE CRITERIA :

Criterion	Definition
1. Malar rash	Fixed malar erythema, flat or raised
2. Discoid rash	Erythematous raised patches with keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash as an unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulcers, usually painless, observed by physician
5. Arthritis	Nonerosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling, or effusion
6. Serositis	a. Pleuritis (convincing history of pleuritic pain or rub heard by physician or evidence of pleural effusion) *or* b. Pericarditis (documented by electrocardiogram, rub, or evidence of pericardial effusion)
7. Renal disorder	a. Persistent proteinuria (> 0.5 g/day or > 3 +) *or* b. Cellular casts of any type
8. Neurologic disorder	a. Seizures (in the absence of other causes) or b. Psychosis (in the absence of other causes). Look for renal involvement ❼ HTN encephalopathy . ➔ In the absence of offending drug ,or known metabolic derangement .
9. Hematologic disorder	a. Hemolytic anemia *or* b. Leukopenia (< 4000/µL on two or more occasions) *or* c. Lymphopenia (< 1500/µL on two or more occasions) *or* d. Thrombocytopenia (< 100,000/µL in the absence of offending drugs)
10. Immunologic disorder +Ve ANA with at least one of :	-Anti–double-stranded DNA *or* b. -Anti-Sm -Positive finding of antiphospholipid antibodies based on (1) an abnormal serum level of immunoglobulin G or M anticardiolipin antibodies, or (2) a positive test result for lupus anticoagulant using a standard method, or -False-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test
11. Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any time and in the absence of drugs known to be associated with "drug-induced lupus syndrome"

10+11 → serology . 1-9 → clinical . NOTE : In 2019 they added fever.

→At least 2 clinical criteria and +ANA and another serological markers (anti ds DNA activity of SLE SPEC.60-80% , anti SMITH SPEC.30% ,anti phospholipid). 4/11

Sensitivity 96% , specificity 96% , in children 100%.

ANA give result -,+ so it diagnostic not used in follow up .BUT anti ds DNA num. used in follow up +UA ,CBC . ESR CRP, .

New SLICC criteria can dx only by :

✓ +ANA and ,Lupus nephritis by biopsy (membranous GN).

Biopsy of an affected organ (e.g., skin, kidney) can be performed to support the diagnosis but is not required for all patients.

Cause of deaths : 3 time more than healthy person , the highest rate in the first 5 years .

✓ Acute renal failure (renal involvement most prognostic factor)
✓ Infections 25% : indication for admission .
✓ Thrombosis 26%
✓ Sepsis and septic shock
✓ Pulmonary hemorrhage , plasma exchange for TTP or diffuse alveolar bleeding
✓ Active lupus 26%

Patients with SLE have double the cardiovascular risk compared to patients without SLE. Cardiovascular disease is among the most common causes of death in patients with SLE.

Disease severity :

- Mild disease (no vital organs affected): e.g., constitutional symptoms, mild arthritis rash and/or cytopenias .
- Moderate disease (no vital organs affected): e.g., cutaneous vasculitis, serositis,RA-like arthritis, moderate rash and/or cytopenias, or no response to standard therapy .
- Severe or organ-threatening disease: e.g., nephritis, myelitis, pneumonitis, mesenteric vasculitis, severe cytopenias .

Managements :

- Patients with SLE usually require life-long immunosuppressants. Management is guided by disease severity and the systems or organs affected (see also “Specific clinical manifestations”).
- Patients should be frequently monitored for medication-induced adverse effects.

- NSAIDs can provide symptomatic relief. [9]
- Nonpharmacological measures include:
  - Lifestyle modifications for ASCVD prevention (e.g., smoking cessation, aerobic exercise)
  - Avoidance of UV light
- If applicable, optimize management of ASCVD and offer preconception counseling (see also “SLE and pregnancy”).

All patients: **Hydroxychloroquine** is the cornerstone of therapy (regardless of disease activity).

- o Reduce inflammation, protect against organ damage
- o Remission joint , skin and B. vessels involvements
- o Anti lipidemic , Safe in pregnancy
- o SE [Contraindications] : Hyperpigmentation , Myopathy in RF , Retinal and corneal toxicity (halos around lights and photophobia, annual fundoscopy is necessary)

Mild to moderate disease (no vital organs affected): Consider the addition of oral glucocorticoids with or without other immunosuppressive agents to achieve remission.

S**evere or organ-threatening disease :**

- Induction therapy :
  - High-dose IV glucocorticoids and other immunosuppressive agents .
  - Used until symptom remission or low disease activity is achieved .

- **Maintenance of remission** :
  - Hydroxychloroquine with or without lower dose glucocorticoids .
  - AND/OR immunosuppressants or biological agents .

- **Disease flares**: Adjust therapy based on the severity of organ involvement

Prevention and monitoring for medication-induced adverse effects :

- All patients: Offer influenza and pneumococcus immunizations

- Hydroxychloroquine: request ophthalmologic screening at baseline, after 5 years, and yearly thereafter

- Glucocorticoids and immunosuppressants :
  - ✓ Assess for infection.
  - ✓ Monitor for side effects of glucocorticoid therapy

Biological therapy :

Belimumab [Belimta] →to reduce remission

Suppress B cell development (Rituximab) + block B-cell stimulation. We don't use Methotrexate .

Note :

- Treat infection > aggressively , no infection in lupus should go home.
- Malar rash 1. Avoid sun exposure • 2. local steroid
- Avoid NSAID cause interstitial nephritis . diag. by eosinophile in urine.
- Anti-malarial drugs (hydroxychloroquine) keep the patient in remission
- vaccination : if influnza active

Drug-induced SLE: Hydralazine , Procainamide , Quinidine , Methyldopa , Chlorpromazine , Isoniazid.

Not all lupus are SLE , could be : chronic discoid lupus erythema , subacute cutaneous lupus erythema , drug induced lupus .

Which prognosis is better ? SLE or Drug induced lupus ? Drug induced is Better than other SLE , Affect male and female (equal ratio) , No CNS and Renal involvements , -ve ANA and –ve Anti ddDNA ,Treatable with cessation of drug (remission within 3-6 months).

SLE and pregnancy : (worsen with pregnancy)

★Not affect fertility but have higher rates of abortion, premature labor and intrauterine death (esp. with Anti-Phospholipid Syndrome) .

Not affect fertility (as Antiphospholipid antibody syndrome), Worsen with pregnancy so ; If the female is stable (4-6 months S & S-free) > get pregnancy , But if develop any manifestation prevented pregnancy

The pregnancy can induce exacerbation so the patient have renal failure and she can lose her kidney , Avoid sun, smoking, infection . SLE can flare postpartum .should be controlled at least 4 months prior to pregnancy

Neonatal/congenital SLE with Anti SSA/RO : Less than 1%-2% , following pregnancies 20% ☹ , Congenital AV-block (bradycardia) IN ICU , Neonatal rash , Treated by antibiotics and vaccines , +Anti-jo-1 Ab.

- Management :
  - Pregnancy planning and counseling [26]
    - Medical treatment should not be discontinued but the drug regimen may be changed. Preconception, pregnancy, and breastfeeding: hydroxychloroquine and/or azathioprine
    - Disease flares: hydroxychloroquine and/or prednisolone
    - Low-dose aspirin from 12 weeks' gestation reduces the risk of preeclampsia. [27]
    - Teratogenic immunosuppressive drugs (e.g., methotrexate, mycophenolate, cyclophosphamide) should be avoided.

- Avoid estrogen-containing hormonal contraceptives in patients with antiphospholipid syndrome because of the increased risk of thrombosis.
- Educate patients of reproductive age about contraceptive methods, planned pregnancy, and the potential teratogenic effects of pharmacological treatment.

- Anti SSA/RO : anti–Sjögren's-syndrome-related antigen A autoantibodies.
- +Ve ANA Life long , so it's for diagnosis not for follow upppp or activity assessment !!!
- Disease Activity assessed by : Fever , hemolysis , anemia , arthritis , pleurisy , pericarditis ,
- increased ESR , CRP , active sediment in urine .

Anti-phospholipide syndrome : DVT , thrombocytopenia , recurrent miscarriage.

Neonetal Lupus Syndrom :

- Etiology: associated with the transfer of maternal antibodies (anti-Ro/SSA and anti-La/SSB)
- Clinical features
  - First- to third-degree congenital AV block
  - Periorbital or diffuse rash (often presents in the first weeks after birth)
  - Cytopenia
  - Hepatitis, elevated liver enzymes
- Diagnostics
  - The following two criteria must be present at birth:
    - Antibodies (anti-Ro/SSA or anti-La/SSB) in either the mother or child
    - Heart block, characteristic rash, and/or hematologic/hepatic involvement with no identifiable cause in the newborn/fetus
- Treatment: directed at specific organ involvement
- Prognosis: Symptoms usually resolve within a few months.

Neonatal lupus syndrome

Antiphospholipid syndrome :

- Def.: Multisystem vasculopathy manifested by recurrent thromboembolic events, **spontaneous abortions** and **thrombocytopenia.**

- **Types:**

1- Primary APS: no detectable causes (Associated with genetic marker HLA-DR7)

2- Secondary APS develops in: SLE (most common), other connective tissue diseases, malignancy, drugs (hydralazine, procainamide, phenytone, interferon, quinidine), infections (HIV, hepatitis C, TB, infectious mononucleosis)

Pathophysiology :

- **Formation of procoagulatory antiphospholipid antibodies** :

- Antibodies form complexes with anticoagulant proteins, thereby inactivating them (e.g., protein C, protein S, antithrombin III**).**

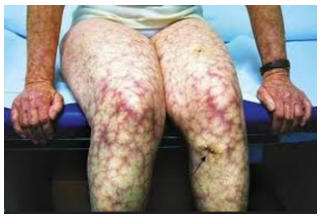
- Antibodies activate platelets and vascular endothelium.

- **Induction of a hypercoagulable state → ↑ risk of thrombosis and embolism**

Clinical features :

APS usually manifests with recurring thrombotic events that may affect any organ.

- **Venous** :
  - Deep venous thrombosis
  - pulmonary embolism
  - ulceration
  - livedo reticularis →



- **Arterial :**
  - stroke and TIA
  - Occlusion of organ arteries (e.g., myocardial infarction)
  - Occlusion of distal extremity arteries (ischemia and gangrene)
- **capillaries :** splinter hemorrhage
- **Pregnancy-related: recurrent miscarriages and premature births**
- **Nonthrombotic manifestations:** may include valvular heart disease, neurocognitive disorders

Diagnosis :

- Consider diagnostic testing based on the presence of typical symptoms, e.g.: Thrombotic complications , Recurrent miscarriages
- Obtain antiphospholipid antibody testing to confirm diagnosis.
- Consider testing for associated autoimmune diseases (e.g., SLE), neoplasms, and infectious diseases.
- Involve rheumatology early.

Thrombosis in APS is typically unprovoked (e.g., unprovoked DVT), recurrent, and/or manifests in unusual sites (e.g., kidneys, liver, retina). It is most commonly seen in younger individuals (< 50 years of age) and in individuals with comorbid autoimmune diseases (e.g., SLE).

- **Routine laboratory studies** :

Obtain for all patients; results are nonspecific but may support the diagnosis.

- CBC
  - Thrombocytopenia
  - Leukocytopenia
  - Hemolytic anemia (may be AIHA or MAHA)
- CMP: may reveal laboratory evidence of hemolysis and/or nephropathy
- Coagulation panel: prolonged aPTT (caused by lupus anticoagulant)
- Urinalysis: may show proteinuria, e.g., in patients with thrombotic microangiopathy

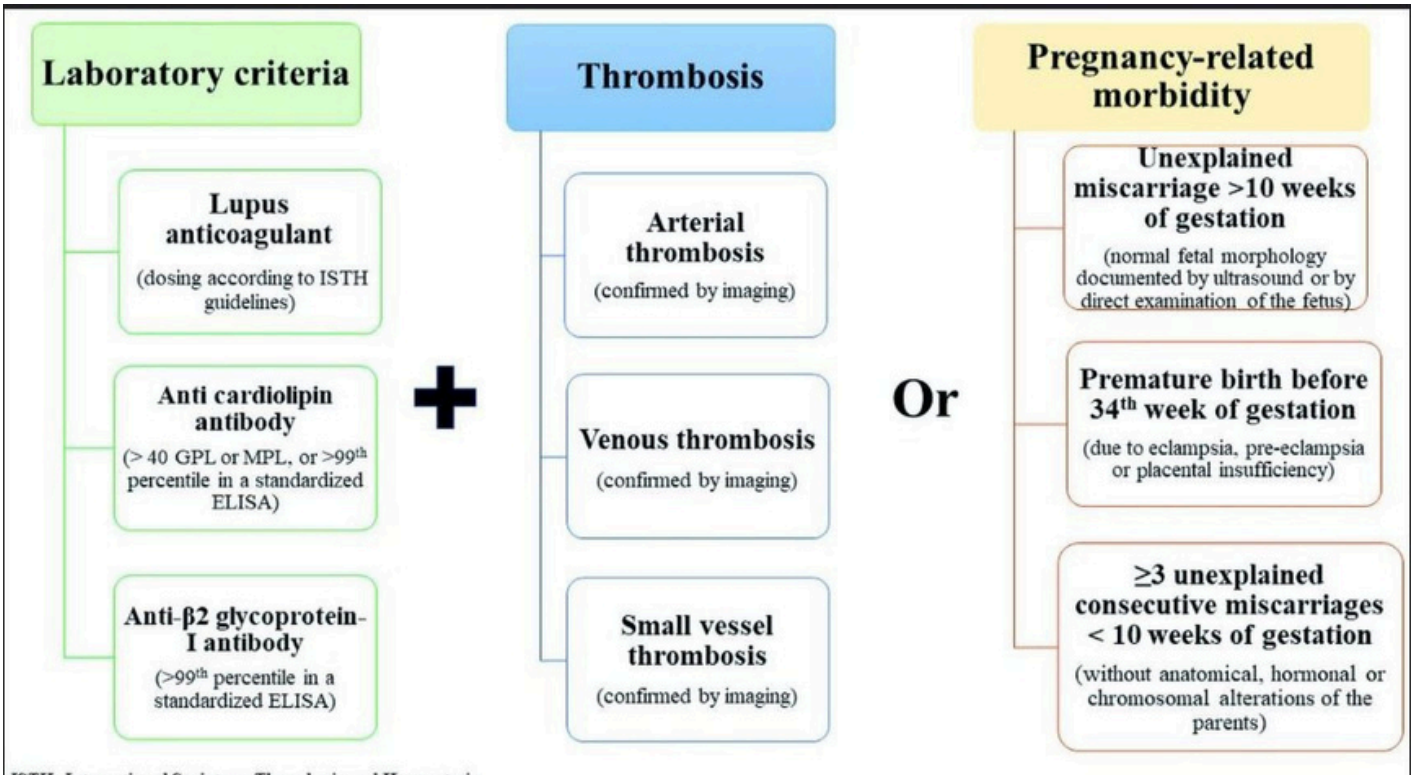
- **Antiphospholipid antibodies (aPL antibodies) :**
  - ***Lupus anticoagulant*** (LA): antibodies against certain phospholipids in cellular membranes
  - **Anticardiolipin antibodies (IgG and IgM)**: antibodies against cardiolipin, a phospholipid in cellular membranes
  - **Anti-β2-glycoprotein antibodies (IgG and IgM)**: antibodies directed against the cardiolipin binding factor β2 glycoprotein I that have prothrombotic effects

Patients with APS can test false positive for syphilis (positive VDRL or RPR) because the antigen used in syphilis tests is cardiolipin.

Interpretation :

- **Symptomatic patients:** The presence of ≥ 1 type of aPL antibody supports the diagnosis.
- **Asymptomatic patients :**

The presence of associated antibodies is not sufficient to establish a diagnosis.
Persistent positivity is associated with a higher risk of thrombotic and obstetric complications.



Approach :

- Treat acute thrombotic events (e.g., DVT, MI).
- Provide urgent management for CAPS in acutely ill patients with multiorgan failure due to thrombosis**.**
- **Initiate long-term thromboprophylaxis.**
  - **Primary thromboprophylaxis(** Consider for patients with no history of thrombosis**): Low-dose aspirin therapy**
  - **Secondary thromboprophylaxis (**APS with a history of thrombosis)
    - **First-line: warfarin**
    - **Second-line: LMWH or UFH**
      - **Treatment duration**
        - **Unprovoked thrombosis: Continue long-term.**
        - **Provoked thrombosis (e.g., after surgery):**

First Provoked venous (DVT ,PE) : 3-6 months if persistent risk factor (e,g lupus ,high risk APS Profile) lifelong anti Coagulation

Recurrent Provoked: lifelong anti Coagulation

Arterial thrombosis (stroke, MI) : generally treated for lifelong

- **Thromboprophylaxis in pregnant individuals: low-dose aspirin therapy PLUS heparin (LMWH or UFH)**
- **Provide supportive care.**

Sjögren syndrom

- **Sex: m > f (9:1) [1]**
- **Age of onset: typically 40–60 years**

Etiology :

- Primary Sjogren syndrome: idiopathic (association with HLA-DR52) [2]
- Secondary Sjogren syndrome: associated with another autoimmune disease, e.g., rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, polymyositis, or primary biliary cirrhosis

Clinical feature :

Clinical presentation varies widely, from isolated *sicca syndrome* to *systemic involvement*

- **Sicca syndrome** :
  - **Ocular symptoms**
    - **Xerophthalmia**: **dry eyes** due to decreased secretion of tears (daily, persistent)
    - Keratoconjunctivitis sicca
      - Conjunctival injection
      - Eye itching or burning sensation
      - Blurred vision
      - Recurrent sensation of sand or a foreign body in the eyes
  - **Oral symptoms**
      - **Xerostomia**: **dry mouth** due to decreased secretion of saliva (daily, persistent) which may lead to: **Dental caries** and oral infections
      - Parotid gland enlargement, often bilateral
      - Tongue fissures
    - Frequent need to drink liquids to aid swallowing and/or speaking
  - **Other glandular symptoms**
    - Vaginal dryness, leading to **dyspareunia** and an increased risk of infections
    - Nasal dryness, leading to chronic rhinitis and epistaxis
    - Pharyngeal, tracheal, and bronchial dryness, causing persistent dry cough
    - Xerosis: abnormal skin dryness and pruritus (secondary to hypohidrosis or anhidrosis)

- **Systemic disease :**
  - Arthralgias and/or arthritis (most common systemic symptom)
  - **Raynaud phenomenon**
  - Constitutional symptoms: fever, weight loss, fatigue
  - GI involvement, e.g., dysphagia , dyspepsia, reflux esophagitis
  - Pulmonary involvement: interstitial lung disease
  - Vasculitis
    - Mainly cutaneous: palpable purpura in the legs, recurrent urticaria, skin ulcerations
    - Glomerulonephritis
  - Autoimmune thyroiditis
  - Neurological involvement, e.g., peripheral neuropathy, myelitis
  - In patients with secondary Sjogren syndrome: features of a concomitant autoimmune condition, e.g., malar rash in patients with SLE

Systemic symptoms are present in 50–60% of patients with Sjogren syndrome.

Labratories studies :

- Routine studies: may show nonspecific supportive findings
  - CBC: normocytic anemia, leukopenia, eosinophilia
  - ↑ ESR
  - Urinalysis: proteinuria and/or RBC casts may indicate glomerulonephritis or interstitial nephritis
- Autoantibodies
  - Anti-Ro/SSA antibodies (positive in 70% of cases) and anti-La/SSB antibodies (positive in 50% of cases): target ribonucleoprotein antigens (Ro/La) in epithelial cells, especially in the salivary glands
  - Antinuclear antibodies (positive in up to 80% of cases)
  - Rheumatoid factor (positive in 50% of cases of primary Sjogren syndrome)

- Prognostic markers: associated with a poor prognosis
  - Cryoglobulinemia
  - Hypergammaglobulinemia
  - ↓ Complement C3 and/or C4

Diagnosis :(SSASSS)

- Schirmer test (assess tear flow) (for Xerophthalmia)
- S: Slit lamp exam with Rose-Bengal stain (for Xerophthalmia)
- A: Autoantibodies (anti-Ro and-La)
- S: Salivary flow measurement
- S: Sialography
- S: Salivary gland biopsy (gold standard)

Treatment :

- **Xerophthalmia**

Advise all patients to maintain adequate eye lubrication and avoid dry environments (e.g., shield eyes from wind, increase indoor humidity).

- **First line**: artificial tears for volume replacement and lubrication
- **Second-line therapies**: usually reserved for refractory or severe disease because of their potential adverse effects
  - Stimulation of lacrimal gland function with oral muscarinic agonists, i.e., pilocarpine or cevimeline
  - Topical immunosuppressive agents, e.g., topical **cyclosporine**, short-term (2–4 weeks) topical glucocorticoids
  - Serum eye drops

- **Xerostomia**

- **All patients**
  - Frequent water intake
  - Caries prophylaxis, e.g., regular dental hygienist visits, topical fluoride or chlorhexidine
  - Avoidance of irritants (e.g., coffee, alcohol) and acidic beverages (e.g., herbal tea, cola) [10]
  - Artificial saliva
    - Preferred treatment for patients without residual glandular function
    - May be considered for all patients
- **Patient with residual glandular function**: stimulation of salivary flow
  - **First line**: nonpharmacological stimulants, e.g., sugar-free lozenges or gum, acidic candy, xylitol
  - **Second line**: oral **muscarinic agonists**
    - Usually reserved for moderate or severe salivary dysfunction because of their potential adverse effects and the lack of strong evidence supporting their benefit
    - Options: pilocarpine, cevimeline

- **Managment of systemic disease**

Complication :

- Development of associated conditions
  - Autoimmune diseases, e.g., systemic lupus erythematosus, rheumatoid arthritis
  - B-cell lymphomas, e.g., **MALT lymphoma**
    - Prevalence 5% [3]
    - Frequently manifests as unilateral, persistent parotid enlargement
    - Predictors of lymphoma include lymphadenopathy, palpable purpura, and cryoglobulinemia.
  - Renal tubular acidosis type 1 [12]
- **Corneal scarring**, ulcer, rupture, and infection
- **Pregnancy: fetal loss, infant with neonatal lupus syndrome and associated complete heart block** (common with anti Ro/SSA antibody) مهم

{ Juvenile idiopathic arithritis }

Epidemiology

- **Prevalence: 1:1000 children (** The most common arthritis is seen in pediatric patients < 16 year olds)
- **Sex: f > m**
- **Age of onset: < 16 years of age**

Etiology

- Idiopathic
- Immunological predisposition: different HLA associations [2][3]
  - **Oligoarticular JIA**: HLA-DR8, HLA-DR5
  - **Polyarticular JIA**: HLA-DR4
  - **Enthesis associated and psoriatic JIA**: HLA-B27
- Possibly triggered by a viral or bacterial infection
- Exposure to antibiotics during childhood may increase the risk of JIA.

Usually presents with:

- Daily spiking fevers.
- Salmon-pink macular rash.
- Anterior uveitis.
- Arthritis (commonly 2+ joints).
- Frequently presents with leukocytosis, thrombocytosis, anemia, ↑ ESR, ↑ CRP.

Systemic juvenile idiopathic arthritis (Still disease)

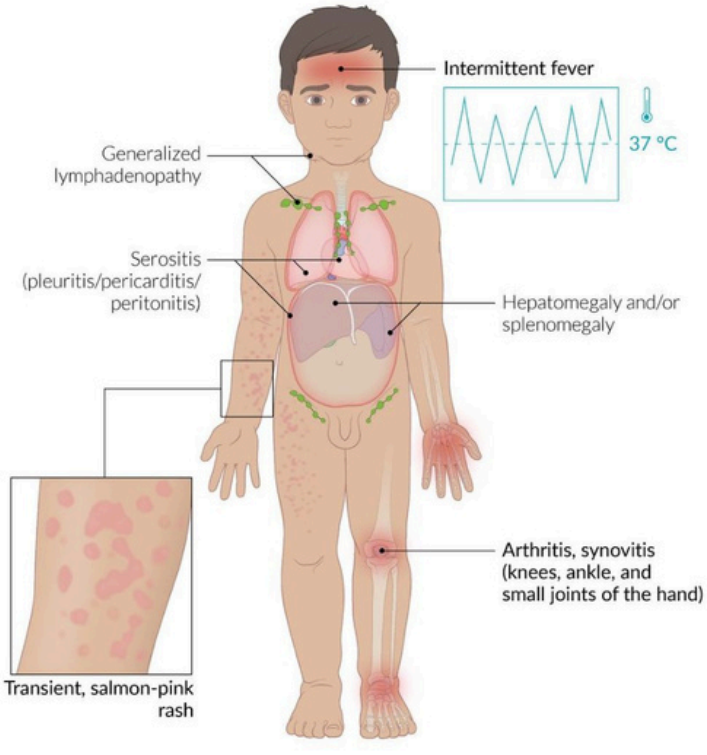
Etiology
Idiopathic

Epidemiology
♀ = ♂
Peak age of onset: 2–4 years

Serology
Typically negative for autoantibodies

Laboratory studies
Anemia, leukocytosis, thrombocytosis

Complications
Macrophage activation syndrome (MAS)



Types

1. Oligoarticular JIA (Most Common – 50%)

Affects fewer than five joints in the first six months.

Often involves large joints (e.g., knees).

Associated with chronic anterior uveitis, especially in ANA-positive patients.

2. Polyarticular JIA (30–35%)

Affects five or more joints within the first six months.

Can be RF-positive (similar to adult rheumatoid arthritis) or RF-negative

3. Systemic JIA (Still's Disease) (10-15%)

Characterized by daily fevers, transient pink rash, and hepatosplenomegaly.

May present with pericarditis or pleuritis.

Increased risk of macrophage activation syndrome (MAS).

4. Enthesitis-related arthritis

Associated with inflammation of entheses (where tendons/ligaments attach to bones).

Often linked to sacroiliitis and axial arthritis.

Treatment: NSAIDs, steroids, Methotrexate, TNF inhibitors.

Vasculitis

Inflammation of blood vessel wall (intima) by inflammatory cells, (any blood vessel can be involved so it gives wide manifestation). It is an autoimmune disease (unknown cause), which can be fatal (esp. Wegener). The inflammation occurs in areas where vascular wall antigens are not recognized as normal.
It's patchy lesion but wide spread so we take a sample along BV
Because of the pathology (inflammation) it will cause fever , weight loss and other disease manifestations depend on size of damaged blood vessels & the affected organs:
kidney: Renal artery stenosis >> HTN , Renal failure
Lung : pulm. artery >> pulm. HTN
CNS + **skin** manifestation .
GI: GI bleeding

Vasculitis is classified according to either

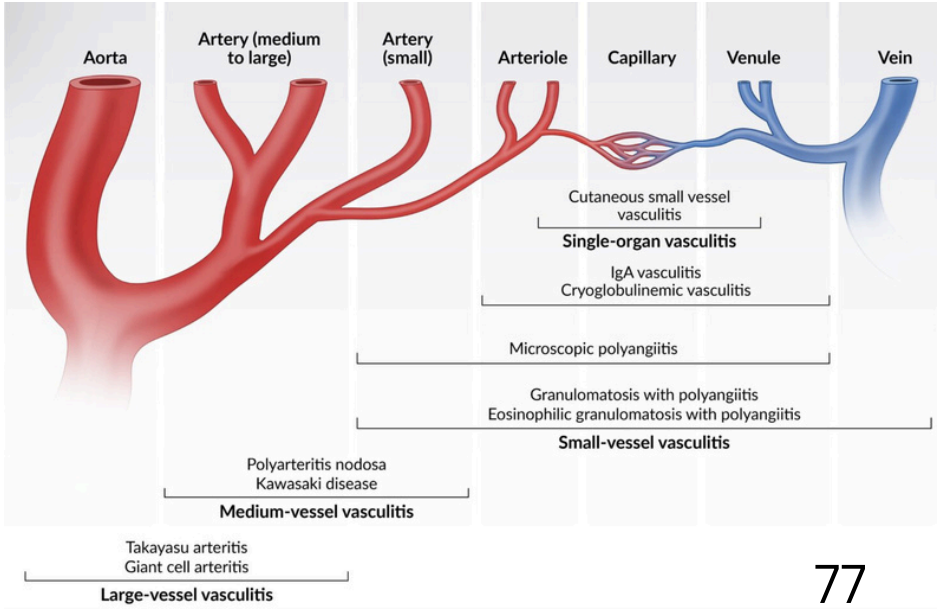
1• size of affected blood vessels
✓ Common Small vessel Vasculitis : HSP , GPA , MPA
✓ Common medium vessel Vasculitis : PAN , Kawasaki disease , churg Strauss syndrome
✓ Common Large vessel Vasculitis : Takayasu arteritis , Giant cell arteritis

2• The underlying cause
- Primary (idiopathic)
- Secendary to an underlying disease (e.g., HBV infection, cancer, systemic lupus erythematosus) or drug use.

* CT disease [SLE , RA , Behcets disease (manifested by mouth ulcer , digital ulcer , eye complications , uveitis , skin lesions)] ,
*Viral illness [Hepatitis B , C , HIV , EBV , CMV , Parvovirus B19 (cause pleurisy chest pain , mimics RA)] .

when we see **purpura or petechial rash >>> look to platelet count if it normal then look at platelet function (bleeding time) if it also normal >>> it is probably **vasculitis** .
***purpura of Vasculitis will be painful , elevated (palpable), distribution over dependent area .

Note : What will happen if the blood vessel get inflamed ?
SMALL:
1) edematous friable (subcutaneous blood oozing ➔ petechial rash) and may rupture ➔leaking of blood ➔ **bleeding** .
2) edematous swollen stagnation of blood ➔ ischemia (**infarction**)
MEDIUM AND LARGE :
1) Aneurysm : dilatation of vessels
2) Healing and fibrosis ➔ narrowing ➔ claudication of extremities [femoral , axillary A
→During active phase of inflammation
→GI / SC bleeding OR Aneurysm

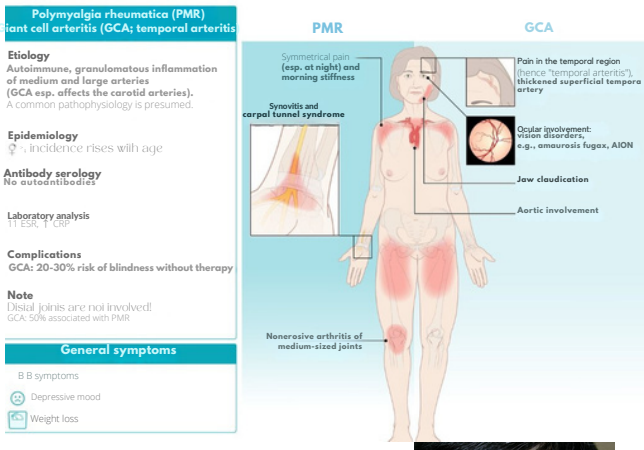


Vasculitis

large-vessel

Giant cell arteritis

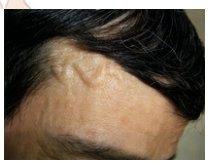
temporal arteritis



Clinical features:

- Most commonly affects women **> 50 years of age**
- **Affect intracranial branches of carotid (presented by unilateral headache)**
- Visual impairment: may result in **abrupt blindness" early complication"**

If the pt. get one eye blindness ➔ emergency ➔ to protect the other eye , risk of other eye blindness within 1-2 weeks



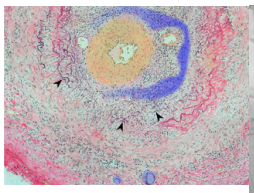
- New-onset headache
- Tender temporal artery
- Jaw and tongue(lingual art.) claudication 50% (when talk and when masticate) , arms claudication.
- Associated with polymyalgia rheumatica (50% of patient with Temporal arteritis have Polymyalgia rheumatic [pain , stiffness in shoulder area] , and 15% of patient with Polymyalgia rheumatic (PMR) have Temporal arteritis .)
- **Clue of temporal arteritis** : (unilateral sudden headache 2/3 of patients , sudden blindness , polymyalgia rheumatica , FUO , anemia with high acute phase reactant , age>50) .
- **50% of pt." esp. in elderly think about Temporal arteritis !!!**

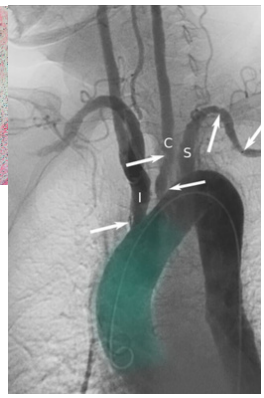
treat then take biopsy to avoid eye involvement , High ESR with blindness start treatment before biopsy (needs 2-3 days) .

Diagnostics:

- **↑ ESR (≥ 50 mm/hour), ↑ CRP**
- **Negative autoantibodystudies**
- **Duplex sonography: halo sign around the vessel**
- **Temporal artery biopsy(gold standard[1.25 -1.5 cm due to patchy**
- **phenomena]): granulomatous inflammation**
- **CXR :JUST AORTIC DILETATION**

Great vessels stenosis





Management:

- **High-dose(1-2 mg/kg) glucocorticoidsto prevent permanent vision loss**
- **immunosuppressive drugs "steroid sparing /protect from steroid side effect withdrawal) (methotrexate)**
- **bilogical agent (anti-B cell agent : rituximab)**

Typical case :

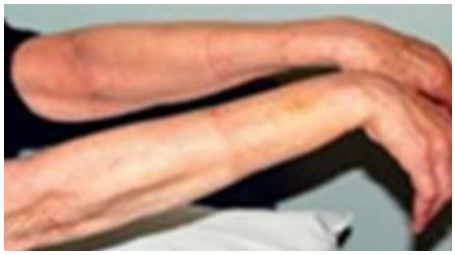
>50 years , headache , sudden blindness , PMR , UOF , anemia of chronic disease , increased ESR , CRP—>temporal arteritis treatment then biopsy , may we do Reentry via US without biopsy .

Vasculitis

large-vessel

NOTE :

FUO ' fever of unknown origin 'DDx in elderly : -lymphoma -TB and Brucellosis -Temporal arteritis -Infective endocarditis.
→ Mononeuritis multiplex MNM (FOOT , WRIST DROP) DDx:
-DM (commonest)-PAN in young age after exclude DM-Leprosy
-Infiltration (compression)



Takayasu arteritis

Etiology:

- Most commonly affects Asian **women < 40** years of age "**if older → atherosclerosis not Vasculitis**"
- Affect Large vessel esp. aorta and its major branches (brain and upper limb). In 50% affect Abdominal , Pulmonary vessels . More in japan
- **"most common cause → post streptococcal"**

Clinical Manifestation:

- claudication in upper extremities and → (unequal pulses >10 (diminished) "radio radial and radio femoral delay)→ in subclavian involvement .Disparity in blood pressure between arms (Takayasu arteritis is also known as **pulseless** disease)

Pulse delay DDx. : coarctation of aorta and Takayasu .

- Bruit over the subclavian arteryor abdominal aorta
- May involve renal a and cause HTN → 50%
- Syncope (Vertebral artery involvement (narrowing))
- **angina pectoris**
- **erythema nodosum : painful indurated nodule in lower limb , Pyoderma gangrenosum.**
- **Subclavian steal syndrome : aneurysm in the origin of vertebral artery >> cause wide area W low pr. >> so retrograde flow of blood from vertebral artery to subclavian artery**

Diagnostics:

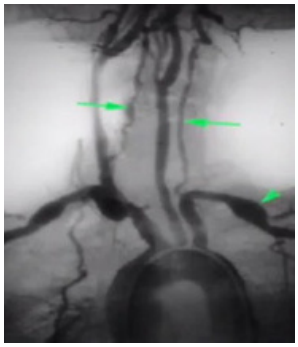
- **↑ ESR, ↑ CRP**
- **albumin -ve " always in acute phase reactant "**
- **MR angiography(preferred study): vascular wall thickening with luminal stenosis or occlusion of the aorta and major branches**
- **Angiography: aneurysm , beading "زي المسبحة ",stenosis of the aortic arch and proximal great vessels (if it chronic : collateral)**
- **x-ray (aneurysm dilatation or widening mediastinum).**
- **PET-scan , CT , MRI**
- **Biopsy: (biopsy of aorta is contraindicated) will be your first choice in case of typical small vessels inflammation and skin lesion**

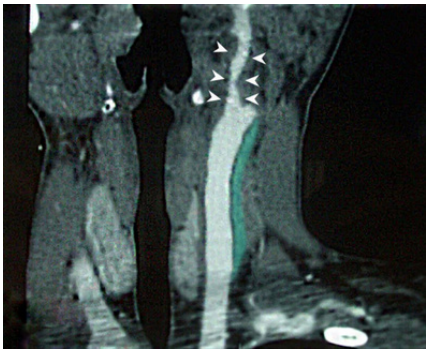
Vasculitis

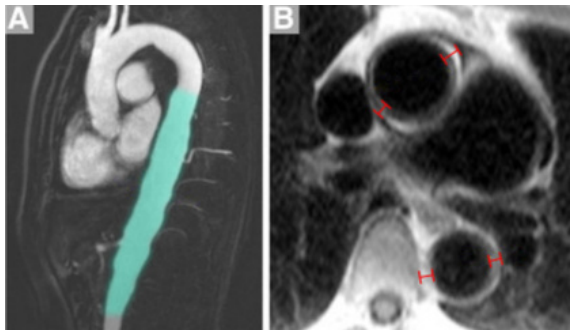
large-vessel

Management:

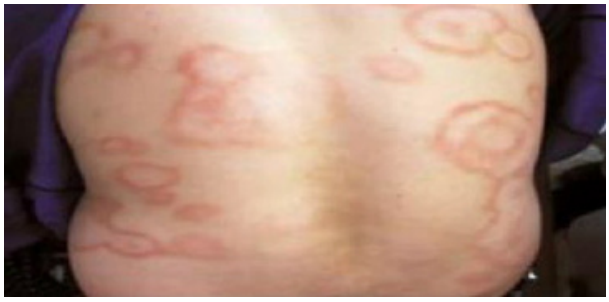
- Glucocorticoids
- PLUS a glucocorticoid-sparing agent(e.g., methotrexate, azathioprine, infliximab)
- bilogical agent (anti-B cell agent : rituximab)
- surgery : revascularization in case of vessel narrowing , Bypass graft



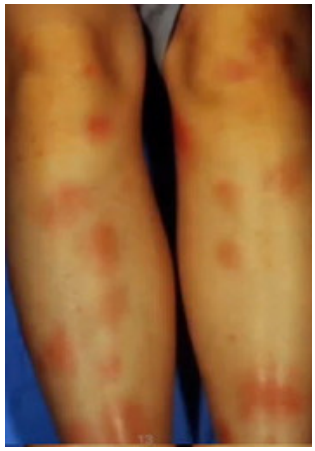




Scattered constrictions and aneurysmal dilatations . DD: Vasculitis if the patient is young (<40 years old). Atherosclerosis if the patient is .old with risk factors (DM)



Erythema annulari : Vasculitis.
Erythema marginatum : Rheumatic fever.

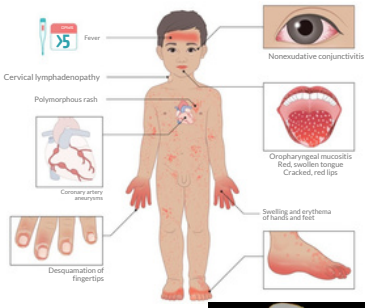


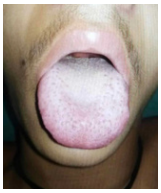
Erythema nodosum
(Painful and Indurated skin lesions)
DD: Vasculitis. Sarcoidosis (Lofgren syndrome). Inflammatory bowel disease. TB , post strep, behcet

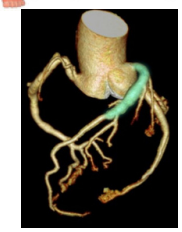
Vasculitis

Medium -vessel

Kawasaki disease







Clinical features:

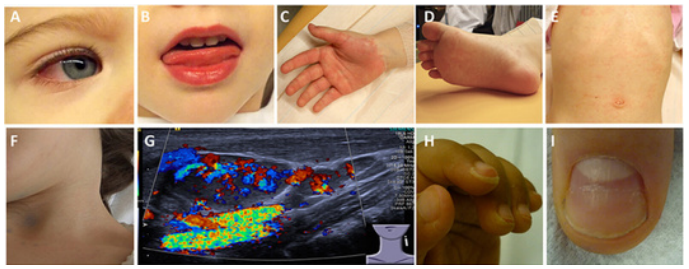
- Most often occurs in children < 5 years of age
- **"CRASH** (Conjunctivitis, Rash, Adenopathy, Strawberry tongue, Hand-foot changes) and BURN (≥ 5 daysof fever)"
- not ANCA associated

Diagnostics:

- **↑ ESR, ↑ CRP, thrombocytosis**
- **Echocardiography: coronary arteryaneurysms**

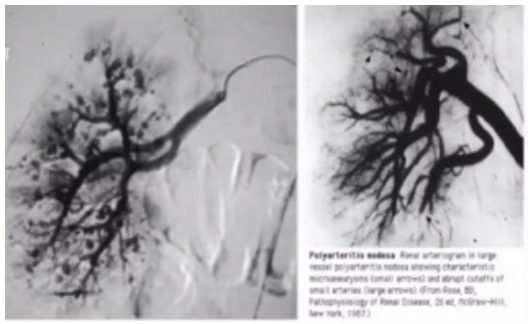
Management:

- **High-dose aspirinPLUS IVIG**

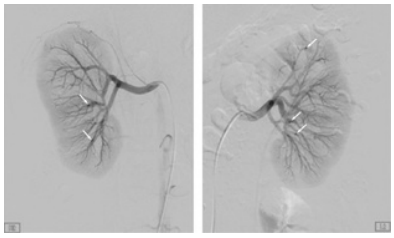


Polyarteritis nodosa PAN

Clinical features:



- Most often occurs in adults 45–65 years of age; m > f
- Fever, malaise
- Abdominal, muscle, and jointpain
- Renal impairment
- Neurological dysfunction (e.g., polyneuropathy, stroke)
- Rash, ulcerations, nodules
- Gangrene in tips of fingers and toe .
- Livedo reticularis (network of vascular dilatation) , we can see it also with SLE and more common with Antiphospholipid syndrome .
- Radial nerve injury (mononeuritis multiplex) OR polyneuropathy [both hands] →HTN (if involve the renal artery) , new onset of diastolic pressure >90 mmHg .
- **Spares the lungs**



Renal A microanurysms

Diagnostics:

- **Associated with positive HBVand/or HCVstudies**
- **ANCA: negative MC TYPE OF IT**
- **Muscle biopsy: transmuralvasculitis**
- **angiograph (multiple micro aneurysms)**

Management:

- **GLUCOCORTICOIDSPLUS CYCLOPHOSPHAMIDE**
- **Renal transplant + control HTN (with CCB , not by ACEI (renal stenosis))**

Vasculitis

ANCA-associated small -vessel

[MPA ,GPA , eosinophilic granulomatosis with polyangiitis (Churg- Strauss Syndrome – like Ashtma presentation)]

Granulomatosis with polyangiitis

"Wegener Granulomatoses "

Etology :

- Most often occurs in adults 40–60 years of age; m > f
- Mainly affect small vessels , to lesser extent affect medium size , venules ,arterioles.

Clinical features:

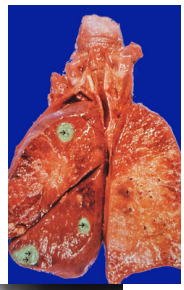
- Upper respiratory tract symptoms (oral and nasal) with lower respiratory tract (pneumonia) and **renal** involvement .
- Chronic sinusitis/rhinitis, **saddle nose deformity(ddx : Wegener , lupus , trauma , syphilis , relapsing polychondritis)**
- Chronic otitis media and mastoiditis
- Treatment-resistant pneumonia-like symptoms such as cough, dyspnea, and hemoptysis
- Rapidly progressive **glomerulonephritis**

Diagnostics:

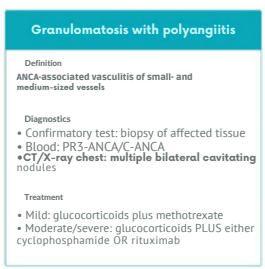
- **PR3-ANCA +ve**
- **Biopsy of the affected organs: granulomatous, necrotizing vasculitis, glomerulonephritis, lung involvement**
- **Chest x-ray or CT: multiple bilateral cavitating nodular lesions**

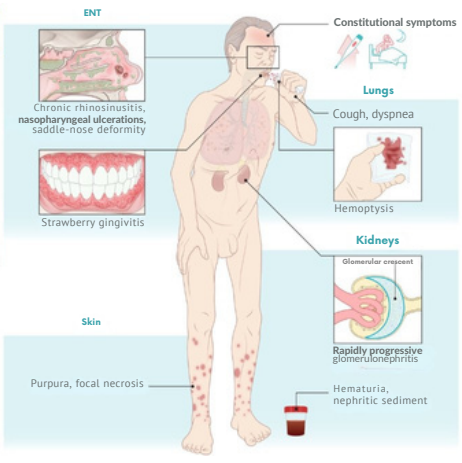
Management:

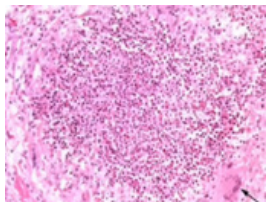
- **Glucocorticoids**
- **PLUS methotrexate OR cyclophosphamideOR rituximab**

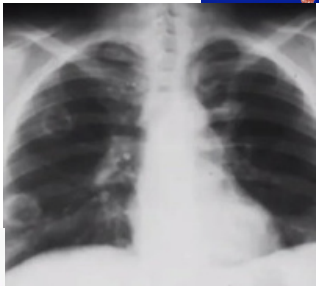


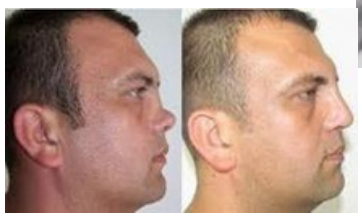
Granulomatosis with polyangiitis is the 'C' disease: Curvy nose (saddle nose deformity), Chronic sinusitis, Cough, Conjunctivitis and Corneal ulceration, Cardiac arrhythmias, non-Caseating granulomason biopsy, cANCA, Corticosteroids and Cyclophosphamide as treatment.











Vasculitis

الدكتور ما ركز عليهم
بس اجوا أرشيف

ANCA-associated small -vessel

Eosinophilic granulomatosis with polyangiitis

Churg- Strauss Syndrome

Clinical features:

- **Severe allergic asthma, sinusitis**
- Skinmanifestations (e.g., tender nodules)
- Peripheral neuropathy
- Gastrointestinal, cardiac, and/or renal involvement

Diagnostics:

- **MPO/p-ANCA (40% of patients)**
- **Peripheral blood eosinophilia**
- **↑ IgE**
- **Biopsy(confirmatory test): tissue eosinophilia, necrotizing granulomas**

Management:

- **GlucocorticoidsPLUS cyclophosphamide**

Microscopic polyangiitis

Clinical features:

- Pauci-immune glomerulonephritis
- Hypertension
- Palpable purpura
- Similar to granulomatosis with polyangiitisbut spares the nasopharynx

Diagnostics:

- **MPO/p-ANCA**
- **Biopsy: inflammation, no granulomas**

Management:

- **Glucocorticoids**
- **PLUS rituximab**

Vasculitis

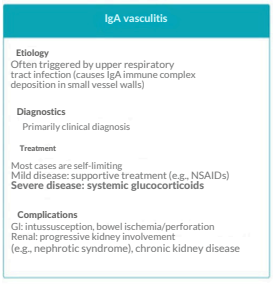
Non ANCA-associated small -vessel

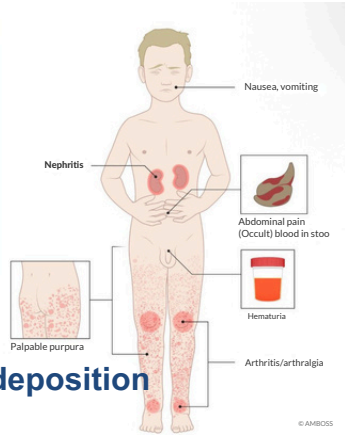
And Anti – GBM disease : Goodpasture syndrome , cryoglobulinemic Vasculitis , IGA vasculitis (HSP) ,Hypocomplementemic urticarial Vasculitis .

IgA vasculitis(Henoch-schonlein purpura)

Clinical features:

- Most often affects children (90% of patients are < 10 years of age)
- **Palpable purpuraon lower limbs**
- Arthritis and/or arthralgia
- Abdominal pain
- Hematuria if IgA nephropathy is present
- Often secondary to URTIs



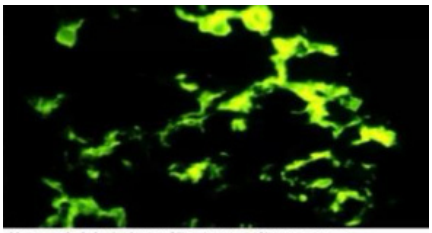


Diagnostics:

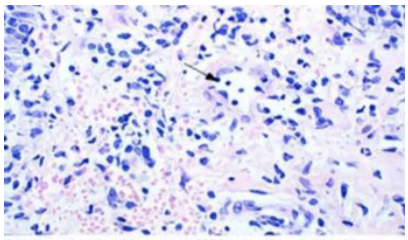
- **↑ IgA in serum**
- **Biopsy: leukocytoclastic vasculitis with IgA and C3 immune complexdeposition**

Management:

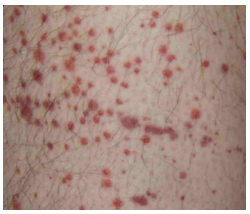
- **Mild cases: symptomatic treatment (e.g., with NSAIDs)**
- **Severe cases: glucocorticoidsPLUS IV hydration**
- **IVIG plasmaphersis**

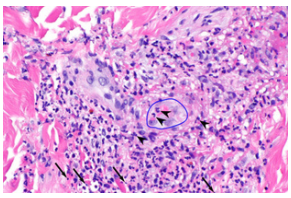


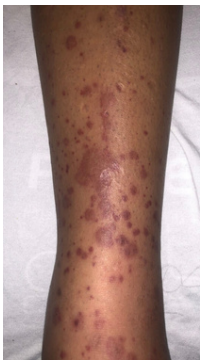
Mesangial IgA deposits Immunofluorescence microscopy demonstrating large, globular mesangial IgA deposits that are diagnostic of IgA nephropathy or Henoch-Schönlein purpura. Note that the capillary walls are not outlined, since the deposits are primarily limited to the mesangium. Courtesy of Helmut Rennke, MD.



Leukocytoclastic vasculitis Leukocytoclastic vasculitis involving the dermal papillae capillaries and venules, a finding that probably reflects an Arthus type III immune complex reaction. Courtesy of Cynthia Magro, MD.







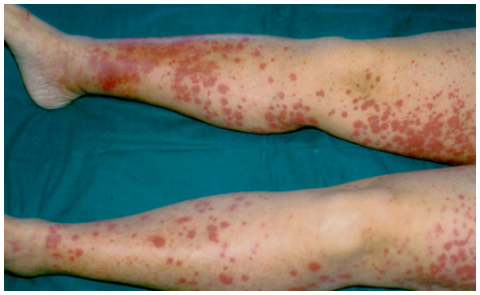
leukocytoclastic vasculitis

Cryoglobulinemic vasculitis

Clinical features:

الدكتور ما ركز عليها

- Fatigue
- Arthralgia
- Palpable purpura
- Glomerulonephritis
- Most cases are secondary to cryoglobulinemiadue to **HCVinfection**.



Diagnostics:

- **Cryoglobulinemiain serum**
- **Cutaneous or renal biopsy**

Management:

- **Mild cases: symptomatic treatment (e.g., with NSAIDs)**
- **Moderate or severe cases: glucocorticoidsPLUS either rituximab OR cyclophosphamide**
- **Treatment of the underlying etiology (e.g., DAAs for HCV infection)**

Vasculitis

variable -vessel الدكتور ما ركز عليها

Behcet disease

Clinical features:

- Most commonly occurs in individuals from Turkey, the Middle East, and Japan
- **Oral and genital ulcers**
- Uveitis
- Erythema nodosum

Diagnostics:

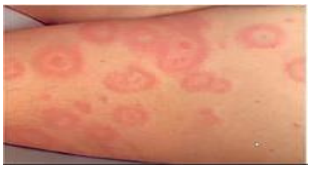
- **Positive pathergy test**

Management:

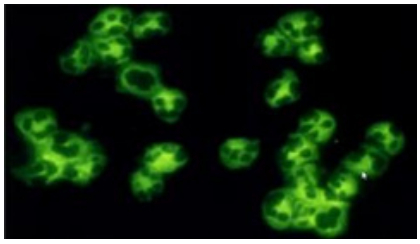
- **Glucocorticoids**
- **PLUS other immunosuppressive agents based on the type and severity of manifestations**

How to approach vasculitis : مهم

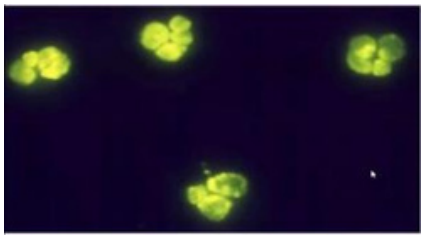
hx of medication , hep C,B >> esp in PAN , SLE manifestation , female , lab test (cbc , ESR, CPR) , KFT (proteinuria 150 mg/d, hematuria, cast) , creatinine , complement , ANA for lupus , ANCA test (PR3 ,MPO) , nerve conduction ,, EMG (electromyogram) in case of MNM>> dermatomyocyte and PAN ,tissue biopsy >> small vessel vasculitis , skin rash , angiogram>> takayasu, PAN .



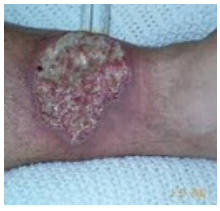
Erythema chronicum migrans (Bull's eye rash) DD: Lyme disease , Vasculitis.



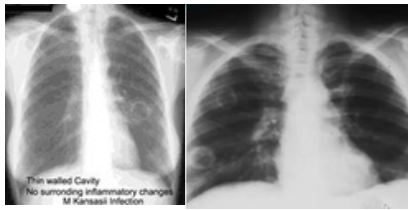
C-ANCA (Pr3) → protease 3



P-ANCA(MPO) → Myeloperoxidase Positive in Microscopic polyangitis



→Pyoderma gangrenosum : ass. With arthritis , IBD , vasculitis .



→ring lesion >> abscess , TB, Cavitating pneumonia (Staph , Anaerobes) ,Wegener , hydatid cyst

Systemic sclerosis (SSc)

Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by vasculopathy and fibrosis of the skin and other organs like Kidney, lungs and heart

Epidemiology

- F > M (5:1)
- Peak incidence: 30–50 years

Pathophysiology

- Autoimmunologic component
- Inflammatory synthesis of extracellular matrix: fibroblast proliferation and increased synthesis of normal collagen leading to fibrosis
- Noninflammatory **vasculopathy**
- ↑ **Fibroblast** activation → ↑ **Collagen** synthesis & deposition → ↑ Organ **fibrosis**

Clinical Features –

- SSc is most commonly described as **limited** or **diffuse** based on the cutaneous manifestations and symptom progression

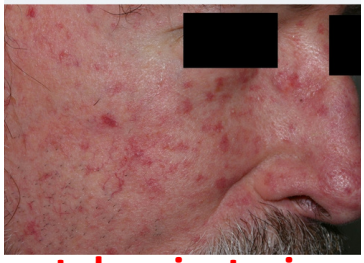
- 1.**Limited SSc :** which is more common, **begins** with cutaneous sclerosis of the **fingers, hands, and face**, which then progresses proximally toward the center of the body. Cutaneous involvement may be followed by internal organ involvement 10–20 years after disease onset. Positive for anti-centromere Abs. Associated with higher risk of Vasculopathy **(pulmonary hypertension)**

- 2.**Diffuse SSc :** which is less common, may be life-threatening in individuals with early involvement of the **heart**, **lungs**(fibrosis, interstitial) or **kidneys**. positive for ve anti-scleroderma 70 antibodies (anti-Topoisomerase)

CREST syndrome :

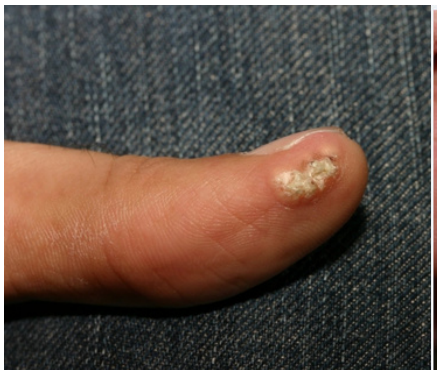
CREST syndrome refers to a constellation of symptoms traditionally **associated with limited SSc** (can also be seen in diffuse SSc)

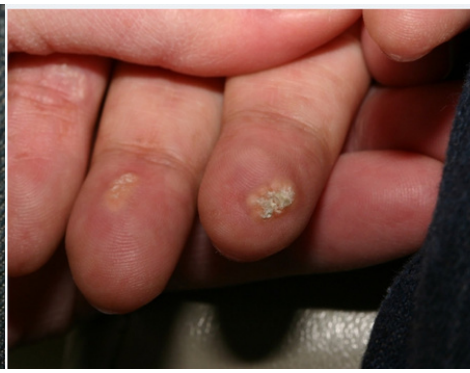
- **C**: **Calcinosis cutis**: small white calcium *deposits* on the pressure points of the extremities (e.g., elbows, knees, fingertips)
- **R**: **Raynaud phenomenon**
- **E**: **Esophageal hypomotility (systemic sclerosis)**: smooth muscle atrophy and fibrosis → esophageal dysmotility and decreased lower esophageal sphincter pressure → dysphagia, gastroesophageal reflux, heartburn → aspiration, Barrett esophagus, stricture
- **S**: **Sclerodactyly**
- **T**: **Telangiectasia**



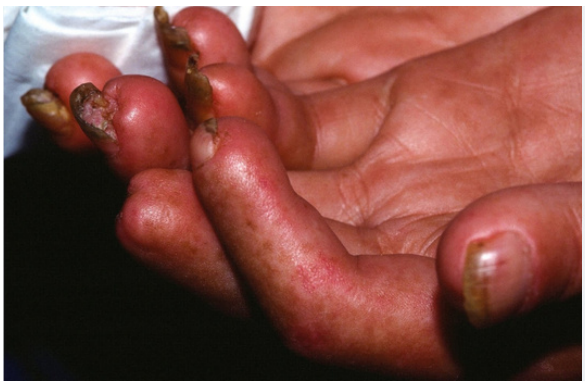
telangiectasia

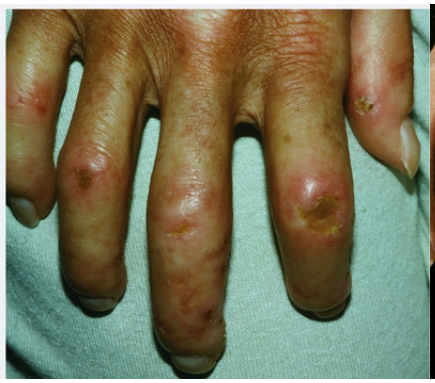
Vasculopathy (Raynaud's)

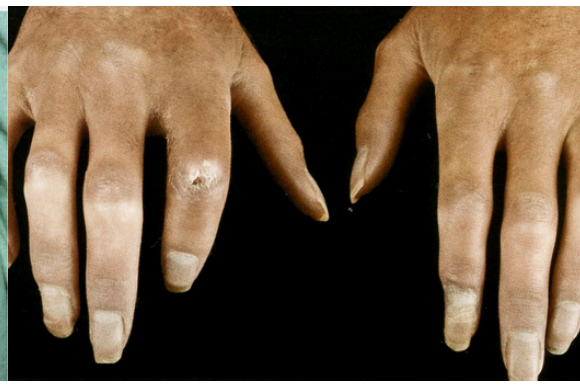




Calcinosis cutis







Sclerodactyly

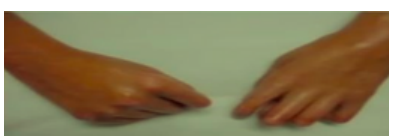
skin over the fingers is **taut, waxy**, and tightly stretched, causing flexure **contractures** and clawing of the fingers

Clinical Features تابع –

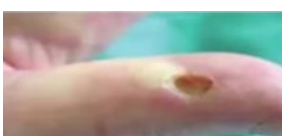
Cutaneous manifestations:

(skin involvement reflects internal organs involvement(if skin involvement is severe, internal organs more affected) and **predicts mortality .)**

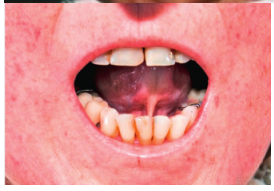
- **Thickening and hardening of the skin**, which appears smooth, shiny, and puffy
- **Sclerodactyly**: fibrotic thickening and tightening of the skin on the fingers and hands
  - Edema followed by fibrosis that results in a waxy appearance of the skin
  - **Limited range of motion**
- **flexed fingers ,** Hypopigmentation in fingers at the PIP joint.
- Multiple, **painful ischemic digital ulcers** with **atrophy** and **necrotic spots**
- Digital pitting: hyperkeratotic scarring that most commonly affects the **fingertips**
- **Face changes**
  - Loss of expression (**mask-like facies**)
  - Smoothing of deep wrinkles (**loss** of wrinkles)
  - **Microstomia ,**pursed mouth , peaked nose
  - loss of outer (lateral) 1/3 of eyebrows)



Flexed fingers



Digital ulcers



Microstomia, perioral wrinkles,

Renal manifestations:

- **Scleroderma renal crisis (SRC)**: medical emergency
  - **Clinical features of SRC**
    - **Oliguric** acute kidney injury
    - Hypertension with or without symptoms of hypertensive emergency
    - **Microangiopathic hemolytic anemia**
  - Treatment: **ACE inhibitors**

Note : mainly seen in diffuse form esp. if given **steroids** (steroids can precipitate renal crises)

- **Chronic kidney disease**: **reduced kidney function** due to abnormal collagen deposition → thickening of renal arteriolar walls → decreased renal blood flow

Cardiopulmonary :

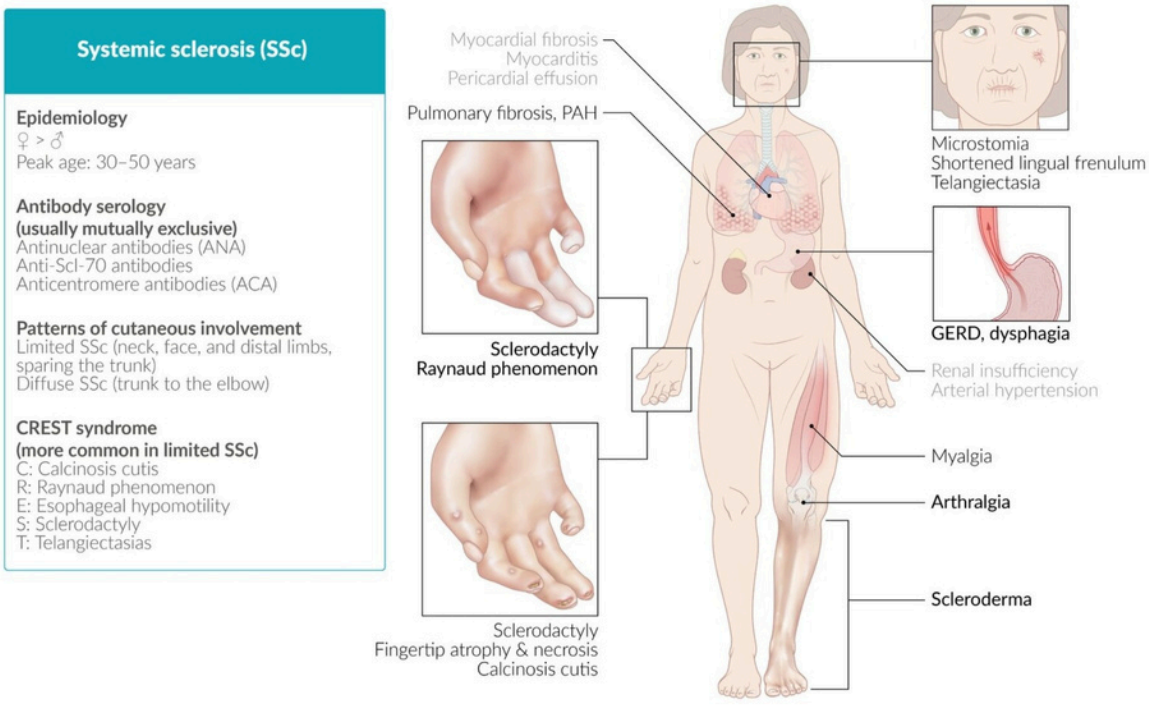
- Interstitial lung disease : (usual interstitial pneumonia)
- **Pulmonary artery hypertension** : (in **limited** form) , silent killer !
- Heart involvement : conduction defect , cardiomyopathies, pericarditis

Other extracutaneous :

- **Gastrointestinal tract**
  - Esophageal dysmotility → **dysphagia** and **reflux GERD**
  - Small bowel dysmotility → **bloating**, gas, **constipation**, fecal incontinence

Most common system involved in scleroderma is GI: 95-99% (almost all) have GI symptoms .

- **Vascular disease**
  - **Raynaud phenomenon**
  - Thromboembolism



Treatment :

General principles

- Treatment focuses on *organ-specific, symptomatic therapy.*
- In **diffuse** cutaneous disease or severe organ involvement, systemic **immunomodulatory** medication is indicated.
- Pathogenesis in each organ isn't the same (neuro vascular , inflammatory , fibro proliferative changes in skin) , and no single drug can treat it !

Cutaneous disease

- **Raynaud phenomenon** (RP)
  - calcium channel blockers
- **Cutaneous fibrosis**
  - Early diffuse SSc; **methotrexate (**skin softening - fibro proliferative agent), or **mycophenolate mofetil**
  - Severe or refractory fibrosis: **cyclophosphamide.**

■ usually after several years (5 years and beyond): **Skin soften** (it happened usually with treatment) so it occurs **after 5 years (at least**) of disease onset as adaptation of immune system .

Renal disease

- **Scleroderma renal crisis**
  - **ACE inhibitors** (ACEIs)
  - Captopril is most commonly used

Cardiopulmonary disease

- **Pulmonary disease**
  - Pulmonary hypertension
    - combination of **ambrisentan and tadalafil**
    - **Endothelin receptor antagonist(Bosentan)** : cause V.D
  - Interstitial lung disease: systemic immunomodulatory medications, e.g., **mycophenolate mofetil**

Notes :

- **For GI symptoms : Antibiotics (bacterial overgrowth) , PPI , Laxative , Motility agents**
- **TNF inhibitors useless in skin and lung (increase fatality in ILD) , it is effective in arthritis but increase risk of malignancy**
- **Biologics like "Ritoximab(anti CD20") improve both skin and lung (interstitial lung disease)**
- **MMF (mycophenolate) used in skin and lung involvement .**
- **azathioprine , cyclosporine (Oral or IV) OR IVIG may be effective in some patients (severe disease ,failed or contraindicated methotrexate , MMF) .**

Diagnosis:

- **Laboratory studies**
  - Antinuclear antibodies (**ANA**): present in 90% of patients
  - SSc-**specific** autoantibodies ;
    - **Anticentromere antibodies**
    - **Anti-Scl-70** (anti-topoisomerase I antibody)
    - **Anti-RNA polymerase III**
- **Cardiopulmonary assessment**
  - High-resolution CT (HRCT) chest: findings suggestive of ILD

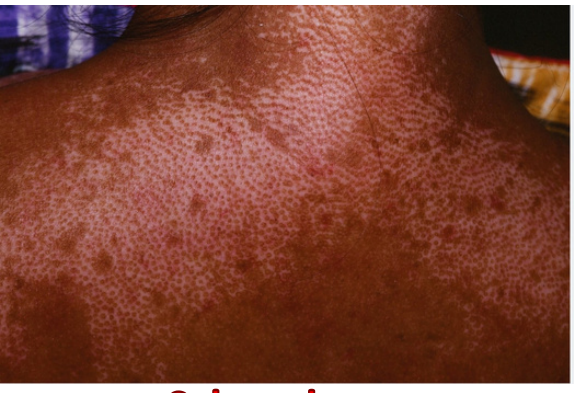
Major criteria for scleroderma (1980):

- **Proximal diffuse truncal sclerosis(just sclerosis or tight skin) and this is the hallmark of scleroderma where the skin proximal to the metacarpophalangeal joints in the hand or the metatarsophalangeal joints in the foot is indurated (non-pitting) , thickened, and hard and is often shiny with loss of skin surface markings. Loss of skin elasticity also occurs.**
- **A "salt and pepper" pattern of hyperpigmentation (excess pigmentation of the skin) and hypopigmentation (reduced pigmentation of the skin) is common.**

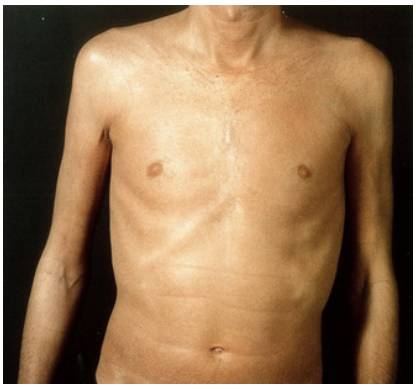
Minor criteria for scleroderma :

- **Sclerodactyl stiffness and tightening of the skin of the fingers (Acrosclerosis)**
- **Digital pitting with scars and ulcerations loss of substance of the finger pad**
- **Pulmonary fibrosis(bibasilar fibrosis)**

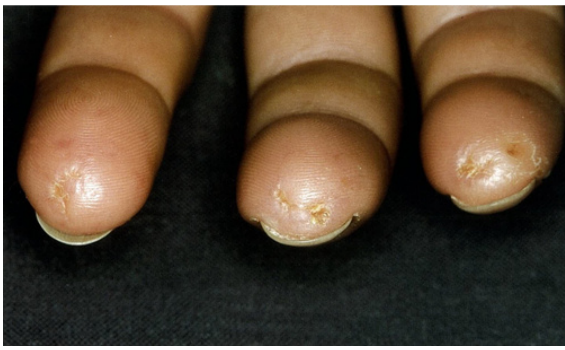
To diagnose scleroderma: 2 from 3 of minors / or 1 major



Salt and pepper



Torso of SSc patient



Digital pitting

Common SSc subtypes

	Limited SSc	Diffuse SSc
Cutaneous distribution	• Neck, face, and distal limbs • Sparing of the trunk	• Trunk, face, and extremities
Extracutaneous manifestations [8]	• May occur ◦ PAH ◦ Severe gastrointestinal involvement (e.g., bloating, constipation)	• Commonly occur ◦ Scleroderma renal crisis ◦ Cardiac involvement ◦ ILD
Onset of systemic symptoms [5]	• Slow: years after Raynaud phenomenon	• Rapid: simultaneously with Raynaud phenomenon or within weeks to months

Differential diagnoses :
Mixed connective tissue disease (MCTD, Sharp syndrome)

- **Definition**: a syndrome characterized by **overlapping symptoms** of **three** autoimmune diseases: systemic sclerosis (SSc), systemic lupus erythematosus (SLE), and polymyositis

- **Clinical features**: Course is usually milder than that of other connective tissue diseases (CTD) but may progress into another CTD.
  - Initial presentation: usually nonspecific symptoms (e.g., fatigue, arthralgia, low-grade fever)
  - Characteristic symptoms, usually manifesting over the course of several years, include:
    - **Raynaud phenomenon** (90% of patients)
    - Polyarthralgia, arthritis
    - Acrosclerosis, synovitis, and overlapping features such as myositis
    - Gastroesophageal reflux disease
- **Diagnosis**
  - Patients are **positive** for **ANAs** and **anti-U1 RNP** (see "Antibody diagnosis of autoimmune diseases.").
    - ANA patterns help determine the type of immune disease.
    - Generally, all ANAs have a speckled pattern on immunofluorescence.
- **Complications**: increased risk of *pulmonary hypertension* and *interstitial lung disease*

Raynaud phenomenon

Summary

Raynaud phenomenon (RP) is an exaggerated vasoconstrictive response of distal arteries and arterioles (most commonly in the fingers and toes) to cold or emotional stress. Primary RP is idiopathic, whereas secondary RP is caused by underlying systemic diseases (e.g., mixed connective tissue disease, vasculitides, medications). Both types typically manifest with the sequential discoloration of fingers and/or toes from white (ischemia) to purple-blue (hypoxia) to red (reactive hyperemia). Episodes of vasoconstriction usually last for 15–20 minutes after removal of the trigger. Ischemic episodes in secondary RP can be more prolonged, leading to tissue loss (ischemic ulcers) and rarely, gangrene. Trigger avoidance is the main aspect of managing RP. In patients with secondary RP, the underlying etiology should be identified and treated. Pharmacotherapy (preferably with calcium channel blockers) may be considered for RP refractory to trigger avoidance. Intravenous prostaglandins or interventional therapy (e.g., selective digital sympathectomy) may be required for patients with severe or refractory disease.

{ Dermatomyositis and Polymyositis }

Dermatomyositis (DM) and Polymyositis (PM) are idiopathic inflammatory myopathies.

Characterized by muscle weakness, inflammation, and in DM, skin manifestations.

Associated with autoimmune processes and, in some cases, malignancy.

Epidemiology

- Incidence: Rare, approximately 2 in 100,000 per year.
- Peak age of onset: PM : 30 - 60 years.
  DM : Bimodal distribution (children 5-15 years, adults 40-60 years).
- Female predominance (~2:1 ratio).

Pathophysiology

DM: Complement-mediated microangiopathy leading to muscle and skin damage and paraneoplastic antibody-mediated vasculopathy, associated with malignancies (non-Hodgkin lymphoma; lung, stomach, colorectal, or ovarian cance

PM: T-cell-mediated muscle inflammation chiefly affecting the endomysium.

Autoantibodies play a role (e.g., Anti-Jo-1, Anti-Mi-2, Anti-SRP, Anti-MDA5).
(may be associated with lupus , overlap syndrome (lupus cause myositis and skin manifestations).

Clinical Features – Polymyositis

- Symmetric proximal muscle weakness Commonly affects pelvic and shoulder girdle muscles, leading to difficulties combing hair , climbing stairs (upper limb) , standing up from a sitting position(lower limb) .
  Gower sign(when patient want to get up from sitting , he move to lateral then he will climb on himself)

- Can also affect neck muscles (flexors more than extensors)
- Progressive over weeks to months.
- No cutaneous involvement.
- Dysphagia due to esophageal muscle involvement.
- Associated with interstitial lung disease (ILD).

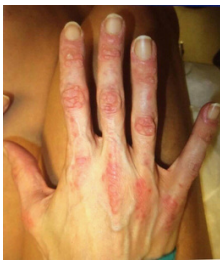
Clinical Features – Dermatomyositis

Muscle weakness similar to PM

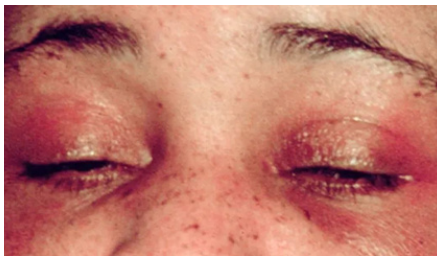
- Symmetric erythematous rash on the: (may be preceded or accompany muscle disorder)
  - Extensor surfaces of the hand joints, elbows, and knees (Gottron sign); scaly papules may form (Gottron papules) (if elevated it papules not sign)
  - Upper eyelids (heliotrope rash); often associated with periorbital edema
  - Mid-face
  - Upper back, posterior neck, and shoulders (shawl sign)
  - Upper chest and anterior neck (V sign)
  - Hips and lateral thighs (Holster sign)

- Poikiloderma may be seen in chronic disease.
- Mechanic's hands: thickened and cracked skin on the sides of the fingers and palms (horizontal fissures may appear darkened or dirty, hence the name)
- Periungual telangiectasias
- Calcinosis cutis (in children) as sclerodema

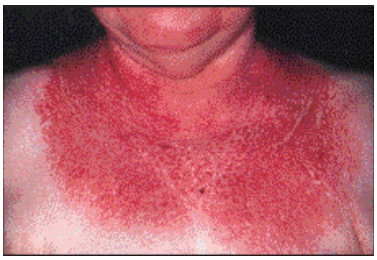
Increased malignancy risk (~15-20%).



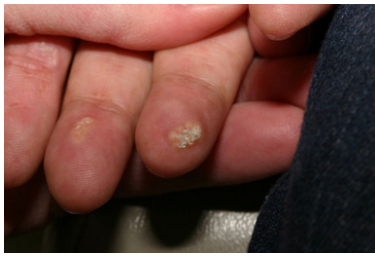
Gottron sign



Heliotrope rash



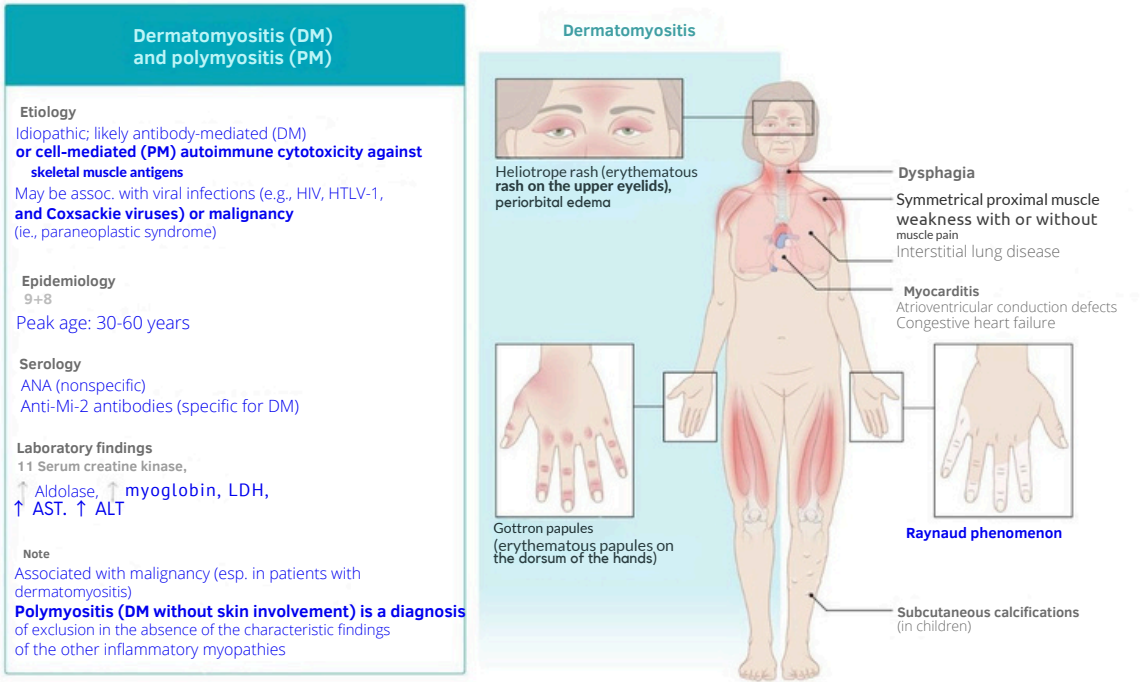
V sign



Calcinosis cutis

Systemic manifestations

- Interstitial lung disease
- Cardiac involvement (primarily in dermatomyositis and polymyositis), including:
  - Myocarditis
  - AV block
  - Heart failure
- Constitutional symptoms (may be fever weight loss)
- Increased risk of malignancy (DM, PM, IMNM)
- Raynaud phenomenon
- Arthritis
- Gastrointestinal symptoms (e.g., abdominal pain, hematemesis, melena)



- Laboratory Tests:
  - ESR and CRP: normal or mildly elevated
  - Elevated muscle enzymes (CK, aldolase, AST, ALT, LDH).
  - Autoantibodies: Anti-Jo-1, Anti-Mi-2, Anti-SRP.
  - TSH: to rule out myopathy secondary to hypothyroidism
- Electromyography (EMG): Myopathic changes and fibrillation.
- Muscle Biopsy (Gold standard):
  - PM: Endomysial inflammation with CD8+ T cells.
  - DM: Perifascicular atrophy with CD4+ T cells.
- Skin Biopsy (DM): Interface dermatitis.
- Imaging: MRI shows muscle edema and inflammation.

NOTE : All patients diagnosed with DM, PM, and IMNM should be tested for malignancies if you see dermatomyositis after age of 40 coming first time : this could be paraneoplastic manifestation [Lung - [lambert-eaton syndrome]) so screen for underlying malignancy.

Differential Diagnosis

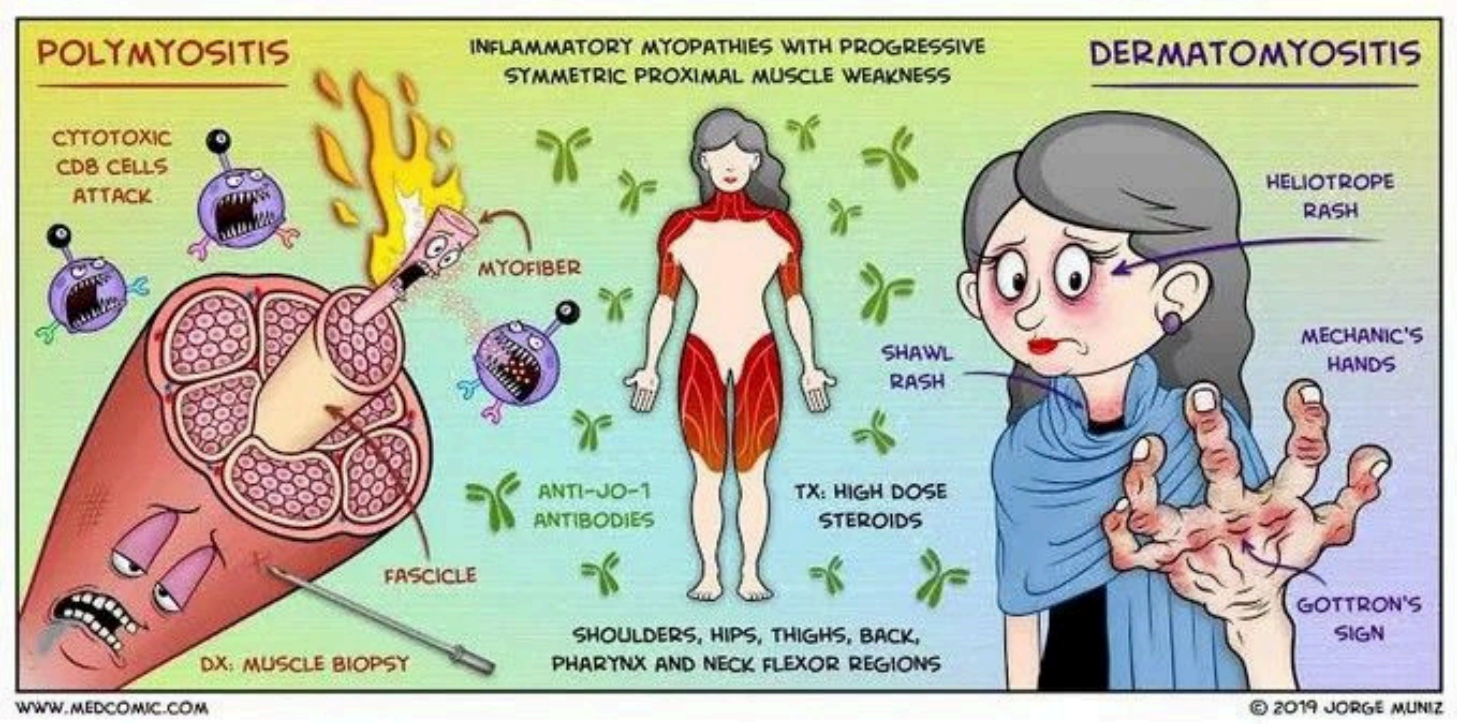
- Muscular dystrophies.
- Myasthenia gravis.
- Steroid drugs (prolonged high doses)
- hypothyroidism , Cushing
- Sarcoidosis
- Inclusion body myositis.
- Metabolic myopathies.
- Drug-induced myopathy (statins, steroids).
- Polymyalgia rheumatica
- fibromyalgia

Treatment

- First-line: Corticosteroids (prednisone 1 mg/kg/day).
- immune suppressant: Methotrexate, Azathioprine, Mycophenolate mofetil.
- IVIG (Intravenous immunoglobulin): For refractory cases.
- Biologics: Rituximab in severe cases.
- Physical therapy: Prevents contractures and improves function.
- Cancer screening: Especially in DM.

Prognosis

- 5-year survival >90% with treatment.
- Worse prognosis with malignancy, ILD, or cardiac involvement.
- Relapses common, requiring long-term immunosuppression.

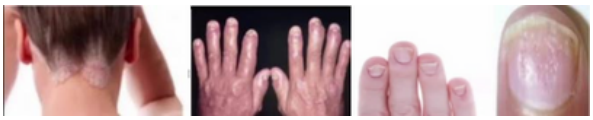


ARTHRITIS AND RASH

Not all rashes in people with rheumatoid arthritis are related to their RA. For instance, rashes from shingles, psoriasis and contact dermatitis are common.

1- Autoimmune and Rheumatological disease

- Systemic Juvenile Idiopathic Arthritis (sJIA) - Still's Disease. → A salmon-pink, evanescent (comes and goes) rash, usually appearing with fever spikes. (see later)
- Rheumatic Fever (post-streptococcal disease) → Erythema marginatum (pink, ring-like rash with central clearing , reproduce by hot bath).
- Systemic lupus Erythrematoses. → Malar (butterfly) rash and discoid lesions.
- Psoriatic Arthritis. → Psoriasis (scaly plaques, nail pitting)



- Dermatomyositis. → Heliotrope rash (purple eyelids), Gottron's papules (over knuckles)
- Reactive Arthritis. → Keratoderma blennorrhagicum (hyperkeratotic rash on palms/soles), circinate balanitis.
- Kawasaki Disease. → Polymorphous rash (non-specific, maculopapular).
- Henoch-Schönlein Purpura (HSP) → Palpable purpura, usually on lower extremities and buttocks.

NOTE : erythema nodosum (painful , tender , indurated u can fell a mass) Ddx : Sarcoidosis ,IBD , TB , BEHCET , fungul.

NOTE 2: psoriatic + septic + reactive make hint about HIV

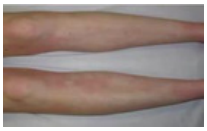
NOTE 3: rash if it with arthritis fever leukocytosis Liver enzyme elevation DDX: (JIA, CMV , viral hepatitis).

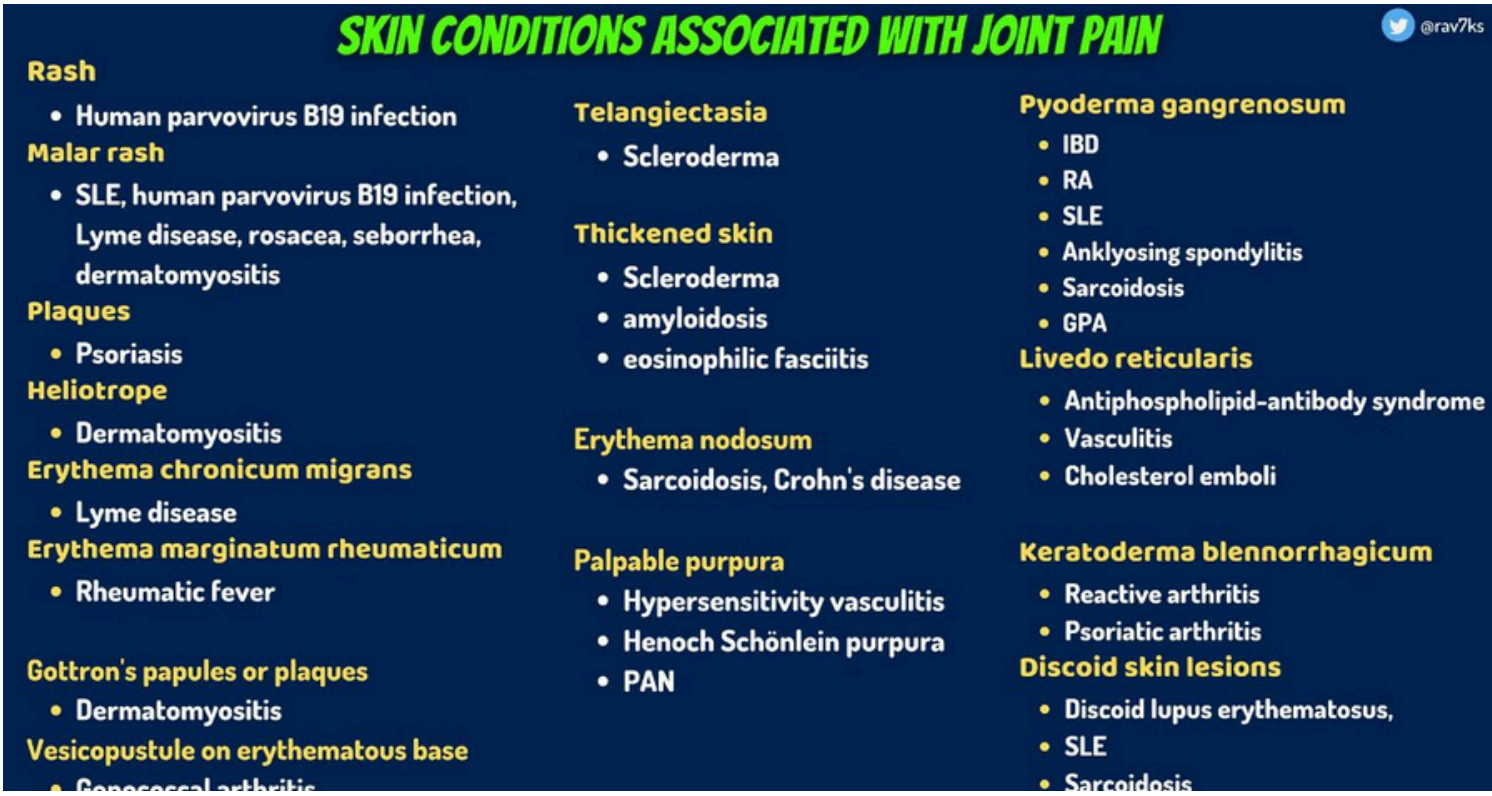
2- **Infectious Causes** (if it for low duration ,acute)

- Viral Arthritis (flu , EBV , CMV , Parvovirus B19, Hepatitis A/B/C(mcc of rash and artharlgia - not arithritis - , enterovirus (maculopapular rash and pleurisy sore throat , conjunctivitis , Rubella, HIV (more than 2 weaks))
- Bacterial Sepsis (Meningococcemia, Gonococcemia, Endocarditis)
- Lyme Disease (Borrelia burgdorferi Spirochetal bacteria): Erythema migrans (bull's-eye rash).→ECG – first degree AVblock – Mobitz I 2 degree AV block -mobitz II →3 degree AV block (pt came w syncope ,bradycardia).

Tick-borne

3- **Vasculitis & Other Inflammatory Syndromes :**

- Henoch-Schönlein Purpura (HSP):
- Kawasaki Disease
- Still's Disease [Triad of :Arthritis +Rash(come and go together) which is salmon pink colored , non-itchy + Recurrent fever. hepatosplenomegaly , leukocytosis. Marker to diagnosis :ferritin very high . Usually the fever and rash come together then disappear together, Negative RF , ANA , Anti-CCP] 



{ Overlap syndrom }

Overlap syndrome : refers to a condition where a patient meets the classification criteria for two or more well-defined connective tissue diseases (CTDs) simultaneously

Example :

1. Sclerodermatous Lupus

Involved Diseases: Systemic Lupus Erythematosus (SLE) + Systemic Sclerosis (SSc)
Key Features: SLE symptoms (malar rash, arthritis, nephritis) with skin thickening and Raynaud's phenomenon from systemic sclerosis.

2. Rhupus Syndrome (rare)

Involved Diseases: Rheumatoid Arthritis (RA) + SLE
Key Features: Erosive arthritis (RA-like) with positive ANA and lupus features like photosensitivity, serositis, and nephritis.

3. Scleromyositis

Involved Diseases: Systemic Sclerosis (SSc) + Myositis (Polymyositis/Dermatomyositis)
Key Features: Skin fibrosis and Raynaud's (SSc) with proximal muscle weakness and elevated CK (myositis).

4. Myositis-Sjogren Overlap

Involved Diseases: Polymyositis/Dermatomyositis (PM/DM) + Sjogren's Syndrome
Key Features: Proximal muscle weakness (PM/DM) along with dry eyes and dry mouth (Sjogren's).

5. Antisynthetase Syndrome

Involved Diseases: Polymyositis + Interstitial Lung Disease + Arthritis
Key Features: Associated with anti-Jo-1 antibody, presents with mechanic's hands, arthritis, and interstitial lung disease (ILD).

6. Sharp Syndrome (formerly considered MCTD) مهم

Involved Diseases: SLE + SSc + PM and Raynaud's phenomenon

Key Features: Features of all three but with anti-U1 RNP positivity (now classified as MCTD, not overlap syndrome).

☆ Better than lupus or scleroderma alone, but complications (like pulmonary hypertension) can develop.

Diagnosis

Diagnosis is based on clinical features and serologic markers. Key tests include:

- ANA (antinuclear antibody) – Usually positive in most CTDs
- **A**nti-dsDNA, anti-Smith – Specific for SLE
- Anti-Scl-70, anti-centromere – Systemic sclerosis markers
- Anti-Jo-1 – Antisynthetase syndrome (myositis + ILD)
- RF, anti-CCP – Rheumatoid arthritis markers
- Muscle enzymes (CK, aldolase) – Elevated in myositis
- Pulmonary function tests & HRCT – Evaluates interstitial lung disease (ILD)

Treatment :

Treatment depends on the dominant disease features:

{ Fibromyalgia }

Incidence:

- **F : M ≥ 3 : 1**
- **Ages 25 0 45, some adolescents**
- **2-5% in general population (overlaps with chronic fatigue syndrome)**
- **Strongly associated with psychiatric illness**

ETIOLOGY :

The pathophysiology of fibromyalgia is not fully understood; its etiology is likely multifactorial. The interaction of the following factors may play a role: [3]

- Genetic predisposition
- Autoimmune [4]
- Environmental triggers (e.g., physical or psychosocial stress)
- Dysregulation of the neuroendocrine and autonomic nervous systems

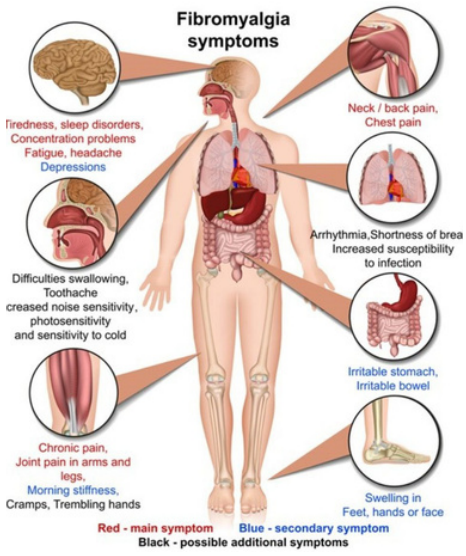
Clinical features

Cardinal symptoms of fibromyalgia

- Diffuse chronic musculoskeletal pain
  - Distribution: all or most regions of the body
  - Character: variable, often neuropathic, without objective pathologic findings
- Fatigue
- Unrefreshing sleep

Common additional symptoms

- **Fibro fog**: a form of cognitive dysfunction that includes difficulty concentrating and lack of clarity of thought
- Headaches (e.g., migraine)
- Morning stiffness
- Paresthesias
- Memory deficits
- Abdominal pain or cramps
- Autonomic changes
  - Xerostomia, xerophthalmia
  - Blurry vision, photophobia
  - Raynaud phenomenon
- Restless leg syndrome
- Pain at tender points (used historically): 18 sites on the body, primarily where muscles and tendons attach to bone



Diagnosis

The diagnosis of fibromyalgia is based on symptoms alone. Imaging studies and biomarkers (e.g., ESR) are typically normal

Consider the diagnosis in patients with cardinal symptoms of fibromyalgia (± fibro fog) for ≥ 3 month.

- Limit additional studies to specific conditions being considered (for exclusion), e.g:
  - Rheumatoid factor, antinuclear antibodies, myositis-specific antibodies
  - Thyroid-stimulating hormone
  - Sleep studies

Treatment

Non phamacological :

- Patient reassurance: disease is benign, non-deforming and does not progress
- Biofeedback, mediation, acupuncture, physiotherapy may be helpful
- Exercise program (walking, aquatic exercises)
- Support the back and the neck- Psychotherapy

pharmacological :

- Severe pain: pregabalin. (NSAIDs not recommended)
- Sleep disturbance: low dose amitriptyline and/or cyclobenzaprine and/or pregabalin (antidepressan drug)

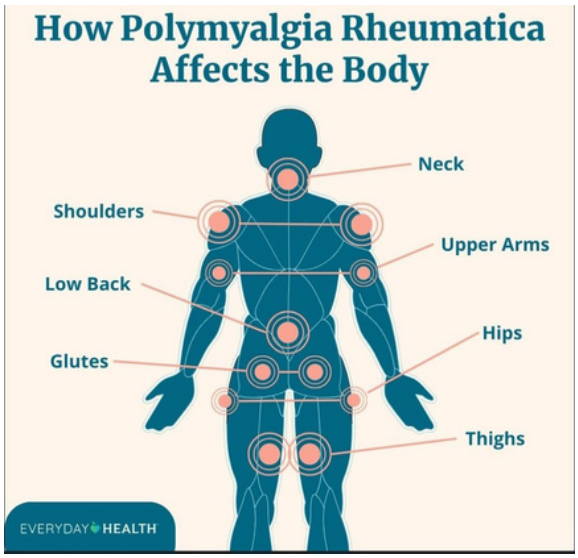
{ polymylagia Rhumatica }

Epiddemiology

- **Sex: F > M (3:1)**
- **Age of onset: > 70 years (very rare in individuals < 50 years)**

Etiology

- **Unknown**
- **Possible contributing factors are:**
  - **Genetic predisposition (e.g., human leukocyte antigen HLA-DR4)**
  - **Association with GCA(gaint cell artrites): Approx. 20% of individuals with PMR also have GCA.**



clinical features

- **Systemic features [3][4]**
  - **Constitutional symptoms:**
  - **Fatigue and malaise**
  - **Depressed mood**
  - **Symptoms of anemia**
- **Musculoskeletal features: shoulder girdle, neck, and pelvic girdle**
  - **Pain: acute onset, bilateral usually, worse at night**
  - **Morning stiffness (> 45 minutes)**
  - **Muscular atrophy and weakness: not directly caused by PMR but resulting from reduced activity due to pain and stiffness**
- **Features of GCA: GCA and PMR share clinical features and may occur simultaneously.**

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Diagnosis

- **PMR is a clinical diagnosis.**
- **Laboratory test :**
  - CBC: thrombocytosis, normocytic anemia
  - Inflammatory markers: ↑ ESR and/or ↑ CRP; normal levels of both suggest a different diagnosis.
  - Serology: absent autoantibodies (including rheumatoid factor)
  - Muscle enzymes: normal levels of creatine kinase and other enzymes.(Normal creatine kinase levels and the absence of autoantibodies help differentiate PMR from other rheumatic diseases (e.g., polymyositis, dermatomyositis, rheumatoid arthritis).

Diagnostic criteria
- Age > 50 y
- > 2 muscle groups
- ≥ 2 week duration
- Increased ESR
- Rapid response to corticosteroids
- Exclusion of others (RA, SLE, PAN or malignancy)

Tratment

- **symptomatic therapy**
- **steroid therapy : Glucocorticoids (low to medium dose)**

Dose adjustment is based on response to treatment

- **supportive therapy**

	Fibromyalgia	PMR
Age	30-50 yrs	> 50 yrs
ESR	Normal	High (>100)
Morning Stifness	Absent	Present
Tender Points	Present	Absent
Related Conditions	Stress, Anxiety, Depression	Temporal Arteritis
Treatment	Analgesics /Antidepressants, Anxiolytics	Cortiosteroids

BEHCET DISEASE

WHAT IS BEHCET DISEASE?

- Behcet disease is a type of variable vessel vasculitis that most commonly affects young adults (20–40 years of age) from the Mediterranean region to eastern Asia. Patients typically present with recurrent, painful oral and/or genital ulcerations; uveitis and erythema nodosum are also common in patients with Behcet disease.(more commone in male than female♂ > ♀)

- Possible autoimmune and infectious triggers (e.g., precipitating HSV or parvovirusinfection)
- Strong HLA-B51 association

PATHOPHYSIOLOGY:

- As we mentioned before it is an Autoimmune systemic vasculitis that can involve arteries and veins of all sizes.
- Characterized by the deposition of immune complexes, proliferation of CD4+ T cells, and increased cytokines

CLINICAL FEATURES:

- Recurrent painful oral aphthous ulcers (95–100%)
  - Typically the initial presenting symptom
  - Usually last about 1–4 weeks
- Recurrent genital ulcerations (60–90%)
  - Single or multiple ulcers that resemble oral aphthous ulcers and heal with scarring
  - Most commonly affect the vulva and the scrotum
  - Ocular disease (50–80%) Uveitis (iridocyclitis, chorioretinitis), keratitis, and/or retinal vasculitis
  - Typically bilateral
  - More common and severe among men
  - Usually occurs 2–3 years after the onset of oral and/or genital ulcers
- Skin lesions (35–85%)
  - Erythema nodosum, papulopustular lesions, pyoderma gangrenosum, pseudofolliculitis, or acneiform eruptions
  - Dermatographism: formation of urticaria after minor pressure is applied to the skin, likely mediated by local histamine release
  - Positive pathergy skin test: the appearance of an erythematous papule or pustule 48 hours after a 5 mm skin prick with a 20-gauge needle (usually on the forearm)

Continue clinical features

- Arthritis (30–70%)
  - Non-erosive, non-deforming, asymmetric monoarthritis or oligoarthritis
  - Usually affects the knees, ankles, hands, and/or wrists
- Gastrointestinal disease: abdominal pain, anorexia, diarrhea, lower GI bleeding, nausea, vomiting
  - Vasculopathy Superficial thrombophlebitis
  - Thrombosis of large veins (e.g., deep vein thrombosis, Budd-Chiari syndrome)
  - Arterial thrombosis
  - Aneurysms (e.g., pulmonary artery aneurysms)
- Neuro-Behcet syndrome (5–10%)
  - Parenchymal CNS disease: behavioral changes, ataxia, hemiparesis, sudden hearing loss
  - Non-parenchymal CNS disease: cerebral venous thrombosis, intracranial hypertension

A cool mnemonic :

PATHERGY: Positive pathergy test, Aphthous oral ulcers, Thrombosis (arterial and venous), Hemoptysis (pulmonary artery aneurysm), Eye lesions (uveitis, retinal vasculitis), Recurrent Genital ulcers, Young at presentation (3rd decade)

DIAGNOSIS :

Diagnostic criteria:

International Study Group diagnostic criteria for Behcet disease [9][2]	
Mandatory criterion	• Recurrent (i.e., ≥ 3 episodes within a 12-month period) oral aphthous ulcers
Additional criteria	• Recurrent genital ulceration • Ocular manifestations (e.g., uveitis, retinal vasculitis) • Cutaneous lesions • Positive pathergy test after 24-48 hours
A diagnosis may be established in patients who fulfill the mandatory criterion PLUS ≥ 2 of the additional criteria.	

Laboratory studies

- CBC: leukocytosis
- Inflammatory markers: ↑ ESR, ↑ CRP
- Serology: Autoantibodies (e.g., ANA, ANCA, rheumatoid factor) are usually absent.
- Genetic studies: HLA-B51 testing is not routinely recommended.

SOME DIFFERENTIA DIAGNOSES:

- Aphthous stomatitis
- GI diseases, e.g., Crohn disease, celiac disease
- Infectious diseases, e.g., tuberculosis, herpes infections, HIV
- Rheumatological diseases, e.g., reactive arthritis, SLE
- Dermatological diseases,

TREATMENT:

Pharmacotherapy

- Ocular disease, CNS disease, and/or vasculopathy
  - Systemic glucocorticoids
  - Glucocorticoid-sparing agents (e.g., azathioprine, infliximab, cyclosporine A, cyclophosphamide, IFN-α, methotrexate)
- Mucocutaneous lesions
  - Topical glucocorticoids (e.g., triamcinolone) can accelerate the healing of oral and genital ulcers.
  - Immunomodulatory agents
    - Consider colchicine to prevent lesion recurrence.
- Arthritis
  - First line: colchicine

Behcet disease

تلخيص

→A systemic Vasculitis that is characterized by the deposition of immune complexes in arteries and veins all sizes.

Epidemiology : Most common from the Mediterranean region to eastern Asia, with the highest prevalence observed in Turkey and Japan , Peak incidence: 20–40 year.

Etiology : Autoimmune and infectious triggers (e.g., precipitating HSV or parvovirus infection) have been suggested. Strong HLA-B51 association.

Clinical features:

Recurrent painful oral aphthous ulcers (95–100%) Usually last about 1–4 weeks Typically the initial presenting symptom	Recurrent genital ulcerations (60–90%) -Single or multiple ulcers that resemble oral aphthous ulcers and heal with scarring -Most commonly affect the vulva in female and the scrotum in male individuals	Ocular disease (50–80%) -Uveitis (iridocyclitis, chorioretinitis), keratitis, and/or retinal vasculitis -Typically bilateral -More common and more severe among men -Usually occurs 2–3 years after the onset of oral and/or genital ulcers	Skin lesions (35–85% -Erythema nodosum -Papulopustular lesi - Pyoderma gangren - Pseudofolliculitis or acneiform eruptions -Dermatographism: formation of urticar minor pressure is ap the skin, likely medi local histamine relea
Arthritis (30–70%) -Non-erosive, non-deforming, asymmetric mono-/oligoarthritis -Usually affects the knees, ankles, hands, and/or wrists	Vasculopathy -Superficial thrombophlebitis -Thrombosis of large veins (e.g., deep vein thrombosis, Budd-Chiari syndrome) -Arterial thrombosis -Aneurysms (e.g., pulmonary artery aneurysms	Neuro-Behcet syndrome (5–10%) -Parenchymal CNS disease: behavioral changes, ataxia, hemiparesis, sudden hearing loss -Extra-parenchymal CNS disease: cerebral venous thrombosis, intracranial hypertension	Gastrointestinal dis ileocecal ulceration abdominal pain, ano diarrhea, lower GI b nausea, vomiting

Diagnostics :-Positive pathergy skin test: erythematous papule or pustule 24–48 hours after a needle prick to a depth of 5 mm -Autoantibodies (e.g., ANA, ANCA, rheumatoid factor) are usually absent. -Nonspecific markers of inflammation may be present during flares (e.g., ↑ ESR, ↑ CRP).

→PATHERGY: Positive pathergy test, Aphthous mouth ulcers, Thrombosis (arterial and venous), Hemoptysis (pulmonary artery aneurysm), Eye lesions (uveitis, retinal Vasculitis), Recurrent Genital ulcers, Young at presentation (3rd decade). Diagnostic criteria (International Study Group criteria) Recurrent oral ulceration at least three times within a 12-month period AND ≥ 2 of the following : Recurrent genital ulceration , Eye lesions , Skin lesions , Positive pathergy test . Differential diagnosis Crohn disease , Aphthous stomatitis (e.g., due to vitamin B12/folate/iron deficiency, gluten- sensitive enteropathy) , Herpes infection , Sweet syndrome , Reactive arthritis , SLE . Treatment →Oral ulcers and/or genital ulcers: topical corticosteroids →Topical lidocaine for pain relief →Skin lesions : Papulopustular lesions: "Treatment" of "Acne vulgaris". Erythema nodosum: colchicine →Arthritis: colchicine →Ocular disease, CNS disease, and/or Vasculopathy : Systemic corticosteroids + Immunosuppressant therapy (e.g., azathioprine, infliximab, cyclosporine A, cyclophosphamide, IFN-α, methotrexate)

THANK YOU