Rheumatology Dossier

Updated 2022/2032

Introduction – patient with joint pain

SERONEGATIVE ARTHRITIS

Rheumatoid Arthritis

Crystal Induced Arthritis

ARTHRITIS AND RASH

Systemic Lupus Erythematous

Vasculitis

Scleroderma

Dermatomyositis

Behcet disease

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Rheumatology- Introduction

→Arthralgia : joint pain. Arthritis : inflammation , redness, most important in it [pain / swelling (most important) / limitation of movement due to effusion .

→According to number of joints involve:

1- Monoarticular joint the causes:

*Trauma *Septic arthritis[infection] *Crystal induced arthritis [gout and pseudo gout]

*TB *Hemarthrosis[blood in joint].
NOTE : Oligoarthritis and poly arthritis could be started as Monoarthritis

2- oligoarticular[2-3]:
*Seronegative arthritis- asymmetrical

3- polyarticular [more than 3]:

*RA – symmetrical, morning stiffness more than 1 h

*SLE - symmetrical and may be asymmetrical.

→ Seronegative arthropathies –spondyloarthropathies:

1- Rhematoid factor is negative

2- Anti-ccp [cyclic citrullinated peptide] is negative.

→Seronegative arthritis types :

1 – Ankylosing spondylitis 2 – reactive arthritis 3 – psoriatic arthritis

4 – enteropathic-arthropathy.

Features of seronegative arthritis: Autoimmune , chronic , inflammatory , systemic , Oligoarthritis , large joint , lower limb mostly , lower limb pain , low back pain , asymmetrical.

Rheumatoid factor+ Anti-CCP are negative # Axial involvement SI joint
Eye ,Heart ,Skin # Treatment peripheral arthritis as in RA.

 # psoriatic differ in its effect small joint of the hand[DIC] distal

interphalangeal joint and is polyarthritis

DIC >>>> psoriatic and osteoarthritis (primary) .

Joint pain questions:

1 –what is the joint involved and how many joint [oligo or poly]?

2 – arthralgia or arthritis? 3 –
symmetrical or not?

4 – relation to movement?

[pain increase with movement this mean is mechanical not inflammatory like OA] but [pain increase after rest this mean inflammatory]

5 – morning stiffness [inflammatory]?

6 – duration of morning stiffness [significant duration more than 30 m . more than 1 h this RA] . We mean by STIFFNESS (limited motion not pain)

7 – back symptoms (SI joint , Epiphyseal joint , disc plate)

8 – systemic symptoms [constitutional] fever (almost in all rheumatic disorders (non-discriminator symptoms)) / sweating/ weight loss] it's a systemic inflammation .

❼Arthritis and sweating = TB or Brucellosis

Facial rash – cheeks

Rash on forehead and chin – photosensitive rash

SLE – painless ulcer and pleuratic chest pain (

Serositis)

❼ 50% of SLE have renal involvement !! 🙈 🙈 We

don't use NSAID in this case because it induce

interstitial nephritis. **Investigation of**

Rheumatology: 1 – rheumatoid factor

2 – anti – ccp [cyclic citullinated peptides] 3 – ANA 4 – ANCA.
→in case of inflammation : morning pain is the worst ☹ .

Pattern of joint involvement :

1– **migratory** : the first joint improve or completely resolve then migrate to another joint as Rheumatic fever and SLE [no period w/o pain]

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

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

→Typically back pain is in seronegative in sacroiliac joint [sacroilitis] > ankylosing spondylitis (IBD)

→The **age** is important : **Rheumatic fever: childhood 5-15** .

SLE: menarche to menopause

Definition :

Rigor: shaking chills – transient passage of micro organism through blood [uiremia/bacteremia]

Chills: feeling of coldness

Significant weight loss : 10%of weight during 6 months without intention

The most common risk of significant weight loss present in rheumatology is – lymphoma and TB spec. in old age.

Note: usually females affected with rheumatoid disease ☺

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 359/24h**

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**

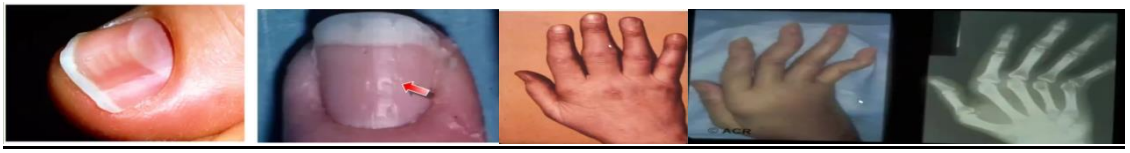
Hemophilia A - factor 8 def, Hemophilia B – factor 9 def, Hemophilia C – factor 11 def
NOTE : Hemophilia A doesn't cause joint disease , unless in case of joint bleeding and cause Hemarthrosis

physical examination : Inspection , palpation , movement range and special maneuver !

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

Skin : color , texture (thick as with scleroderma)

Swelling and deformities: Swollen PIP joint , swan-neck deformity : hyperextension of the PIP joint with flexion of the DIP joint , Ulnar deviation , Swollen (MCP) joint [typically involved in RA] , Osteopenia (decreased bone density in x-ray).



2-**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): mild effusion

Patellar tap , fluctuation →moderate to severe .

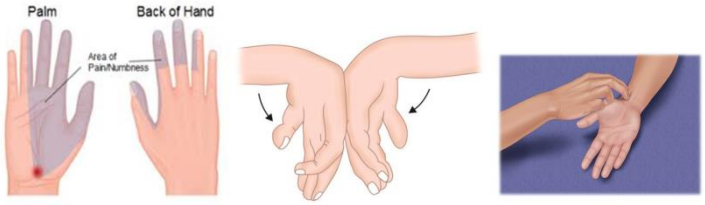
3-**Movement** range : we examine range , types of movement and power .

Active VS passive : in case of normal passive and abnormal active : think of **periarticular problem** (tendon , nerve ,ligaments , muscles)

In case of abnormal both active and passive : **joint pathology**

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

Practical examination : **cervical spine and TMJ** (inspection , palpation , range of motion) :Flexion , Extenion , rotation , lateral bending .

Shoulders : inspection , palpation , Range of motion : identify the following : Sternoclavicular joint , Acromioclavicular joint , biceptal groove , subacromial space .

Wrist , Elbow and hands : inspection , palpation , range of motion :

Elbow [extension , flexion , supination , pronation]

Wrist [flexion , extension ,radial and ulnar deviation]

Palpate : DIP , PIP , MCP and wrists .

Muscle strength : Upper limbs and lower , compare both sides .

Back : **Deformities** : Kyphosis تحدب : Anterior bending of spine .

Scoliosis جنف : lateral bending of spine

Lordosis: Posterior bending of spine .

Examine for **scars and swelling** (para spinal or midline), tenderness , muscle spasm , spinosum process .

NOTE : TB is localized to lower thoracic and upper lumber , Pott's disease or brucellosis .

Ankylosing spondylitis involve all spine and start from lower spine (SI joint) .

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

Knee: Meniscus test , LCL test , cruciate ligament test , joints [subtalar and tibiotalar].

Foot : metatarsal squeeze test : swelling , redness , tenderness of 1 MTP → Gout ,OA .

→Hematological findings : Leukopenia : liable to infection

Anemia : common in rheumatic diseases

Thrombocytosis in RA : platelets are acute phase reactant .

Thrombocytopenia in SLE

CHRONIC ARTHRITIS

Primarily , 40% of patients are RA

→SERONEGATIVE ARTHRITIS (Seronegative spondyloarthropathy)

1-ANKYLOSING SPONDYLITIS (can present with apical lung fibrosis).
2-REACTIVE ARTHRITIS : comes usually after URTI or GU , GI infections after 2 weeks of infections . also known as **Reiter's syndrome**
3-PSORIATIC ARTHRITIS in DIP .
4-ENTEROPATHIC (IBD RELATED) ARTHRITIS.
5- undifferentiated spondyloarthropathy :just spine arthropathy without any other manifestations.

Characteristics:

1-Asymmetrical (unilateral) ,large joints , oligo-arthritis(less than 4 joints involvement) **except** for **PSORIATIC ARTHRITIS** which is involving the small joints (Distal interphalangeal joint) , Poly-arthritis(4 or more) and symmetrical (bilateral) involvement.

2-Can present with mono-arthritis.

3-Can present with extra-articular manifestations : Eyes(uveitis) , Lung (fibrosis) , Heart , Skin (psoriatic plaques).

4-Axial involvement (Sacroiliac joint) then extends to the lumber , thoracic and cervical vertebrae (Back symptoms).

5-Enthesitis :inflammation of the sites where the tendons or ligaments inset into the bone.

6-Rheumatoid factor /anti CCP are negative.

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 .

RHEUMATOID ARTHRITIS

Most Rheumatic diseases are : chronic , inflammatory , systemic (not a mechanical (joint) disease that affects primarily the joints) , autoimmune , affect joint with variable extent with unknown etiology .

Most joints affected here are small joints : PIP , MCP , wrists , MTP , ankles , knees

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**) :DIP→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 .
- **CHRONIC** : long duration
- **Pattern** : additive (today complain tow joints , next week 5 joints …)
- **Fluctuating curse over weeks to months (comes and goes)**
- **Non-remitting** : don't remit alone without treatment (DMARDs) except in rare cases .

And so : The old criteria for diagnosis require persistent symptom for six weeks at least ; to exclude viral and reversible arthritis .

→Rheumatic fever : don't cause chronic joint symptom (more than 1 month) **, it cause short lived arthritis (less than 1 month)**

NOTE : if you see that joint symptoms persist for more than month **most likely you're not dealing with Rheumatic fever !**

→Morning stiffness : - since it's an inflammatory process

- due to edema inside the joints and the intra articular pressure is high .

- (duration **more than** 1 hour)

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

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]

In old criteria [7] , 1987 :

→ Symptom must last for 6 weeks at least

→ **Patient must exhibit <u>four</u> of them**

→ **you can diagnosed here by history only !**

→ **CCP anti No** !? ما كان مكتشف وقتها

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

Rheumatic fever	Rheumatoid arthritis
Large / major joints On the joint itself (olecranon process).	Small joints 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) .

In new criteria [4] , 2010 :

→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 :→ The new criteria follow SCORING system

→ * allow you to make an early diagnosis (how) as it not require the duration just to be more than 6 weeks .

•to be diagnosed with RA in new criteria you need score of more or equal to 6/10 .

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

X rays findings : Erosions , osteopenia , narrowing of joint space , soft tissue swelling.

→Other manifestation of RA : Extra-articular

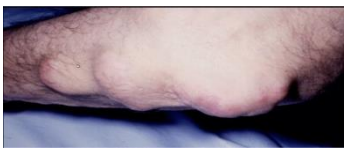
-pericarditis -neuropathy -scleritis - Vasculitis -Subcutaneous nodules

-**felty's** syndrome (RA , splenomegaly , neutropenia)

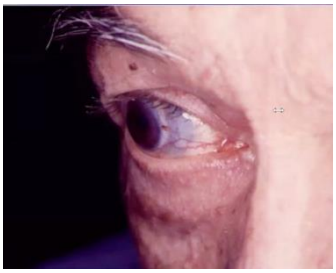
-**sjogren** syndrome can be a complication of secondary involvement in RA (xerostomia + xerophthalmia) , they called Sicca symptoms (Dry eye , Dry mouth) , parotid enlargement ,

-**pulmonary** involvement (interstitial fibrosis)

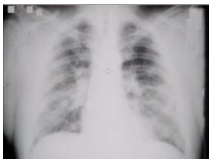
→ nodules on extensor aspect and large >>> nodules of RA



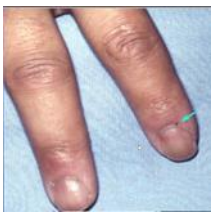
→ scleromalacia : thinning in sclera (dangerous sign ! it can cause rapture of globe and loss of vision) blue in color due to exposure of the choroidal veins; due to Scleritis which could rupture and lead to blindness.



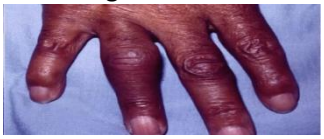
→ chest x- ray show interstitial lung disease (bilateral reticular nodular shadow) sarcoidosis



→ digital infarction / vasculities



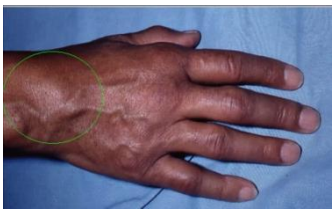
→ PIP joint swelling 4th & swan neck 5th



>> swan neck deformity : extension of PIP , flexion of DIP

>> boutonniere deformity : extension of DIP , flexion of PIP

→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

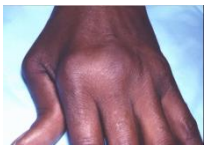


→NOTES : RA age (30-55), **incidence : 30/100.000**, **F:M 2-3:1** : as patient younger think of SLE , as older think in RA , so age is important in ddx here ! No morning stiffness in SLE . x-ray of bone show joint erosion >> destruction >> deformity (70% of joints erosions occur in first 2 years of disease so early treatment and diagnosis very important) , Most have fluctuation course (exacerbation + remission), active disease 10-20% through its course .

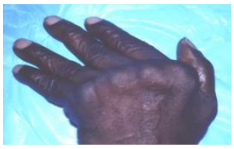
5% of patients > 65 years .

Older than 65 years and presented as RA : you have to rule out : chronic infection as TB + Malignancy manifested by para neoplastic syndrome .

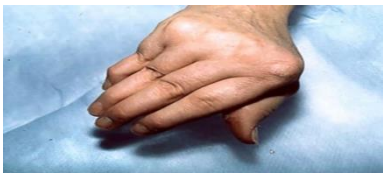
→ Z-deformity of thumb, Swelling in the MCP of 2nd and 3rd fingers. Muscle wasting (arrows).. Late case patient



→ 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) .

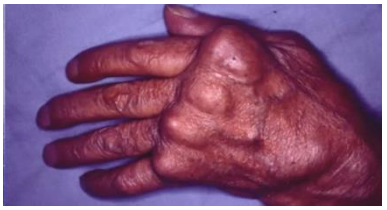


→Swan-neck deformity in the in the 3rd ,4th and 5th fingers
Ulnar deviation , Swollen MCP , Tobacco stained fingers , Hyper keratotic lesion

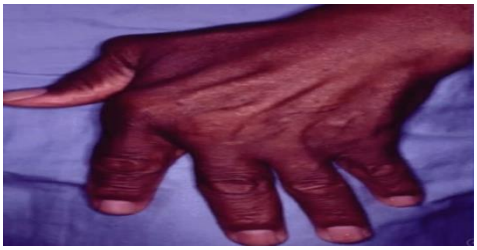


→ Volar subluxation of MCP joint (step sign) & clubbing !!! why ? lung fibrosis of RA .

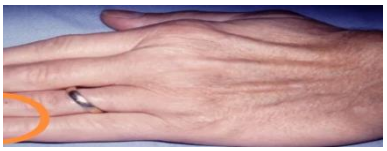
Thin and shiny skin ; elderly or taking steroids



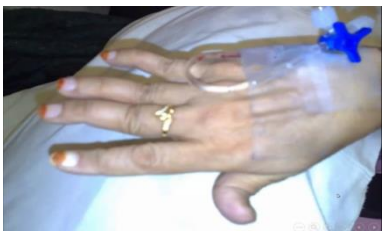
➔ Ulnar deviation , Muscle wasting(dorsal interossus muscle) , Z deformity



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

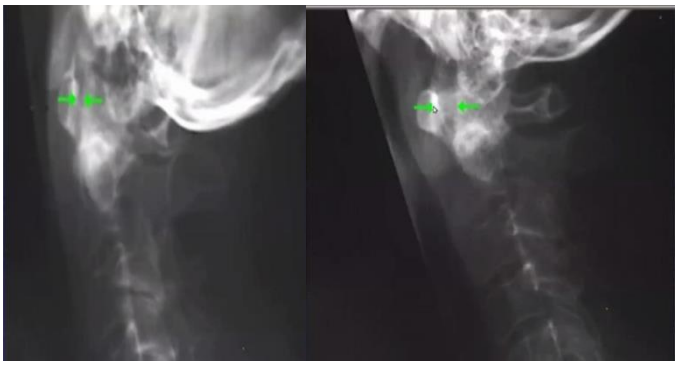


→Swan-neck deformity , Muscle wasting , Finger clubbing



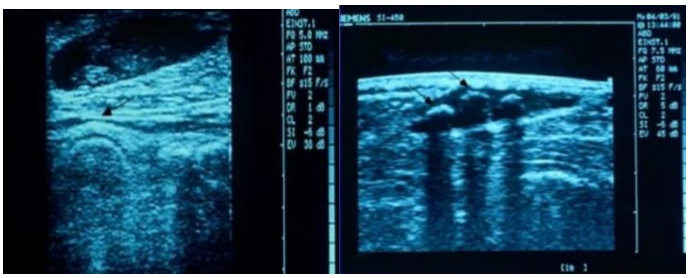
→ Neck sub laxation in C1 & C2 (patient come with electric like pain in back when he looking down) can compress the pyramidal tract leading to quadriparesis.

After movement of the neck ; the distance is increased ; Subluxation of c1 ,c2



→ BAKER cyst : knees (arthritis with effusion) fluid in the posterior popliteal region

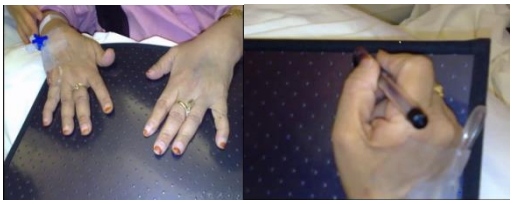
sitting with completely flexion might lead to its rupture; fluid will diffuse to the calf muscle leading to acute inflammation that simulates DVT



→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)



→ 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, haemarthrosis)

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

GENETIC PREDESPOSITION :HLA-DR4 ⟶ most common . HLA – DRB1 ⟶ bad prognosis (here the Anti CCP positive : worse disease)

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

→increase evidence of infection , cardiovascular disease and lymphoma.

→PATHOLOGY :

•Unknown trigger → Active T-cell activate macrophages :

•cytokine TNF alpha , IL-6 , IL1 (high inflammatory cytokine) that activate :

1- Osteoclast : bone destruction , RANK-RANK ligand → decrease OPG .

2-Chondrocyte : cartilage destruction and apoptosis .

3-Synoviocyte hypertrophy &inflammatory cell

PANUS (highly destructive pathology)

→B-cell : produce RF & Anti ccp → more immune complex and complement.

→Endothelial cells : more adhesion and expansion through blood vessels .

NOTES: RF & Anti ccp mean → **worse prognosis**

→ anti ccp is **specific** factor for RA

- Rheumatic factor : IG reactive against Fc portion of IgG . Mostly IgM pentamer is big molecule can accumulate cells and augment RA !
- IgM against IgG .

The Importance of CCP : 1- Good for diagnosis 2- Prognosis 3- Help in prediction
REMEMPER → damage of joint start early in course

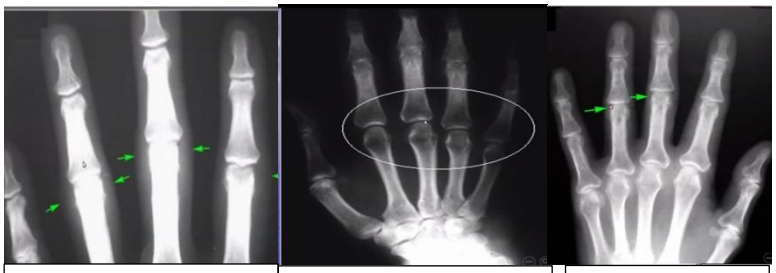
→Pregnancy : RA :70% improve due to placental steroids, and the methotrexate is stopped before **3 month** . most DMARD can be stopped , **HCC and azathioprine are relatively safe (in case of symptomatic pregnant)**

❼ **SLE : mostly worse more and more .**

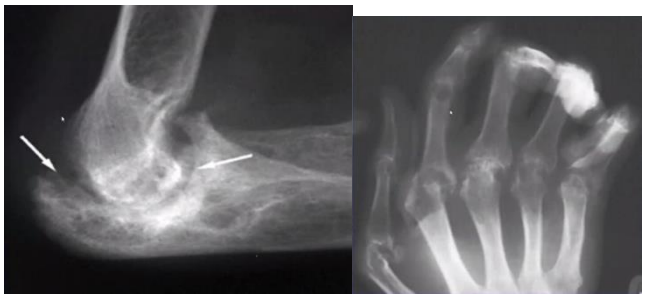
→If you see X-ray of hand you can see :

x ray is usually valid for 6-12 months

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



Joint space narrowing | Peri-articular osteopenia | Marginal erosion

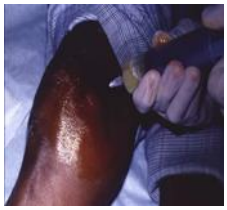


Bone destruction

→Poor prognosis RA in :

1- Poly articular joint disease
2- Persistent active disease
3- Extra – articular manifestation
4 Positive (RF / Anti ccp)
5-Elderly
6-HLA – DRB

We do joint aspiration in case of single joint out of proportional inflamed of other joints:
RA fluid is turbid . Normal fluid : light yellow clear , viscus , transparent , translucent .



Pus from the joint coming out = septic arthritis

→ Turbid (CSF) in RA ! (high inflammatory fluid)

TREATMENT: Non pharmacological : patient education , exercise , rest

- ➔ Extra note : Assessment of activity : DAS28 : Disease activity score : Tender joints , swollen joints , ESR , +/- CRP , patient global health(0-100) zero is the best .
- ➔ **We treat the morbidity , CVD , Stop smoking , treat HTN , DM , Dyslipidemia and so on .**
- ➔ **Our goals : to prevent further loss of joints and permanent SE as liver toxicity .**

Only controlled NOT cured .

Pharmacological : to induce remission , mainstay treatment for all patient except those who are in remission

- ❖ **NSAIDS [don't alter outcome]** → pain control (**selective COX2** : no GI symptom + don't affect **platelet , they end by – COXIB) , increased risk of thrombosis** 💻
- ❖ **DMARDs** [shouldn't be stopped even if the patient in remission] → methotrexate (best initial DMARD), hydroxychoroquine , cyclosporine.

  Methotrexate : modify outcome , slowly act , long term effect , considerable SE , need close monitoring (CBC , LFT , urine analysis , examine eyes)

- ➔ Monitor of MTX by : liver function test (risk of hepatitis) , bone marrow / CBC (risk bone marrow suppression)
- ➔ SE of MTX 💻 : Bone marrow suppression , Hepatitis , folate deficiency , interstitial disease as pneumonitis ,GI ulceration from oral to anus , Teratogenicity .

Corticosteroids in :

strong anti-inflammatory ,
for short duration up to 3
months
can halt progression of
erosion
oral , IV , intra-articular
1 -Acute disease (
exacerbation)
2- Interval (6 weeks) until methotrexate act (bridging)
3- If there is vasculities

Gold injection : not used now (nephrotoxicity)

New – Biological agent [anti TNF] : etanrcept (sc) , infliximab (IV)

Disadvantages of biological agents :
1- Risk to recurrent infection esp. TB
2- Very expensive

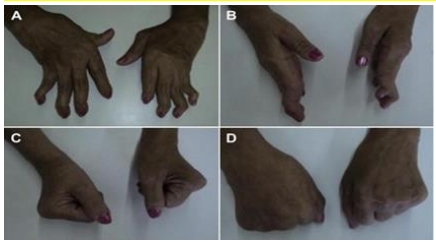
→Abatacept : prevent interaction between T cells
and APC (it blocks the whole cascade)
Rituximab : anti B cells

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

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

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 .

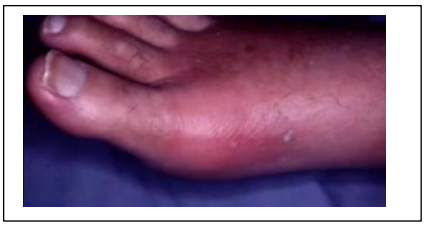
❼ You can see here a reversible sawn neck deformities , which is not considered as RA , instead it's mostly SLE patient !!



Crystal Induced Arthritis :

→caused by precipitation of uric acid crystal in the joint or soft tissue

Three types of crystals can induce "crystal induced arthritis"



1- Mono-sodium urate causing gout
2- Calcium pyrophosphate causes pseudogout
3- Hydroxy-appetite crystals

GOUT and PSEUDOGOUT

→common site is first metatarsophalangeal joint , this joint is involved in 50% of gout patient in their first presentation , and in 90% of patient during their whole disease course , 80% involve one joint mostly in the lower limbs . so if patient have arthritis for 10 years for example and there were no involvement of MTP joint , don't consider gout as much as other possible DDx .

- gout in big toe called podagra
- **DDx of arthritis in this joint** : septic arthritis , cellulitis , and most typically OA
- usually doesn't come to female in their reproductive ages × , usually post menopause poly-articular . it could come in the knee , ankle , shoulder or elsewhere , usually takes large joins in acute attacks not small joints (hand joints for ex.)
- gout is a very painful arthritis , more painful than others , patient with gouty pain will not tolerate the sheet of the bed . the attack lasts for one week to maximum three weeks , usually gout subside with treatment and rarely before one week .
- short onset, develops during hours not days , usually pain develops at night (Saturday evening in الغرب because of alcohol intake at this time. In Arabs they will be at cardiology ward because of usage of *diuretics* that have a side effect of hyperuricemia) .
- It could be acute or chronic arthritis , its cause by precipitation of urate in joints and soft tissues .
- Palindromic rheumatism : arthritis have very short duration (hours).

→Sometimes when a **lady 24 YO** came to the ER with **acute knee arthritis** , it's hard to differentiate whether its septic arthritis OR gout , both have **pain** , **hotness** , **tenderness** , **swelling** , **limitation** of **movement** and **fever** , different points are :

1- Being a female and young is far away from gout .
2- Night time of pain and development time of pain (in gout is hours but in septic is days).
3- Ask about precipitating factors of gout like recent trauma , related medications like diuretics , alcohol consumption .
4- Recurrent or not (if yes it's with gout , if not this can go with both). With gout attacks resolve completely even if untreated in 1-3 weeks
5- Presence of tophi (gout)
6- First MTP involvement (gout)
7- Renal involvement [stones , impaired renal function] → (gout)
8-high grade fever , shaking chills , leukocytosis →(gout)
9- In examination : extension of inflammation in acute gouty attack is more than the joint area , it spread above and below the joint [extend beyond the involved joint , may be mistaken with tenosynovitis , arthritis in adjacent joint area or even cellulitis] . this spread must be acute (within hours) to be characteristic to gout . because septic arthritis if not treated

probably it could spread too but over weeks

Note : think of **Gout** in **Hypertensive** patient who was managed with **Thiazide** .

It has 4 phases :

1-Asymptomatic: high uric acid level without symptoms ,discovered accidentally by blood testing for other reasons . This face ends with the first attack .
The patient may stay asymptomatic for life , may have first attack and never have second one, and may have recurrent attacks (chronic gout).management at this case is **doing nothing** ◆v:◆ except in 2 cases :
1-uric acid level exceeds 10mg in female and 15mg in male ,, because it can precipitate in kidney causing Urate nephropathy or kidney stones. (normal urate in blood is up to 7mg) .

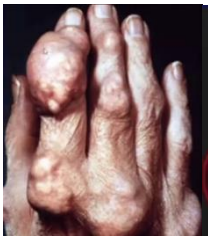
2- OR if the patient have renal impairment or stones or tophi →Urate nephropathy , renal lithiasis may precede 10-40% of 1st attack .

❼Why we don't treat asymptomatic patient with mild elevation in uric acid ? because the risk of treatment side-effects is exceeding the risk of mildly high urate .

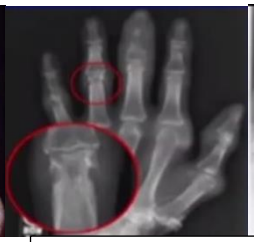
2-Acute first gout : usually start at night or early morning
monoarticular , first MTP joint , usually in the lower limbs , large joints , preferred by previously damaged joints (if a joint is partially damaged by previous OA for example) , usually last for days up to 4 weeks .
•What precipitate acute gouty arthritis ? alcohol [Saturday night] , stressful condition (trauma , surgeries) , HTN , diuretics as Loop diuretics Furosemide (the most common drug known to precipitate gout) , IV heparin , cyclosporine .
Lasts Days → Mild attack , Severe attacks → 2-3 Weeks
Half of the patients will have 2nd attack within 1 year and Frequency of attacks increases with time .

3-Inter-critical gout : period of between first attack and second attack (years).
Usually we don't treat patients after first attack bacause most probably they will not have second one , except in renal impaired patients or patient with renal stones or if patient have critical job like pilots .
50% the patients will have 2nd attack within 1 year , and minority never have any attacks .

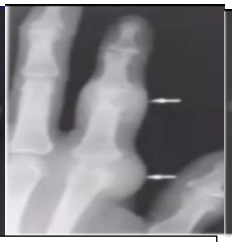
4-Tophitious gout (chronic gout) : Severe Hyperurcemia
appear after at least 10 years from the first attack , involve joints and soft tissues like tendons , ear , subcutaneous tissue .. and it must be differentiated from rheumatoid nodules .[articular and extra articular]
→Gouty tophi is immediately over the olecranon area الكوع (bursitis) , just like rheumatic fever nodules. Gouty ones are soft full with fluid that can be aspirated by needle .
→On X ray It causes erosions that are punched out with over-hanging edges , while erosions in rheumatoid are marginal erosions without punching out.

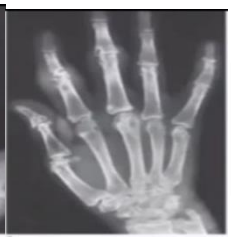


Tophaceous gout



Punched out erosions with over-hanging edges (sparing the margins (Gout))





Marginal erosions (at the joint's tip) RA

❼Hyperurcemia and Kidney :It causes **chronic urate nephropathy** [common] with renal impairment , Na+ Urate deposit in medullary interstitial , and less commonly acute Urate nephropathy except in patient with tumor lysis syndrome .

*Disease causing **acute Urate nephropathy**, precipitate in renal tubules : acute lysis syndrome (patient with tumor undergoing chemotherapy, solid tumors as lymphoma) , in oncology wards patient are on hydration and allopurinol [xanthine oxidase inhibitor] even before chemotherapy to avoid nephropathy .

* **Uric acid renal calculi**

→Hyper-uricemia Is either because under-execration (90% so more common) [chronic RF , Renal tubular defect] or over-production 10% as with enzyme defect .

Uric acid path in kidney : 1- filtered 2-reabsorbe 3-secreted

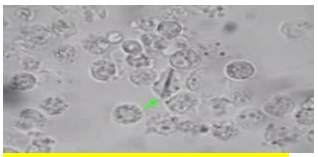
Overproduction in liechnehan syndrome (defenses and mental sub abnormality) , affect female more than male .

Diagnosis : 1-clinically (as mentioned above)

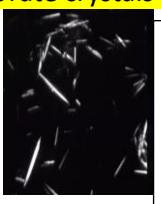
2-lab (Urate serum level , synovial fluid)

❼For all mono-arthritis , the best diagnostic tool is joint aspiration (in gout fluid is turbid with high cellularity , and Urate crystals (intracellular needle shaped crystals) , WBC count is more than 2000-20000 cell , (its normally **less than 200 cell**) and it can sometime cause a count of 100000 , here cell count will not help to distinguish between septic and gout). **And we do culture and glucose level of synovial fluid .**

WBC less than 200cells / mm3 ❼ normal
200-2000 cells / mm3❼ non inflammatory
2000-20.000 cells / mm3❼ Inflammation [Gout]
>100.000 cells /mm3 ❼ Septic , or even more than 50.000 cells /mm3
200-2000 cell / mm3 ❼ Hemarthrosis



Urate crystals under LM.



VE birefringence under polarized light, crystals shine up with dim light [black background], needle shaped

❼Low glucose mean septic (bacterial infection) .

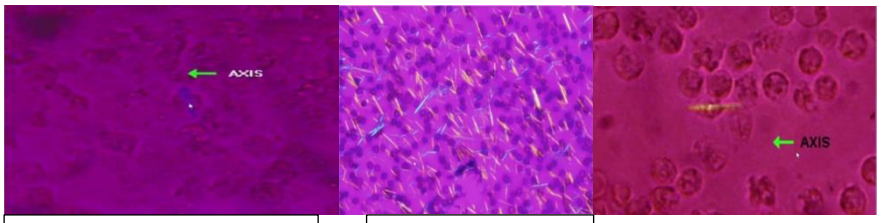
❼Culture is **negative** in gout . but in septic , the probability to have positive culture is 95% , except in patients who had antibiotics before test , or un-usual organism that is difficult to grow .

❼Polarized like microscopy > crystals appear shiny in black background (negative birefringent) .

→When Urate crystals is with the axis > its yellow In color , against the axis it turns blue ,,, opposite in pseudo-gout (which have rhomboid shaped crystals) .

There is also red light microscope (red background).

→Both septic and gout have elevated blood WBC count , but more in septic



Yellow if parallel to the axis

Blue if perpendicular to the axis

Under Red light compensator

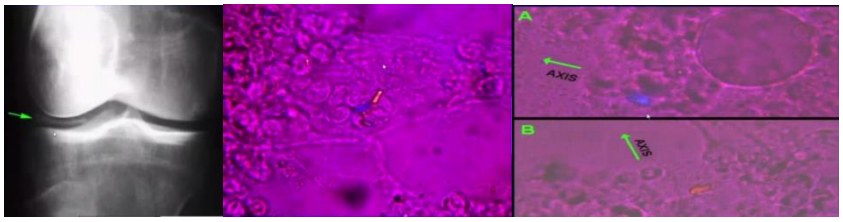
[Pseudo gout] : →Pseudo gout and CPPD **aren't the same term** ! , pseudo-gout is one presentation of CPPD .

patient with CPPD maybe Asymptomatic (most common) OR have pseudo-rheumatoid OR pseudo- OA OR pseudo-neuropathic , Pseudo gout.

CPPD**[** Calcium pyrophosphate crystal deposition] usually in **elderly**, more in **female** , and usually affect **large joint** like **knee** [most common] , wrist , symphysis pupis and shoulders .

❼(On X-ray) Appear like calcification on cartilage of joint > called *chondrocalcinosis* ,this is very typical & cheap to diagnose CPPD ,most patients here asymptomatic !

❼Shape of crystals is short rods (like bacilli organisms , BRICK SHAPED) , the color is **blue when parallel to axis** , and **yellow when perpendicular** (or opposite to axis) .



Management :**Manage risk factors** (drugs , alcohol , …) , give fluid , reducing weight , diet modifications (just to reduce *not stop* uric acid containing food and protein containing food)

NSAID [diclofenac , ibuprofen] in **acute attacks** unless the patient have renal impairment , instead we use **colchicine** (never combine NSAID with colchicine , both together lead to sever GI upset like ulceration and gastritis) OR better to give intra-articular steroids .❼**Systemic steroid rarely used**

❼Allopurinol , never given in acute attack because it may precipitate more attacks , usually in acute attacks we give NSAID or colchicine then we wait for 1 month then give allopurinol if indicated .

→**Indications for allopurinol** :

1-Recurrent attacks 2-Renal impairment 3-If the patient have Tophitious gout 4- first attack in critical jobs

Side effects of allopurinol : hyper-sensitivity syndrome , in 1 for every 1000 patients , so its alternative is febuxostat (xanthine synthase inhibitor) .

→We can use **probenecid** that increase uric acid secretion in urine [in case of under-excretion type] . its contraindicated in patients with renal stones because it increases the risk of stones .

→If you cut protein containing food completely , liver will compensate it and things may get worse.

ARTHRITIS AND RASH

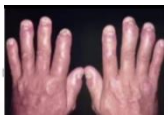
DDX of Syndrome came with : joint pain, swelling ,limitation of movement, rash.

1-Allergy .

2-Infection (if it for low duration ,acute) :viral ,FLU , EBV ,CMV. Hepatitis [A, B , C→ mcc of rash and arthritis [rare arthritis , it's arthralgia for weeks]] , enterovirus [Maculopapullar rash , pleurisy, sore throat , conjunctivitis → less than week] , herpes ,parovirus(it come w arthritis and rash so diff. about RA by duration this infection ended by weeks 1-2 weeks) , HIV >2weeks .

3-SLE ☺☺.

→**Psoriatic plaque** ,**onycholysis**, **Nail pitting , DIP arthritis** [swelling](diag. psoriatic arthritis). If this patient came with manifestation of –[psoriatic + septic + reactive] arthritis Make a hint for HIV →

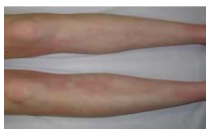



→rash if it with arthritis fever leukocytosis Liver enzyme elevation DDX:

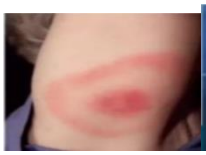
(JIA, CMV , viral hepatitis).

❼JIA (juvenile idiopathic arthritis) came as Rheumatoid or systemic.

→stills 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.



→erythema chronicum migrans ECM or bulls eye (LYME DISEASE (Borreliosis). Spirochetal bacteria called Borrelia burgdorferi ,



Tick-borne

→ECG – first degree AVblock – Mobitz I 2 degree AV block -mobitz II

→3 degree AV block (pt came w syncope ,bradycardia).

→erythema marginatum (reproduce by hot bath)

→erythema nodosum (painful , tender , indurated u can fell a mass) Ddx

:sarcoidosis ,IBD , TB , BEHCET , fungul.

→heliotrope rash , gottron's papules (dermatomyositis)

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.

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

-How it happen?

Apoptosis program cell death spontaneously and cleared by immune sys. (by B cells)

→If we block this (phagocyte clearance process swill not happen) → auto reactive cell will be → autoantibody immune complex → destruction of tissue .

→**Age** at risk : reproductive age F > M 10- 15 :1

→**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** (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 :

1-**malar rash** over checks and bridge the nose :

*Malar rash(regular) ⟶ 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** , hair loss more than 100

3-**Oral ulcer :** Painless , 2-3 days will heal , superficial lesion .

4-Arthritis : No erosion , but can be deformity (tendon and ligament affect) ,deformity it can be **corrected by** prior sign , migratory , mostly ,symmetrical , MCP – PIP could be involve .

→differentiate btw RA and SLE :no morning stiffness , age [younger], no erosion.

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 Bilateral MOST LIKELY SCLERODERMA.**

6-Patechie Thrombocytopenia , vasculitis

7-Livedo reticularis (net like dilated blood vessels) ddx anti phospholipid syn.

8-Renal finding →the most common cause of mortality and morbidity and affect 50% of the cases. Immune complex mediated .

-Glomerulonephritis:

1) Stage I : minimal changes FOOT

2)Stage II : proliferation mesangial

3) Stage III : focal segmental , Focal means less than 50% of Glomeruli , Segmental means : segment of Glomeruli not the whole one .

4)Stage IV : diffuse : the whole Glomeruli , loss of mononuclear cells .

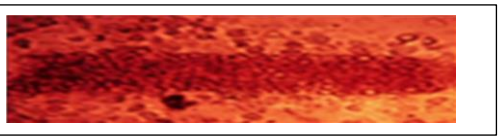
5)Stage V : membranous (HEAVY PROTEINURIA)

6)Stage VI : advanced (sclorosing) Total hyalinized of glomerulus .

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)

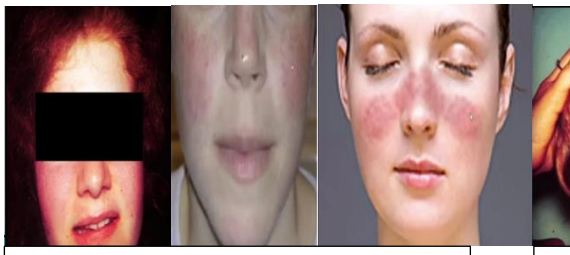


10-Serositis : pleurisy (stabbing , local. , increase with inspiration .) , phenomena , pleural effusion
11-Seizure (it happen because of renal(nephritic) , increase BP , so patient get HTN encephalopathy .

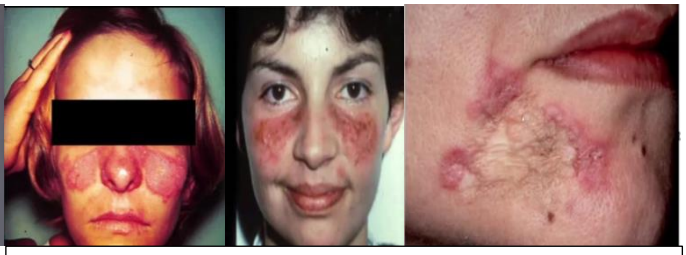
12-Hemolytic anemia and anemia of chronic disease: (HSR II) (increase bilirubin , increase reticulocyte , diagnosed also by coombs test [+ve]) . leukopenia (decrease lymphocyte) ddx HIV
13-Aseptic endocarditis (immune complex non infected cause)

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 .

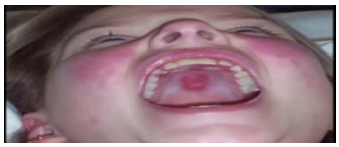
DDx: steroid overdose (rare).
15-lupus started with fatigue , fever , Weight Loss and affect other systems .



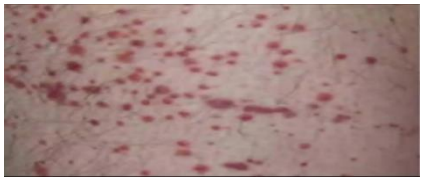
SIMPLE MALAR RASH



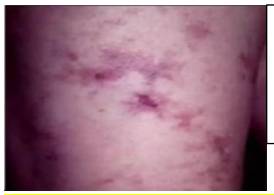
DISCOID MALAR RASH (scales with raised, edges that will heal with hypo or hyperpigmentation, resulting in dermal atrophy , follicular plugging and SCAR FORMATION



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 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

Criterion	Definition
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 DNAactivity of SLESPEC.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).

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%

Managements : depends on the organ .

Skin , MSS, Serositis → NSAID , HCC , Local cortisol . **More serious involved organs [CNS , Renal]** →immunosuppression with high dose of steroid with AZA or cyclosporine

- ✓ Treat **infection** > aggressively , no infection in lupus should go home.
- ❼**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:
  - Reduce inflammation, protect against organ damage
  - Remission joint , skin and B. vessels involvements
  - Anti lipidemic , Safe in pregnancy
  - **SE [Contraindications]** : Hyperpigmentation , Myopathy in RF , Retinal and corneal toxicity (halos around lights and photophobia, annual fundoscopy is necessary)

→Vaccination →influenza (active)yearly , + pneumovax /5years

✉**Biological therapy** Belimumab •Belimta (biliniomab) →to reduce remission

Suppress B cell development (Rituximab) + block B-cell stimulation.

We don't use Methotrexate .

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 : 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 symptoms , the fetus should aborted ☹ , but rare الحمدلله ..If the female unstable > pregnancy is prevented **.** 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**.**

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.

Vasculitis

Inflammation of blood vessel wall (intima) by inflammatory cells (everywhere in the body so it give wide manifestation), its autoimmune disease (unknown cause) , Can be fatal (esp. Wegener). The inflammation depend on the area that is not recognize the Abs as normal ➔patchy involvement .

❼Because of the pathology (inflammation) it will cause fever , weight loss and depend on the organ :

kidney: Renal artery stenosis >> HTN , Renal failure

Lung : pulm. artery >> pulm. HTN

CNS + skin manifestation .

GI: GI bleeding

❼when we see purpura or petechial rash >>> look to platelet count if it normal then look at platelet function (bleeding time) if it also normal >>> its Vasculitis .

❼purpura of Vasculitis will be **painful** , **elevated** (palpable), distribution over dependent area .

➔ WITH Vasculitis maybe preexisting C.T disease ex. lupus RA.

Note : What will happen if the blood vessel get inflamed ?

✓ In small vessels :

1) edematous friable (subcutaneous blood oozing ❼ petechial rash) and may rupture ➔leaking of blood ➔**bleeding** .

2) edematous swollen stagnation of blood ➔ischemia (infarction)

✓ In medium and large size :

1) Aneurysm : dilatation of vessels

2) Healing and fibrosis ➔**narrowing** ➔claudication of extremities [femoral , axillary arteries].

→During active phase of inflammation →GI / SC bleeding OR Aneurysm

** systemic manifestation : Fever, weight loss and tiredness

✓ Common Small vessel Vasculitis : HSP , GPA , MPA

✓ Common medium vessel Vasculitis : PAN , Kawasaki disease

✓ Common Large vessel Vasculitis : Takayasu arteritis , Giant cell arteritis

→ **Vasculitis can be** : primary or Secondary to other disease as : * **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)] .

Other classification : ANCA+ve [MPA ,GPA , eosinophilic granulomatosis with polyangiitis (Churg-Strauss Syndrome – like Ashtma presentation)] , ANCA –ve .

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

Takayasu Arteritis :

- Young age Less than 40 [10-40] (if older ➔atherosclerosis not Vasculitis !!) , more in female 80%-90% (F:M ❼ 10-1).
- Affect Large vessel esp. **aorta** and its major branches (brain and upper limb).
- In 50% affect Abdominal , Pulmonary vessels . More in japan
- Manifestation :
  - ✓ claudication in upper extremities and ➔(unequal pulses >10 (diminished) "radio radial and radio femoral delay)➔in subclavian involvement .

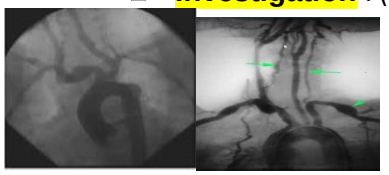
    Pulse delay DDx. : coarctation of aorta and Takayasu .
  - ✓ May involve renal a and cause HTN ➔50%
  - ✓ erythema nodosum : painful indurated nodule in lower limb , Pyoderma gangrenosum.
  - ✓ Subclavian steal syndrome : aneurysm in the origin of vertebral artery >> cause wide area W low pr. >> so retrograde flow of blood from vertebral artery to subclavian artery
  - ✓ Angina pectoris : Patient presented with chest pain , SOB , HTN , Hemoptysis.
  - ✓ Bruits over subclavian , brachial , abdominal vessels .
  - ✓ **Vertebral artery involvement (narrowing) → patient presented with syncope attack .**
  - ✓ General symptoms : Fever , Fatigue , Weight loss

"most common cause ➔post streptococcal"

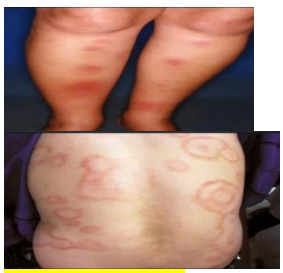
- **dx.:**
  - Angiogram (aneurysm , beading , narrowing{after healing and fibrosis}) , (IF it's chronic ➔collateral)
  - x-ray (aneurysm dilatation or widening mediastinum).
  - PET-scan , CT , MRI .

    Note: (biopsy of aorta is contraindicated)

    ❼**Biopsy will be your first choice in case of typical small vessels inflammation and skin lesion**
- **Investigation** : (ESR+CRP →+ve) , (albumin →-ve) .



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

Erythema annulari : Vasculitis.
Erythema marginatum : Rheumatic fever.

Treatment:

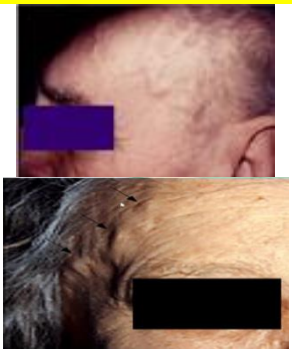
1- steroids high dose 1-2mg/kg

2- immunosuppressive drugs (methotrexate , Azathioprine , Mycophenolate)

3- bilogical agent (anti-B cell agent : rituximab)

4- surgery : revascularization in case of vessel narrowing , Bypass graft

Temporal arteritis :



Signs for temporal arteritis?
Palpable and tender temporal artery
First investigation to do?
ESR

- ✓ Large vessel /age >50 , F:M ❼ 3:1 ,
- ✓ Affect intracranial branches of carotid (presented by unilateral headache)
- ✓ Presented by headache 70% , tender vessel with fever (FUO).
- ✓ Jaw and tongue(lingual art.) claudication 50% (when talk and when masticate) , arms claudication.
- ✓ The important early complication (**abrupt** blindness) by involving ophthalmic vessel .12%
- ✓ If the pt. get one eye blindness ➔emergency ➔to protect the other eye , risk of other eye blindness within 1-2 weeks .

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 ❼ statrt treatment before biopsy (needs 2-3 days) .

Diagnosis:

- ✓ Temporal : biopsy from temporal (**1.25 -1.5 cm** due to patchy phenomena)
- ✓ CXR ➔JUST AORTIC DILETATION
- ✓ **HIGH ESR AND CRP (most important and the first one)**

➔ 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 .

Treatment : 1- steroids high dose 1-2mg/kg

2immunosuppressive drugs “steroid sparing /protect from steroid side effect withdrawal) (methotrexate)

3bilogical agent (anti-B cell agent : rituximab)

❼Typical case : >50 years , headache , sudden blindness , PMR , UOF , anemia of chronic disease , increased ESR , CRP ❼ temporal arteritis treatment then biopsy , may we do

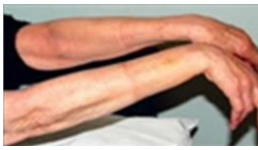
Reentry via US without biopsy .

NOTE : FUO DDx in elderly : -lymphoma -TB and Brucellosis -Temporal arteritis -Infective endocarditis.

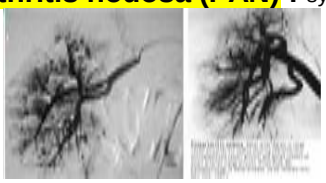
→ Mononeuritis multiplex MNM (FOOT , WRIST DROP) DDx:

-DM (**commonest**)-PAN in young age after exclude DM-Leprosy

-Infiltration (compression)



Bilateral wrist drop
(radial nerve palsy)

Polyarthritis nodosa (PAN) : systemic necrotizing Vasculitis 

✓ **mainly MEDIUM** size , can affect small size , involve up. Limb more .

✓ Manifestation :

1-Gangrene in tips of fingers and toe .

2-**Livedo reticularis** (network of vascular dilatation) , we can see it also with SLE and more common with Antiphospholipid syndrome .

3-Multiple ring lesions in the lungs

4-Radial nerve injury (mononeuritis multiplex) OR polyneuropathy [both hands]

→HTN (if involve the renal artery) , new onset of diastolic pressure >90 mmHg .

High urea > 40mg/dL , High creatinine > 132µmol/L

✓ 25-40% of Patient ➔HBV surface ag +ve (that's why many people says that hep.B is a cause of PAN .

✓ -ve ANCA

Diagnosed : by angiograph (multiple micro aneurysms)

→**typical of PAN .**

➔**Treated :** as above (but immunosuppressive ➔Cyclophosphamide not others !), Renal transplant + control HTN (with CCB , not by ACEI (renal stenosis))

- **Small vessel arteritis :**

we take biopsy in case of presence of skin lesions

1.ANCA associated

- **Wegener granulomatosis (granulomatosis with polyangitis)**
- **Microscopic polyangitis .**
- **Eosinophilic Wegener :** Bronchial asthma + high eosinophilia + vasculitis **>> churgstrauss syndrom .**

2.Immune complex vasculitides : cryoglobulinemia → IgA nephropathy and vasculitis ,

hypocomplementemia .

Wegener –granulomatosis : can be fatal ☹

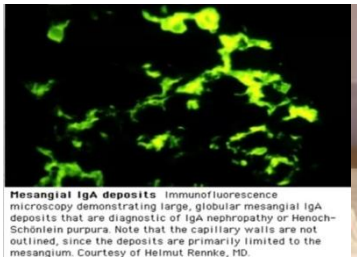
Mainly affect small vessels , to lesser extent affect medium size , venules , arterioles.

- ✓ Upper respiratory tract symptoms (oral and nasal) with lower respiratory tract (pneumonia) and renal involvement .
- ✓ Granulomatous inflammation .
- ✓ Manifestation :
  - sinusitis , epistaxis
  - Saddle-nose due to destruction of nasal septum . (ddx : Wegener , lupus , trauma , syphilis , relapsing polychondritis)
  - skin manifestation
  - CXR showing ring lesion , nodules , alveolar opacity , bleeding , cavitation .
- ✓ **+ve C-ANCA (proteinase 3)**
- **Diagnosis : biopsy , immunofluorescence .**

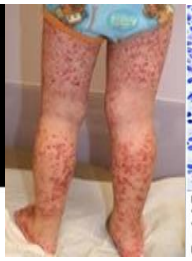
Henoch-schonlein purpura : IGA Vasculitis

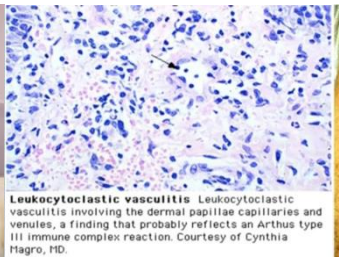
- ✓ Young male pt < 14 year , more in children <5 years .
- ✓ Manifestation :
  - PURPURA (100%) on buttocks and behind the thigh
  - abdominal pain(mesenteric infarction)(63%).
  - Renal (40%) (more severe in older children)and GI bleeding(33%)(very rare) .
  - joint pain(83%).
- ✓ follows RTI .
- ✓ IgA mediated small vessel vasculitis after a viral infection (URT)

- ❖ **Diagnosis : skin biopsy ,** kidney(BIOPSY IgA deposit) not usually.
- ❖ **Treatment :** **steroid** only in case of abdominal pain (abdominal vasculitis) and renal involvement (crescent GN) may we use Cyclophosphamide . otherwise we don't treat .
- ❖ **IVIG plasmaphersis :** type of management

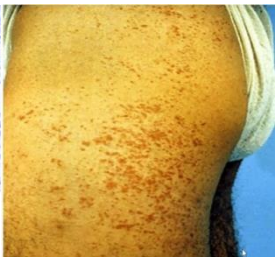


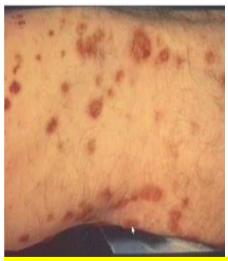
Mesangial IgA deposits Immunofluorescence microscopy demonstrating large, globular mesangial IgA deposits that are diagnostic of IgA nephropathy or Henoch-Schönlein purpura. Note that the capillary walls are not outlined, since the deposits are primarily limited to the mesangium. Courtesy of Helmut Rennke,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



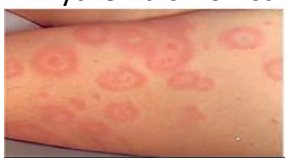


How to approach vasculitis :

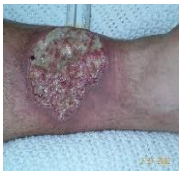
hx of medication , hep C,B >> esp in PAN , SLE manifestation , female , lab test (cbc , ESR, CPR) , KFT (proteinuria 150 mg/d, hematuria, cast) , creatinine , complement , ANA for lupus , ANCA test (PR3 ,MPO) , nerve conduction ,, EMG (electromyogram) in case of MNM>> dermatomyocyte and PAN ,tissue biopsy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

Note : MPO (myeloperoxidase) = P-ANCA +ve in PAN and eosinophilic GPA (eosinophilic Wegener

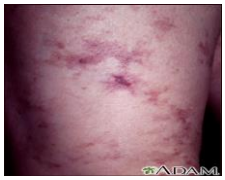
❼Erythema chronicum migrans (Bull's eye rash) DD: Lyme disease , Vasculitis.



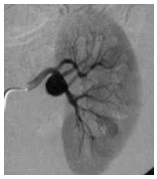
→Pyoderma gangrenosum : ass. With arthritis , IBD , vasculitis .



→ livedo reticularis ass. With anti-phospholipid syndrome(MCC) and PAN , SLE

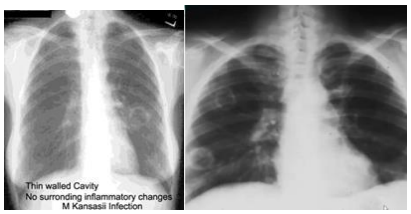


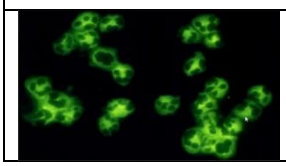
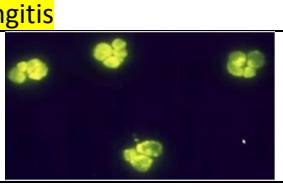
→renal angiogram aneurysm >> PAN



→saddle nose >> wegner , lupus , trauma , syphilis , polychondritis , SLE , leprosy ,

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



C-ANCA (Pr3) → protease 3	P-ANCA(MPO) → Myeloperoxidase Positive in Microscopic polyangitis
	

Scleroderma(systemic sclerosis):

Patient characterized by :Loss of wrinkles , peaked nose , hands are very tight .

So scleroderma: rare connective tissue disorder , more in Females , characterized by:

1) Skin thickening (tightness)
2) Vasculopathy (that's why there is Raynaud's) 95%-99% of patients (triggers :cold , emotional stress)
3) Auto antibodies , 95% +ve ANA , **anti-Jo Ab may be seen with lung involvement**.

There are Two types of scleroderma , Based on cutaneous involvement:

1-limited form: indolent type , associated with higher risk of Vasculopathy (pulmonary hypertension) more than diffuse form , involve Face and distal limbs , with **anti-centromere Abs** ,also **CREST**

Calcinosis	Raynaud's	Esophageal dysmotality	Sclerodactyly	Telangiectasia

2-diffuse(generalized) form : involve all skin and internal organs derangement(lung (fibrosis and interstitial), GI, others) with worse prognosis ☹ . With +ve anti-scleroderma 70 antibodies (anti-Topoisomerase)

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.

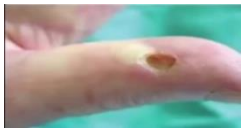
Minor criteria:

1)sclerodactylyl stiffness and tightening of the skin of the fingers (Acrosclerosis)
2)digital pitting with scars and ulcerations loss of substance of the finger pad
3)pulmonary fibrosis(bibasilar fibrosis)

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

Organs that may be involved:

1) Most common system involved in scleroderma is GI: (diarrhea or constipation , flatulence , fecal incontinence, GERD) 95-99% (almost all) have GI symptoms .
2)Pulmonary hypertension (in limited form) , silent killer ☠ with ILD [nonspecific interstitial pneumonia , usual interstitial pneumonia]
3)Renal crises: in diffuse form esp. if given steroids (steroids can precipitate renal crises) resulting in very increased Blood pressure
4)Digital ulcers , painful , at tip of fingers , may we use biological agents with it .



5)Heart involvement : conduction defect , cardiomyopathies as pulmonary HTN (except diffuse forms)

Skin is very important organ to detect scleroderma:

#(tight skin (shiny) , contractures in hand , face(mask shaped with no wrinkles) , pursed mouth , peaked nose , loss of outer (lateral) 1/3 of eyebrows)


Flexed fingers.
Hypopigmentation in fingers at the PIP joint.
Possible Raynaud's phenomenon at the palm

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

#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 .

Raynaud's : vasoconstriction (white color) then cyanosis then vasodilation (and hyperemia).

Treatment of scleroderma:

❼treatment is usually symptomatic , Skin: no effective treatment, 60% improve with time, Calcium channel blockers may help Reynaud's phenomena . ACE is the drug of choice to treat hypertension and to prevent further kidney damage. For GI symptoms : Antibiotics (bacterial overgrowth) , PPI , Laxative , Motility agents

-methotrexate for skin softening (fibro proliferative agent)

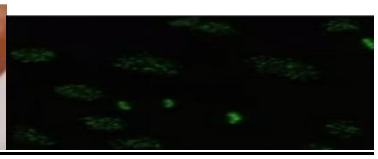
-MMF (mycophenolate) ❼ in skin and lung involvement .
-azathioprine , cyclosporine (Oral or IV) OR IVIG ❼ may be effective in some patients (severe disease ,failed or contraindicated methotrexate , MMF) .
NOTE : Azathioprine : steroid sparing agent to induce maintenance after 1 year of cyclosporine .
-but all of them are not perfect medication 🙈 🙈 🙈

❼**For pulmonary hypertension**: Endothelin receptor antagonist(Bosentan) : very expensive medication/ cause VD so decrease hypertension

❼ **biologics**(Ritoximab(anti CD20)) improve both skin and lung (interstitial lung disease)

❼**TNF inhibitors useless : in skin and lung (increase fatality in ILD) . it is effective in arthritis but increase risk of malignancy .**
NOTE : This disease is so difficult to evaluate , treat and monitor (diverse clinical picture) , usually diagnosed later . Pathogenesis in each organ isn't the same (neuro vascular , inflammatory , fibro proliferative changes in skin) , and no single drug can treat it !!!!





Vasculopathy (Raynaud's) Flexed fingers with stretched thickened skin Immunofluorescent antibodies

Dermatomyositis: inflammatory proximal myopathies

-Show (redness ,violet discoloration on eyelid) . It is an inflammatory myopathy characterized by chronic inflammation and weakness [painful] (usually proximal muscle weakness on:)

→**upper limb** :patient cant undress himself , cant comb hair . Ask patient to abduct shoulder and examine power

❼**lower limb**: patient has (difficulty or cant) get up from standing

Gower sign(when patient want to get up from sitting , he move to lateral then he will climb on himself)

❼This muscle weakness can happen in children [5-15] and adults up to 40 [40-60] (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.

❼skin disease may precede or accompany muscle disorder

❼they may be fever , weight loss

❼patients (children) may have calcinosis (calcification in soft tissues) few years later[1-3 years after onset] : as scleroderma

❼may be associated with lupus , overlap syndrome (lupus cause myositis and skin manifestations).

Differential diagnosis in patient with muscle weakness:

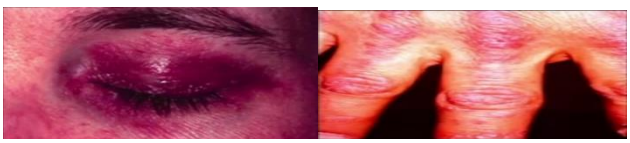
1-steroids (such as patients with lupus taking steroids) , prolonged high dose .
2-hypothyroidism , cushing's , osteomalacia.
3- Sarcoidosis (doctor discuss how to diagnose it)

Diagnosis of Dermatomyositis + clinical picture :

1-muscle enzymes (cpk ,MM ,serum aldolase)
2-abnormal electromyography(EMG) ❼ fibrillation
3- muscle biopsy(pathognomic or inflammation shown in biopsy) , MRI guided biopsy in case of active inflammation or unknown involved muscles

Treatment

-steroids [initial treatment , certain dose and limited period [4-6 weeks] **WITH** immunosuppressive like methotrexate **OR** azathioprine
❼ we can give IVIG in severe cases OR resistant
-if patient still unresponding >>> latest thing: give rituximab



Heliotrope Rash Gottron Papules (elevated erythema)
NOTE : In case of Just erythema ❼ called Gottron sign

Behcet disease

→A systemic Vasculitis that is characterized by the deposition of immune complexes in arteries and veins of 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 o acneiform eruptions -Dermatographism: formation of urticar minor pressure is ap the skin, likely medi local histamine rele
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, and 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:** **P**ositive **p**athergy test, **A**phthous mouth ulcers, **T**hrombosis (arterial and venous), **H**emoptysis (pulmonary artery aneurysm), **E**ye lesions (uveitis, retinal Vasculitis), **R**ecurrent Genital ulcers, **Y**oung 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)