



## SLE

**Systemic lupus erythematosus (SLE)** is a

- Multi-system
- Inflammatory
- Autoimmune disorder (*loss of tolerance to self-antigens*)

### Predisposing factors

1. **HLA region on chromosome 6**
2. **Premenopausal women** are most commonly affected
3. **SHIPP** drugs
4. **Ebstein Barr virus** may be a trigger for SLE

### Pathophysiology

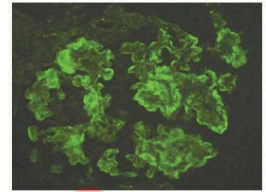
- Exposure of the immune system to **cellular remnants from apoptotic cells**.
- The cellular remnants (self antigens) activate lymphocytes and **Antibodies are produced** against them.
- These antibodies attack other normal tissue across the body.

### Antibodies

1. **Anti nuclear antibody (ANA)**
  - Positive in about **95% of patients** with SLE
  - **Most sensitive** (*entry criterion for SLE diagnosis*)
  - **Non-specific** (*may be seen in other conditions or entirely normal patients*)
2. **Anti Smith antibodies**
  - **Most Specific** for SLE
3. **Anti C1q > Anti DS-DNA antibody**
  - Corresponds to **disease activity (flares)**
4. **Anti histone antibodies**
  - **Drug induced** lupus
  - **SHIPP** drugs cause SLE (*Sulfasalazine, Hydralazine, Isoniazid, Procainamide, and Penicillamine*)
5. **Anti ribosomal P antibodies**
  - **Psychiatric SLE**
6. **Anti glutamate receptor antibody/ Anti neuronal antibody**
  - **CNS SLE**
7. **Anti phospholipid antibodies**  
(*past h/o miscarriage or thromboembolism*)
  - Lupus anticoagulant
  - Anti-cardiolipin antibodies
  - Anti-beta2-glycoprotein-1
8. **C3/C4 level**
  - **Low levels** are seen in SLE
  - Get exhausted due to complement activation in SLE

### Lupus Nephritis

- **Lupus Nephritis** is seen in almost **50%** of patients.
- **Full house effect** seen on IHC in lupus nephritis
- **Type 4** lupus nephritis (*Diffuse type*) is most common
- Risk of **recurrence** after kidney transplant is **low**



IgG, IgM, IgA, C3, C1q  
*Full house effect*



### Joints

(*Musculoskeletal system features*)

- "**Symmetrical**" small joint polyarticular arthritis (*most common clinical feature of SLE, seen in 90% patients*)
- **Jaccoud arthropathy** : Deformity present but **erosions absent** (d/d of RA)



*Jaccoud Arthropathy*

## Dermatological manifestations

- **Photosensitivity** is most common skin manifestation in SLE
- **The butterfly (malar) rash** is characteristic of SLE - *Nasolabial fold sparing (butterfly spares)*
- **Non scarring alopecia** is associated with SLE
- **Discoid lupus** refers to a benign version of SLE confined to the skin (*Scarring alopecia seen with DLE*)

Acute cutaneous lupus ("acute skin lupus")  
"Butterfly rash" (redness across cheeks and nose)

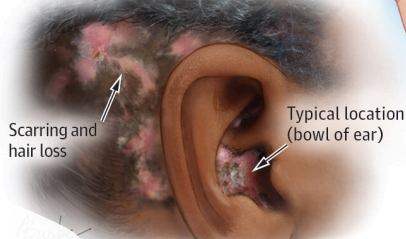


Subacute cutaneous lupus ("subacute lupus")



Red, raised, scaly nonscarring rash on sun-exposed areas

Chronic cutaneous lupus ("discoid lupus")  
Red to purple rash with discoloration and scarring

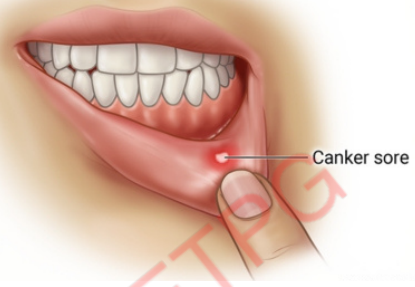


## Heart and Lungs

- The most common cardiac manifestation of SLE is **pericarditis**
- **Pleural effusion** and **pleuritis** seen in lungs
- **Shrinking lung syndrome** (*decreased lung volume*)

## Aphthous Ulcer

- Also known as **canker sore**
- A small, shallow sore inside the mouth or at the base of the gums.
- D/d is "**cold sore**" caused by **HSV-1**



Canker sore

# Rheumatoid Arthritis

Rheumatoid arthritis is a

- Chronic, systemic inflammatory disorder
- Characterised by **inflammatory polyarthritis**

## Predisposing factors

1. **Genetics** : HLA DR<sup>4</sup> (*Room has 4 walls*)
2. **Females** (*Symptoms more severe in females*)
3. **Smoking** : strongest lifestyle factor for development of RA

## Pathophysiology

- Following a suspected triggering event, there is development of **self-citrullination** (*alteration of a positively charged arginine amino acid into neutral citrulline*)
- Immune system then reacts to these citrullinated proteins
- Development of **anti-cyclic citrullinated peptide** (anti-CCP) antibodies
- **At the joint level**, the pro-inflammatory response leads to **synovial membrane hyperplasia**, which subsequently damages cartilage.
- This destructive synovial hyperplasia is referred to as a '**pannus**'

## Antibodies

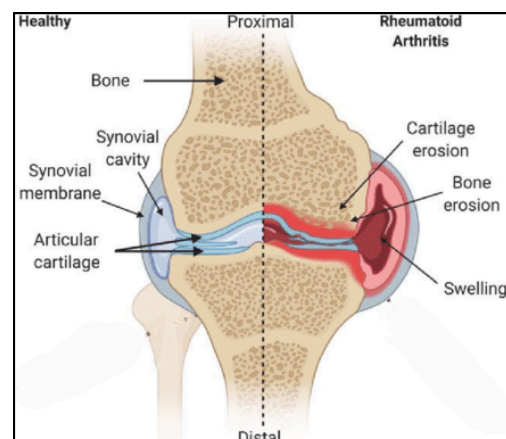
### 1. Rheumatoid factor (RF)

- An **IgM** autoantibody against Fc portion of IgG
- Seen in **60-70%** of patients with RA

### 2. Anti-cyclic citrullinated peptide (CCP)

- Autoantibodies that react to **citrullinated proteins**
- **Low sensitivity** but **high specificity**
- Positivity predicts erosive disease and worse prognosis

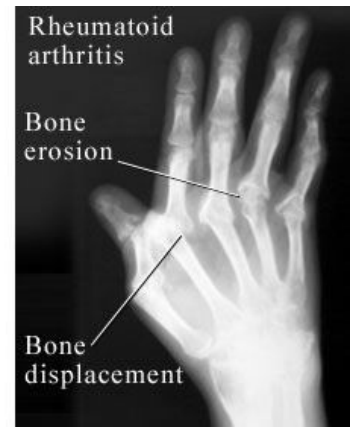
*Presence of RF and CCP : Seropositive RA*



## Joint

### (Musculoskeletal system features)

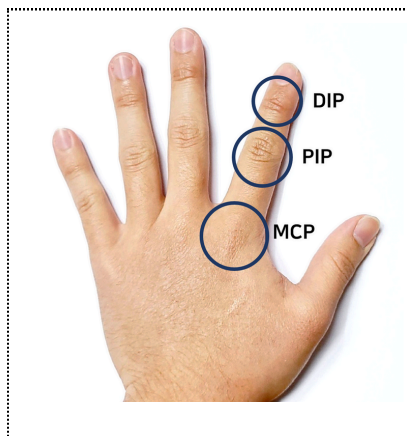
- **Symmetrical** polyarthritis of **small joints** of hands and feet.
- **'Boggy' joint swelling** due to active synovitis, often difficult to palpate joint line
- Joint pain **worse at rest or inactivity** (decreases with exercise/movement)
- **Early morning stiffness** lasting > 1 hour
- **Erosive** arthritis (erosions present)



### Joints affected

- **Metacarpophalangeal (MCP) joints** and **joints of wrist** affected
- **DIP spared** (affected in psoriasis)

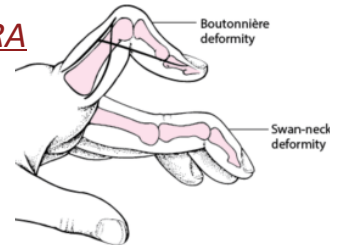
"DIP near the nails : affected in Psoriasis"



### Classical signs in Chronic RA

#### 1. Boutonniere deformity:

- Flexion at PIP
- Hyperextension at DIP



#### 2. Swan-neck deformity:

- Hyperextension at PIP
- Flexion at DIP

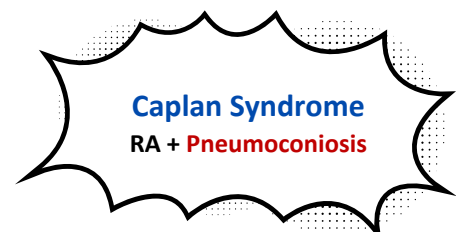
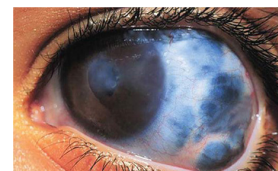
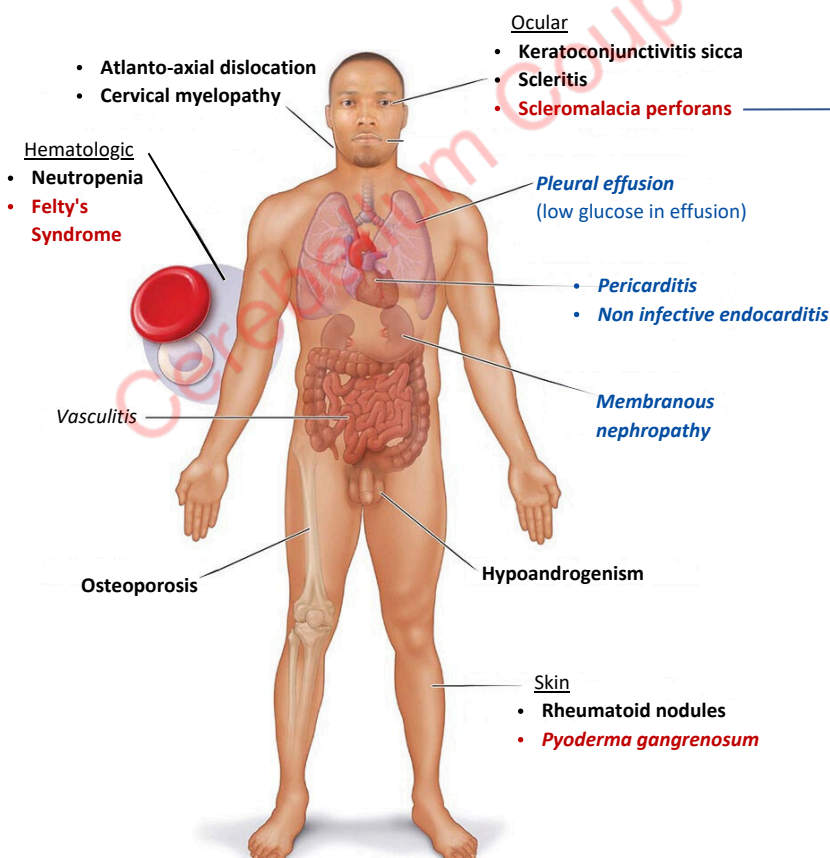


#### 3. Ulnar deviation at MCPs

#### 4. Z-deformity at wrist

Ulnar deviation along with Z deformation at wrist

## Extra-Articular manifestations of RA



## Management of RA

### 1. Initial therapy: **DMARDs**

- **First-line** of treatment
- **Methotrexate, Leflunomide** or **Sulfasalazine**
- **Methotrexate** and **Leflunomide** are **contraindicated in pregnancy** (**DOC in preg** : **Hydroxychloroquine**)

*Add bridging **steroid** therapy and **NSAIDs** (2-3 months),  
which allows time for the DMARD to take effect.*

### 2. Failure to respond: **DMARD "step up"**

- Add another DMARD (*DMARD combination therapy*)

### 3. **Biologics**

- Used as **second-line** in combination with DMARDs
- Initial therapy in patients with **severely active and progressive disease**

**TNF Alpha inhibitors** : **ACE-I** ki **GOLI**

<b>A</b>	Adalimumab
<b>C</b>	Certolizumab
<b>E</b>	Etanercept
<b>I</b>	Infliximab
<b>Goli</b>	Golimumab

*Rule out TB before initiating  
treatment with TNF Alpha inhibitors*

#### Other biologics

- **Interleukin 1R** antagonist : **Anakinra (1-R-kinra)**
- **Interleukin 6** inhibitor : **Tocilizumab, Sarilizumab (Toci Sari Sixy)**
- **CD 20** inhibitor : **Rituximab (ri-2-X-imab)**
- **CTLA-4** inhibitor : **Abatacept (BATA = 4)**
- **JAK** inhibitor (*small mol inhibitor*) : **Tofacitinib, Baricitinib (nib = small)**

### 4. **Managing flares:**

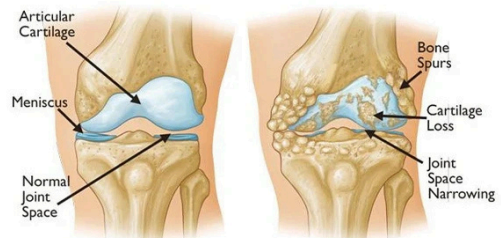
- Acute courses of **corticosteroids** (e.g. prednisolone)

*Consider reducing or stopping therapy in patient who have  
**maintained remission** (or low disease activity) for **> 1 year** without corticosteroids.*

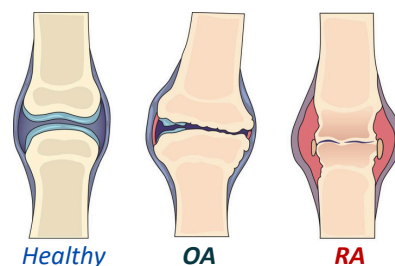
## Osteo Arthritis

- **Non-inflammatory** arthritis (*pain decreases on rest*)
- Occurs as a result of **wear and tear** of the joints (*cartilage mainly affected*)
- Over time, the cartilage breaks down, leading to **pain, stiffness, and reduced joint mobility**.
- Factors like **aging, obesity, repetitive joint stress** can contribute to OA development.
- **Assymetric** joint space reduction
- **Hip** and **knee** more commonly involved along with other joints
- **Named nodules** in osteo-arthritis
  1. **Heberden** nodules : **DIP**
  2. **Bouchard** nodules : **PIP**

**DH and BP**



Osteo-arthritis



# Gout

- **1st meta-tarso-phalngeal** joint m/c affected (*aka Podagra*)
- **Acute red great toe**
- Elderly/Alcoholic
- Deposition of **monosodium urate** crystals
- **Erosions** present (*rat bite erosions*)
- d/d Pseudogout : **calcium pyrophosphate** crystals (m/c in knee)



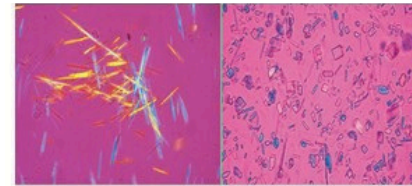
**Martel G sign**  
seen in Gout

- **Rat bite** erosions
- m/c joint : **1st MTP** (*great toe*)



**Pseudogout**  
*aka chondrocalcinosis*

- **Calcification** in joint cartilage
- m/c joint : **Knee**



**Negatively birefringent**

MSU crystals in gout

**Positively birefringent**

Calcium pyrophos. crystals in pseudogout

## Drugs that precipitate Gout

### 'CANT LEAP'

- C** Cyclosporine or cancer drugs
- A** Aspirin (*low dose*)
- N** Niacin
- T** Thiazide
- L** Lasix (furosemide)
- E** Ethambutol
- A** Alcohol
- P** Pyrazinamide

## Management of Gout

### 1. Acute Gout : NSAIDs and Steroids

- First-line of treatment (*except Aspirin because it causes uric acid retention*)
- Preferred NSAID : **Indomethacin** (*PCM not preferred because it has no anti-inflammatory action*)

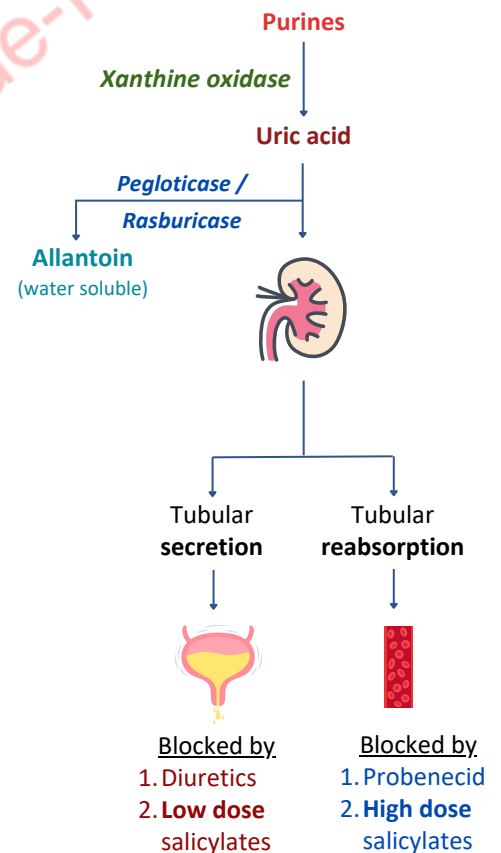
### 2. Colchicine (most effective drug for acute gout)

- Prevents **polymerisation of microtubules**
- Decreases **neutrophil recruitment**, hence stops the inflammatory process
- S/e : **Bone marrow suppression** (*hence not used as first line*)

### 3. Chronic Gout : Drugs that lower Uric acid Levels

- DOC : **Allopurinol** (*Xanthine oxidase inhibitor*)
- **Pegloticase** (*converts uric acid to allantoin*)
- **Probenecid** (*prevents reabsorption of uric acid in renal tubules*)

*Rasburicase is used to manage uric acid levels in Tumor Lysis Syndrome*



# Seronegative spondylo-arthropathies

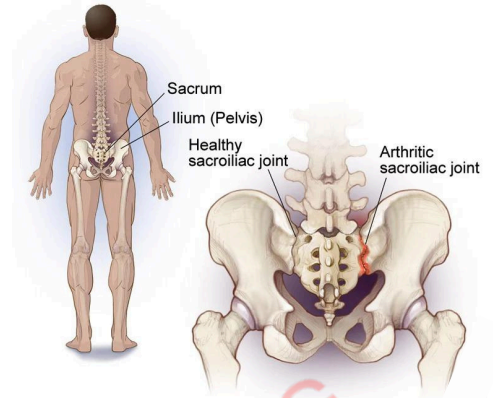
- Inflammatory arthritis which is negative for - RF, Anti CCP antibodies or ANA
- Includes :
  1. **Ankylosing spondylitis**
  2. **Psoriatic arthritis**
  3. **IBD associated arthritis** (aka enteropathic arthritis)
  4. **Reactive arthritis** (aka Reiter syndrome)

## Common features :

- **HLA B27 gene association** (>90% for Ankylosing Spondylitis)
- Inflammatory back pain : **early morning stiffness >1hr** that improves on exercise
- **Assymetric peripheral arthritis** (LL > UL)
- **Thoracolumbar spine** is m/c involved (*spared in RA*)
- **Sacroilitis**
- **Achilles enthesitis** (*not seen in enteropathic arthritis*)
- **Dactylitis** (sausage shaped digits)
- Most common extra articular manifestation is **anterior uveitis**.



**Enthesitis of Achilles tendon**



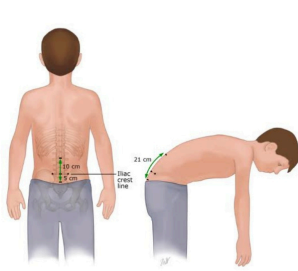
**Sacroilitis**

- Primary clinical feature in ankylosing spondylitis
- **Bilateral** sacroilitis seen with seronegative spondylo-arthropathies

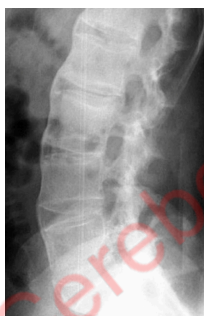
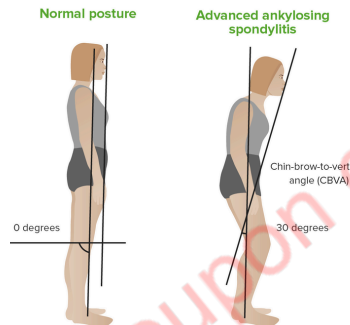
*Unilateral* sacroilitis is seen with Tuberculosis

## Ankylosing Spondylitis

- **Young male**, HLA B27
- **Ankylosing** : Stiffened **Spondylitis** : Inflammation of spine
- Positive **Schöber test** (*assesses decrease in lumbar spine flexion*)
- **Spinal deformity** (*seen in advanced disease*)

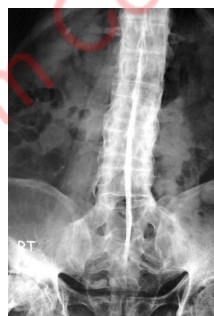


**Schober test** detects reduced flexion



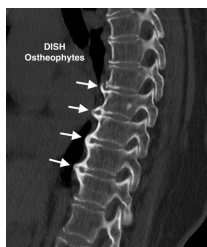
**BAMBOO SPINE**

Vertebral body fusion



**DAGGER SIGN**

Ossification of the spinous ligaments



### Diffuse idiopathic skeletal hyperostosis (DISH)

- **d/d** of ank. spond
- Seen in **elderly**
- Following ossification along **ant. longitudinal ligament**

## Reactive arthritis

- h/o - **GI or Genital infection**
- **Self resolving**
- Asso. with **HLA B27**



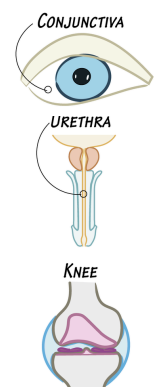
**Circinate balanitis**

**Keratoderma blenorrhagicum**

**CLASSIC TRIAD**  
Conjunctivitis  
(CAN'T SEE)

Urethritis  
(CAN'T PEE)

Arthritis  
(CAN'T BEND THE KNEE)



# Systemic Sclerosis

- Characterised by thickened, hardened skin, hence also known as **scleroderma**.
- **Immune-mediated damage** to vascular structures (e.g. blood vessels) and **excessive synthesis and deposition** of extracellular matrix structures (e.g collagen). This leads to chronic fibrosis, scarring and damage to organs
- Further divided into 2 subtypes :

## Limited Cutaneous systemic sclerosis

*anti centromere Ab*

- **CREST** Syndrome
- Long standing history of Raynaud's
- Internal organ involvement is **very late**
- **PAH** > **ILD**

### CREST syndrome

- C** - **Calcinosis cutis** : calcium deposits in the skin
- R** - **Raynaud phenomenon** (*white-blue-red*)
- E** - **Esophageal dysmotility** : swallowing difficulty
- S** - **Sclerodactyly** : skin thickening and hardening affecting the fingers and toes
- T** - **Telangiectasia** : dilated capillaries.

### Raynauds Phenomenon

- Raynaud's phenomenon is a condition that affects the blood vessels.
- There are periods of time called "**attacks**" when the body does not send enough blood to the hands and feet.
- Attacks usually happen when patient is **cold** or **feeling stressed**.

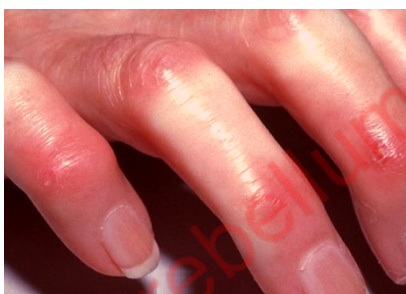


### For screening of systemic sclerosis :

- **ANA** testing is done (*ANA is positive in >95% cases*)
- **Most sensitive** for both limited and diffuse type

### For confirmation

- **Limited cut.** : Anti centromere Ab
- **Diffuse cut.** : Anti Topoisomerase/ Anti SCL 70 Ab



**Sclerodactyly (Sausage fingers)**



**Salt and pepper appearance**



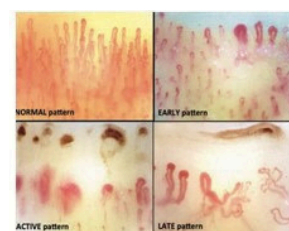
**Capillaroscope**  
Shows changes to capillaries in nail bed



**Perioral skin tightening - fissures can be seen**



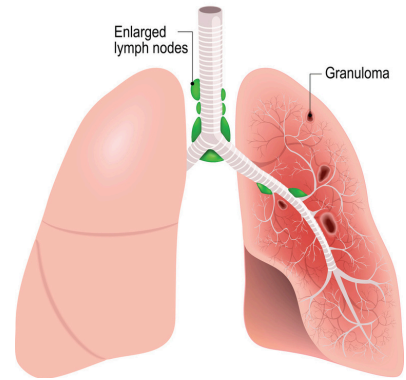
**Calcinosis cutis**



**Nail bed capillaroscopy**

# Sarcoidosis

- **Fever + Cough + hilar lymphadenopathy** = TB or Sarcoidosis
- **Multisystem granulomatous disorder** that mostly affects the lungs.



## 1. Pulmonary Sarcoidosis

- The lungs are affected in **90% of patients**
- **Bilateral hilar lymphadenopathy** is the hallmark finding on CXR
- Both TB and sarcoidosis cause **cavitating lung lesions**
- **Pulmonary fibrosis** in advanced disease

## 2. Cutaneous sarcoidosis

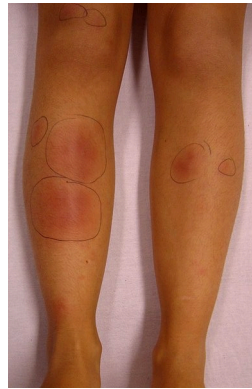
- **Papular sarcoidosis**: multiple papules develop, generally on the head and neck or areas of trauma.
- **Erythema nodosum**: a panniculitis (*inflammation of subcutaneous adipose tissue*) characterised by **red, painful nodules**.
- **Lupus pernio**: a **violaceous, nodular rash** distributed over the nose and cheeks (*pathognomonic but rare*)



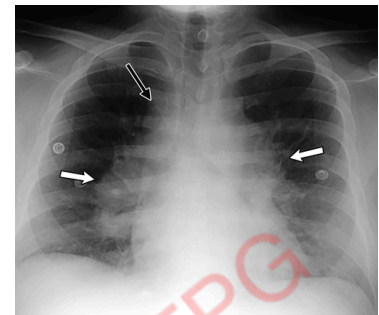
Papular Sarcoidosis



Lupus Pernio



Erythema nodosum

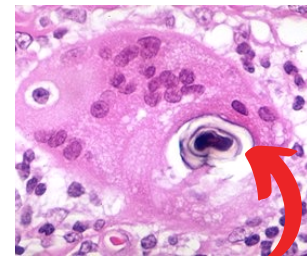


Bilateral hilar and mediastinal lymphadenopathy

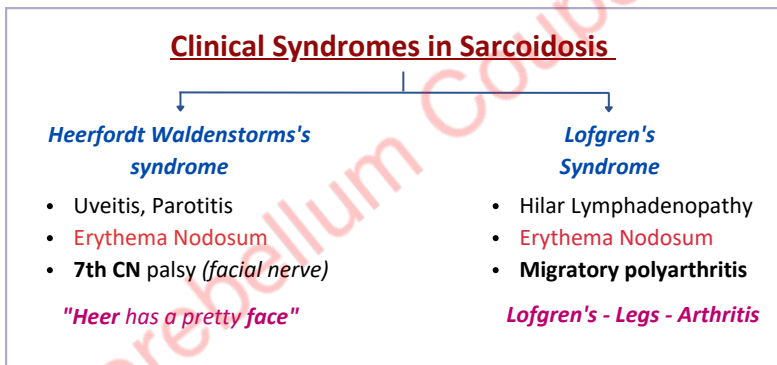
Scadding staging based on CXR findings

## 3. Other manifestations

- **Ocular manifestations** in 30-60% of cases, most commonly in the form of **uveitis**
- **Hypercalcaemia** is seen in around 15% of cases (*due to extra-renal synthesis of calcitriol*)

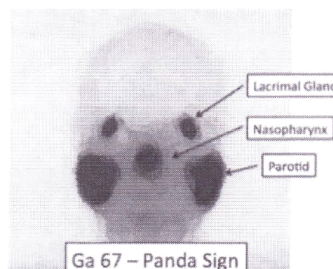


Schaumann body  
due to excess vitamin D



## Diagnosis

1. **Bilateral hilar lymphadenopathy** on CXR
2. Bronchoalveolar lavage : **CD4/CD8 ratio > 4**
3. **Serum ACE** raised
4. **Panda sign** on Gallium 67 scan
5. **Calcium elevated**



Ga 67 - Panda Sign

# Sjogren Syndrome

Associated with auto-antibodies : Anti **Ro**/ Anti **La** antibodies "no **RO**na or **LA**al tapkana"

## Lymphocytic infiltration of exocrine glands

- **B/L parotid enlargement** (rule out lymphoma)
- **Dry eyes** (*Keratoconjunctivitis sicca*)
- **Dry mouth**



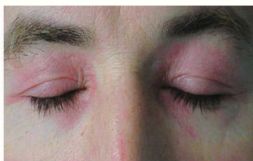
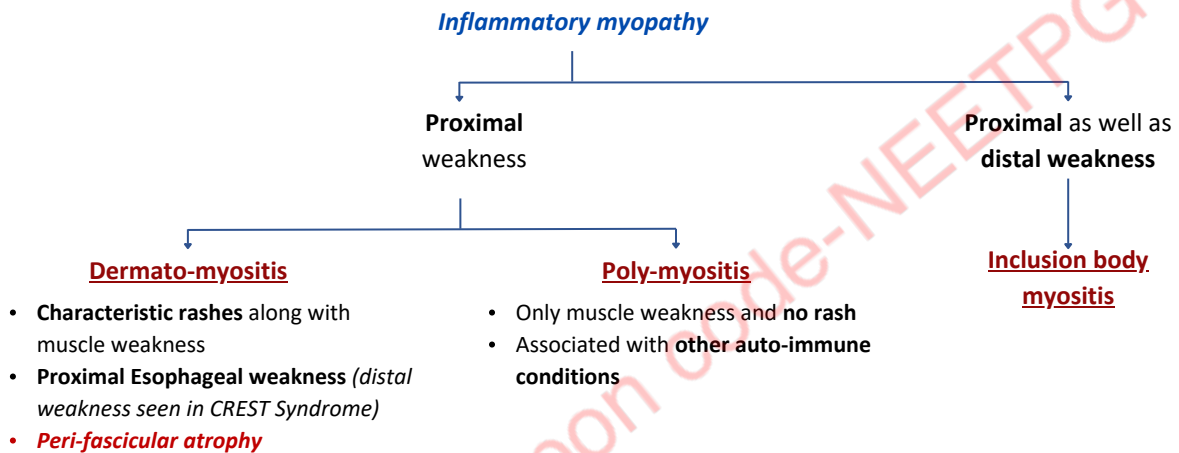
**Schimmer test**  
(uses rose bengal dye)

## Extra-glandular manifestations

- Arthritis (m/c)
- Type - 1 RTA "**Sjogr-one**"
- Vasculitis and Raynaud's phenomenon
- Lymphoma

# Inflammatory Myopathies

- **Auto-immune** disorder
- Muscle inflammation leading to **progressive muscle weakness** and **wasting**
- Raised **Creatine Kinase**



**Heliotrope eyelid rash**



**Gottron's Papules**



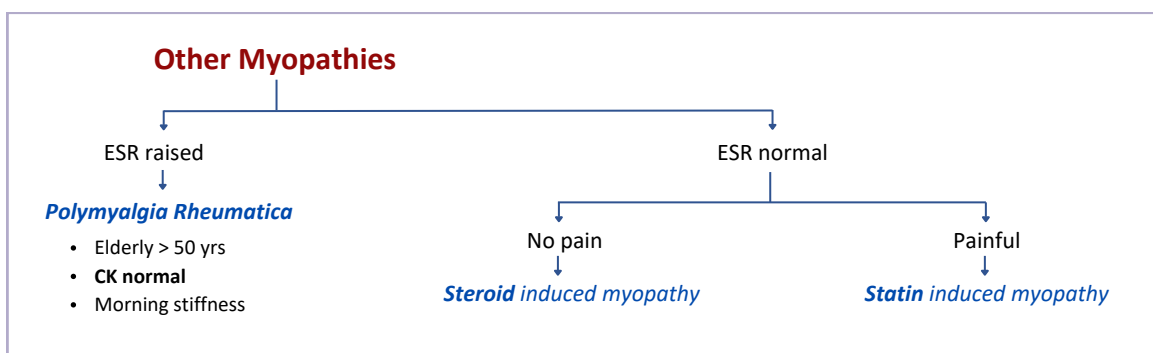
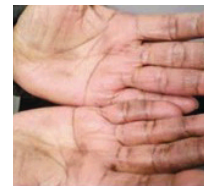
**Nail-bed telangiectasia**



**Shawl Sign**

## Anti synthetase syndrome

- Type of inflammatory myopathy
- **Anti-Jo 1** antibody
- **Mechanic's hands** (hyperkeratotic lesion)
- Associated with :
  1. Arthritis
  2. ILD
  3. Raynaud's phenomenon



# Vasculitis

- **Inflammation** of blood vessels that interrupts blood flow to vital organs.
- Leads to **ischaemia, tissue damage** and **ultimately organ dysfunction** (e.g. gut ischaemia, acute kidney injury)

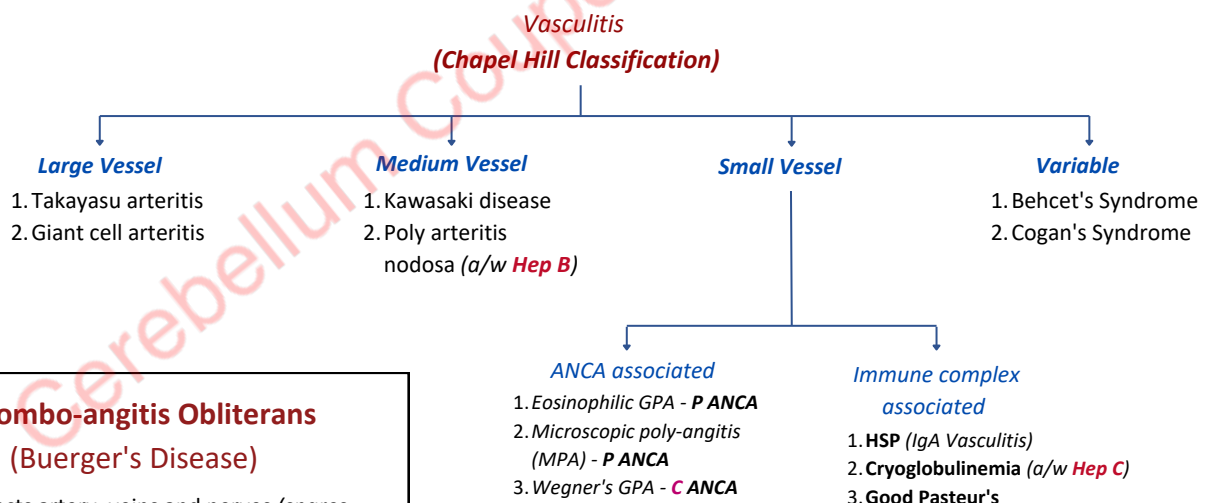
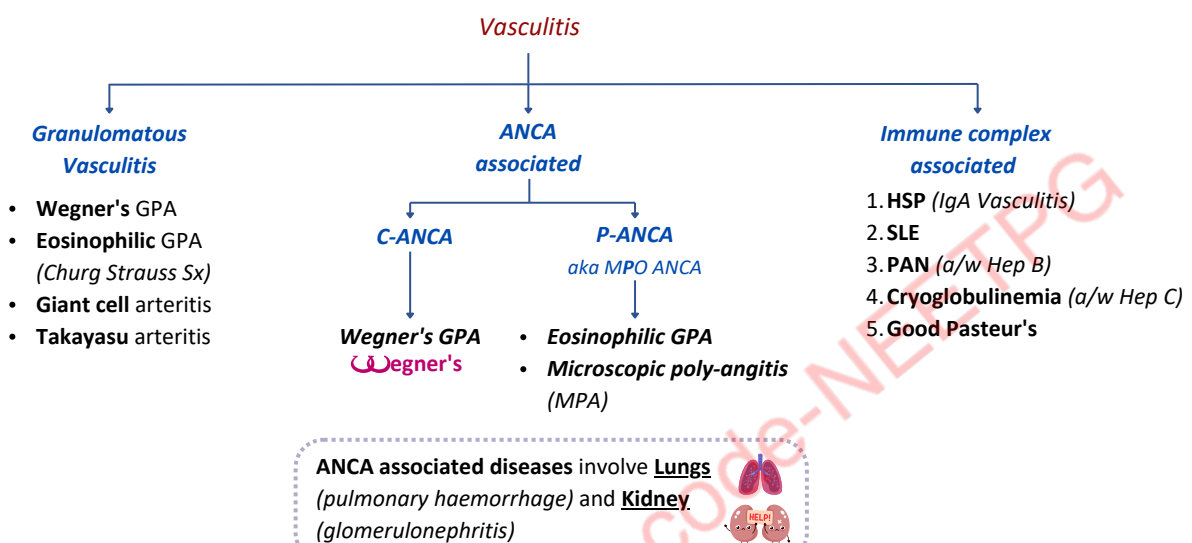
## Clinical features

The clinical features of vasculitis depend on both the **size of the vessels** involved (*large, medium or small*) and the **location of the vessels** involved (*kidney, skin or gut vessels*)

1. **Palpable** purpura
2. **Asymmetrical neuropathies** (damage to the small blood vessels that supply peripheral nerves)
3. Unexplained **bleeding**
4. **Constitutional symptoms** such as fever, weight loss, and fatigue



**Palpable purpura**



## Thrombo-angitis Obliterans (Buerger's Disease)

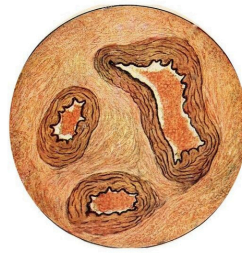
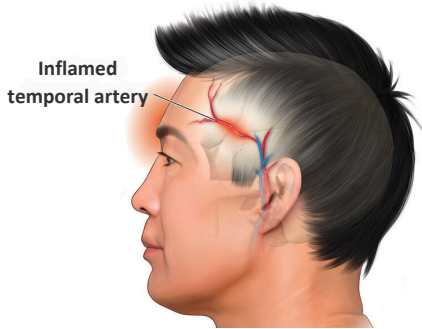
- Affects artery, veins and nerves (*sparing lymphatics*)
- Young adult < 35 years
- **Smoker**
- **Severe limb pain**
- M/c artery : **Radial/Tibial**
- Corkscrew collaterals seen on **DSA**
- T/t : **Stop smoking** (surgery has no role)

## Most common

- Vasculitis in adults : **GCA**
- Vasculitis in children : **HSP** (Kawasaki in Asia)

## Giant cell arteritis

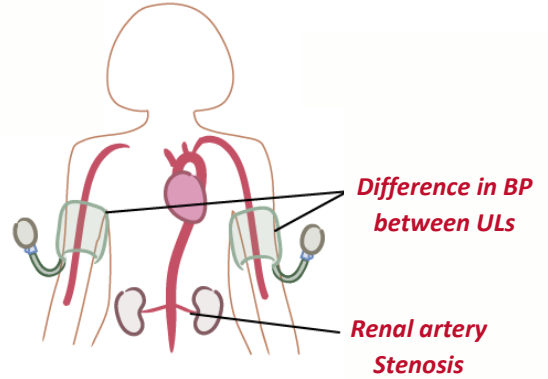
- Also known as **temporal arteritis** (*Superficial temporal artery most commonly affected*)
- **Granulomatous - Large vessel - vasculitis** (*type 4 hypersensitivity reaction*)
- Older adults > 50 years of age
- Associated with **Polymyalgia Rheumatica**
- Characterised by a **unilateral headache, scalp pain, and visual loss** due to involvement of the ophthalmic artery.
- Classical feature : "Jaw pain that occurs while chewing"
- Immediate management : **Start steroids**
- It is considered a **medical emergency**, because without prompt recognition and treatment it can lead to permanent visual loss.
- Gold standard for diagnosis : **Artery biopsy (VVG)**



VVG staining  
(stains elastic fibres)

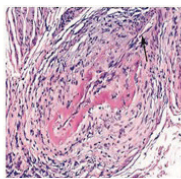
## Takayasu arteritis

- Takayasu arteritis is aka "pulse-less disease" and "aortic arch syndrome"
- **Granulomatous - Large vessel - vasculitis** (*type 4 hypersensitivity reaction*)
- Affects **younger adults < 40yrs**
- Affects **woman (>80%)** and *Asian ethnicity*
- Affects the **aorta and its major branches** (m/c is **Subclavian artery**)
- *BP difference between upper limbs*
- Diagnosis is usually made on **imaging**.



## Poly-arteritis nodosa

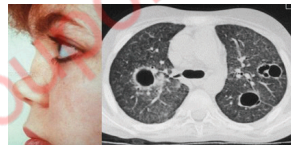
- **Medium vessel vasculitis** (*immune complex mediated*)
- Associated with **Hepatitis B**
- **Segmental, transmural "necrotizing" inflammation** of arteries (*fibrinoid necrosis*)
- It **never affects the pulmonary system** (**PAN - Pulmonary artery never-involved**)



Fibrinoid necrosis

## Wegner's GPA

- ANCA asso. **granulomatous necrotising vasculitis (C-ANCA)**
- **URTI + LRTI + Glomerulonephritis** (triad)
- **Cavitary lung lesions**
- Crescentic RPGN



Saddle nose and Cavitations in lung

## Eosinophilic GPA

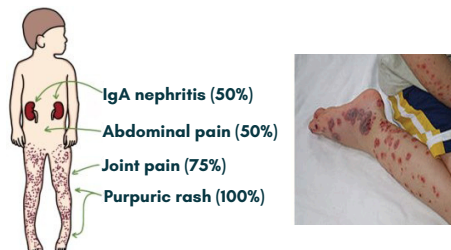
- aka *Churg Strauss Syndrome*
- ANCA asso. **granulomatous vasculitis (P-ANCA)**
- **Asthma and Eosinophilia**
- **Mono-neuritis complex** is an associated condition with EGPA

## Microscopic polyangitis

- ANCA asso. vasculitis (**P-ANCA**)
- Clinical features similar to PAN
- **Glomerulonephritis** with rapid progression to renal failure

## HSP (IgA vasculitis)

- Henoch-Schönlein purpura
- Commonly presents in **childhood**.
- **Viral prodrome**
- **Self limiting** (*can lead to intussusception*)



## Cryoglobulinemia

- Cryoglobulins are immunoglobulins that precipitate in **cold (<37°)** and dissolve upon rewarming.
- Associated with **hepatitis C**

## Good Pasteur Sx

- Refers to clinically evident **glomerulonephritis and pulmonary haemorrhage**.
- **Anti-GBM** antibodies

## Behcet's Disease

- aka **Neutrophilic Vasculitis**
- **Oral and genital ulcers**
- **Erythema Nodosum and anterior uveitis**
- **Oral ulcers are painful** but heal without scarring while **genital ulcers are painless** but heal with scarring.
- Associated with **HLA B-51**



## Differentials

1. **HUS/TTP/ITP** will have thrombocytopenia
2. **JIA** will have erythematous rash + fever

# Auto-antibodies compiled

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## Associated with SLE

1. **ANA** : most sensitive (*entry criterion for diagnosis*)
2. **Anti Smith** : most specific
3. **Anti C1q > Anti ds-DNA** : Corresponds to disease activity in SLE (*Flares*)
4. **Anti histone** : drug induced SLE (*SHIP drugs*)
5. **Anti neuronal / Anti glutamate receptor 2** : CNS SLE
6. **Anti ribosomal P** : Psychaitric SLE

## Associated with other connective tissue disorders

1. **Anti-U1 RNP** : Multiple connective tissue disorder
2. **Anti CCP, Rheumatoid factor** : Rheumatoid arthritis
3. **Anti-Ro / Anti-La** : Sjogren's Syndrome
4. **Anti-Jo1** : Anti Synthetase Syndrome (*Mechanic hands*)
5. **Anti-topoisomerase 1/Anti-scl-70** : Diffuse cutaneous systemic sclerosis
6. **Anti-centromere** : Limited cutaneous systemic sclerosis (*CREST Syndrome*)

## Other auto-antibodies

1. **AchR antibodies, Anti MUSK antibodies** : Myesthania Gravis
2. **Anti TPO** : Hashimoto's Thyroiditis
3. **LATS** (*Long acting Thyroid stimulant*) : Grave's disease
4. **Anti LKM-1** : Autoimmune hepatitis type 2
5. **AMA** : Primary billiary cirrhosis (**AMMA = female, has cirrhosis**) [PSC seen in males, asso with IBD]
6. **P-ANCA** : EGPA, MPA, **Ulcerative Colitis**
7. **C-ANCA** : Wegner's GPA
8. **ASCA** (*Anti-Saccharomyces cerevisiae antibodies*) : Chron's disease

Cerebellum Coupon code-NEETPG