Rheumatology Review

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1. Rheumatoid Arthritis:

- Systemic chronic inflammatory disease mainly affects synovial joints.
- Severity is variable.
- More common in females from **25-59**
- Possibly autoimmune.
- Could be genetic, environmental, infectious.

★ **Associated with HLA-DR4**

❖ **Pathology**:

- Nodules
- Vasculitis
- Synovitis: Joints, tendons, bursa.

❖ **RA is characterized by synovitis leading to PANNUS**

Pathogenesis at cellular level:

- Hereditary and environmental > activate CD4 T cells.
- Endothelial activation, macrophage activation, B cells.
- Recruitment of inflammatory cells, chondrocytes, osteoblasts and osteoclasts, RF and immune complexes.
  - ➢ All lead to destruction of bone and cartilage.

- IL1 plays a pivotal role in inflammatory and destructive process of RA.
- Pro-inflamm effects of IL 1:
  - TNF-a, osteoclast activation, and angiogenic factors.
- Pro inflamm effects on TNF a:
  - IL 1, and cell death.
- Both (IL 1, TNF a):
  - Cyclooxygenase 2, PG E, NO, adhesion molecules, chemokines, collagenases, IL 6

❖ **Signs and symptoms:**

★ **Joints inflammation:**

○ **Warm, swollen, tender, symmetrical pattern**

★ **Pain and morning stiffness of joints**

○ **Lasts 1-2 hours**

★ Nodules, anemia, fatigue, fever, malaise

○ Articular:

Wrist:

- Synovitis, prominent ulnar styloid, subluxation and collapse of carpus, and **radial deviation**

Metacarpo-phalangeal joints:

- **Ulnar deviation**, subluxation, synovitis.

Thumbs:

- Z deformity and synovitis.

Proximal interphalangeal joints:

- Synovitis, **boutonniere deformity (FF)[1], and swan neck (FE)[2].**

○ Extra articular manifestations:

- ○ Fever, malaise, weight loss, fatigue
- ○ Anemia
- ○ Lymphadenopathy
- ○ Palmar erythema, nodules, vasculitis
- ○ Dry eyes, episcleritis/scleritis, Scleromalacia perforans, Choroid and retinal nodules
- ○ Pericarditis, myocarditis, coronary vasculitis, nodules on valves.
- ○ Entrapment neuropathy (carpal tunnel syndrome), Peripheral neuropathy, Mononeuritis multiplex.
- ○ Large granular lymphocyte syndrome and lymphomas.
- ○ **Felty's syndrome: RA + neutropenia + splenomegaly.**
- ○ Pleuritis, nodules, interstitial lung disease, bronchiolitis obliterans, arteritis, pleural effusions
- ○ **Amyloidosis: rare complication > nephrotic syndrome**

  Patient presents with proteinuria

  GN due to SLE would have RBC casts

❖ **Investigations:**

- ○ CBC: microcytic anemia due to Fe def.
- ○ ESR, CRP: may be normal
- ○ RF and ACPA
  - ✓ **ACPA: is more specific to RA**
- ○ US and MRI not required when there are obvious clinical signs
- ○ Abnormal X ray not needed to confirm diagnosis
- ○ LFTs and renal profile to monitor drug safety
- ○ Radiographs to monitor disease damage:
  - ✓ Joints
  - ✓ **Spine: to detect instability is cervical vertebrae**
    - ➢ **During endotracheal intubation > hyperextension > compression of cord**
  - ✓ Chest: fibrosis and effusion

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[1] **F**lexion (of proximal) **F**lexion (of distal)

[2] **F**lexion (of proximal) **E**xtension (of distal)

Criteria: target population:

- At least 1 joint with clinical synovitis
- With synovitis that is not better explained by another disease

❖ **Treatment:**

❑ Goals: Relieve pain, Reduce inflammation, Prevent joint damage, Improve function and quality.

❑ Rationale for early treatment:

- Erosion develops early
- Irreversible
- Activity is strongly associated with joint destruction later in disease course.
- Early treatment > slow down radiographic progress
- Disease activity must be suppressed maximally in its early stages to prevent destruction and preserve function

❑ Medication:

DMARDS:

- Examples:
  - **Methotrexate: best initial (gold)**
    - ✓ CBC and LFTs
  - Hydroxychloroquine
    - ✓ Eye exam
  - Sulfasalazine, leflunomide, azathioprine
    - ✓ Azathioprine > bone marrow suppression
- Uses:
  - **Control symptoms but no immediate relief**
    - ➢ Begin with NSAIDs and DMARDs and then taper the NSAIDs when DMARDs begins to work.
  - **Delay progression of disease**
  - **Effect may not be seen until few weeks – months**

NSAIDs:

Traditional: aspirin, ibuprofen, ketoprofen, naproxen

Cox 2 inhibitors: celecoxib, etoricoxib

Uses:

- **Relieve pain and inflammation**
- Combo with DMARDs
- SE: GI symptoms

Steroids: if NSAIDs don't provide adequate pain relief.

➢ **Avoid long term use**

Biologic response modifiers:

- Before using any drug, you have to make sure the patient doesn't have any infections like latent TB
- TNF Inhibitor**: infliximab** and adalimumab
- IL 6 receptor inhibitor: tocilizumab
- T cell costimulation: abatacept
- Anti CD 20: **rituximab**

❑ Physiotherapy:

- Maintain range of motion
- Strengthen muscle
- Prevent deformities
- Maintain activities of daily living

❑ Occupational therapy

❑ Surgery

2. Scleroderma spectrum disease:

- Characterized by: skin thickening, vasculopathy, and auto-antibody production
- Fibroblast activation > vasculopathy (initial inflammation > hyperplasia + narrowing of lumen) > inflammatory component

❖ **Types:**

- Diffuse: more internal organ involvement
  - Worse prognosis.
  - Ab: anti-topoisomerase/ RNA polymerase III antibodies.
  - Clinical features:
    - ✓ Skin develops more rapidly
    - ✓ Early involvement of other organs like GIT, Renal, Lung
- Limited: indolent
  - Higher risk of pulmonary hypertension
  - Affects parts distal to the elbows and knees with facial involvement.
  - Ab: anti-centromere antibodies
  - Clinical features:
    - ✓ CREST syndrome:
      - Reynaud's (first)
      - Esophageal Dysmotility
      - Sclerodactyly
      - Telangeictasia
    - ✓ Skin is thickened, bound down to underlying structure and the finger taper
    - ✓ Characteristic facial appearance: beaking of the nose, radial furrowing of the lips > limits mouth opening

❖ **Autoantibodies:**

- Scl-70 (anti-topoisomerase): most specific
  - Associated with diffuse subset, ILD, and reduced risk of pulmonary arterial hypertension
- Anti-centromere: limited subset, PAH, and digital ulcer
- RNA polymerase: SRC, malignancy associated SSC and mortality
- Scl-PM: associated with myositis overlap (two CT diseases occur at the same time)
- ANA: positive most of the time but not specific

❖ **Criteria:**

Features
- 1. Symmetrical proximal muscle weakness
- 2. Muscle biopsy evidence of myositis
- 3. Elevation in serum skeletal muscle enzymes
- 4. Characteristic electromyogram pattern of myositis
- 5. Typical rash of dermatomyositis

Polymyositis
- Definite: all of 1–4
- Probable: any 3 of 1–4
- Possible: any 2 of 1–4

Dermatomyositis
- Definite: 5 plus any 3 of 1–4
- Probable: 5 plus any 2 of 1–4
- Possible: 5 plus any 1 of 1–4

first item of the criteria is enough to diagnose SSc

- ***organ involvement:***
  - No single drug to treat everything so it depends on patients' needs
  - Pathogenesis in each organ involved is not the same, it could be Neurovascular, Fibro proliferative, or Inflammatory.
- ***Skin involvement:***
  - Largest and most important organ involved
  - Reflection of internal organ involvement
  - Indicates severity of disease and mortality
  - Always starts in fingers and extends proximally
  - Contracture of the finger and disability are preventable with stretching exercises
  - Patients are advised to use creams and emollients at all times
  - Skin loosening occurs 5 years after the onset of disease
  - Treatment is initiated when active skin inflammation is apparent or progressive skin thickening
- Treatment:
  - Methotrexate
    - ✓ Only if there is no ILD or renal failure
  - Rituximab
  - Mycophenolate
  - Cyclophosphamide
  - Some steroids
- ***Raynaud's phenomenon & digital ulcers:***
  - 2 faces of the same coin
  - RD occurs years before SSc diagnosis
  - DU usually occurs in the first 5 years after development of non RP manifestations
- Secondary RP:
  1. Non pharma therapy
  2. Treat pain
  3. CCB
  4. Prazosin does not work well
  5. oral and IV Prostaglandins
  6. IV iloprost (better than nifedipine)
- DU:
  - Aim of treatment: healing and prevention of new ulcers
  - CCB: used but no evidence in healing DU
  - Endothelin receptor antagonist (bosentan)
  - Phosphodiesterase inhibitor
  - Prostacyclin
- ***ILD:***
  - Chronic, progressive fibrosing interstitial pneumonia leading to progressive loss of pulmonary function and resp. failure
  - Affects bases of lungs
  - Diagnosis made via PFTs
  - Imaging > HRCT
  - Leading cause of death in SSc patients
  - Clinical findings:
    - Tachypnea
    - Tachycardia
    - Cyanosis
    - Clubbing

- Reduced chest expansion
- Fine early inspiratory crackles

- PFTs:
  - Low FVC
  - Low FEV1
  - Normal or high FEV1/FVC ratio
  - Low DCLO
  - Restrictive pattern with low DLCO

❖ **Treatment:**
- ★ Standard: Cyclophosphamide
- ★ Alternative: MMF or rituximab
- ★ Maintenance: MMF, AZA, and RTX
- ★ Steroids to induce and maintain

◆ ***PAH:***
- PAP $\geq$ 25 mmHg with pulmonary wedge pressure $\leq$ 15 mmHg
- PAH can be secondary to ILD
- Solutions to reduce M & M:
  - Early detection
  - Aggressive treatment
  - Early referral for lung (or lung & heart) transplant
- Clinical findings:
  - Desaturation
  - Tachycardia
  - Tachypnea
  - Syncope
  - Palpable P2 and parasternal heave
  - Loud P2
  - Signs of R sided HF
- Treatment:
  - Endothelin receptor antagonist
    - Bosentan
    - Ambrisentan
    - Macitentan
  - Phosphodiesterase inhibitor
  - Prostacyclins

◆ ***GI is the most common internal organ to be involved***
- Esophagus > Dysmotility and reflux > strictures
- Stomach > gastroparesis, watermelon appearance, telangiectasia
  - Treatment for both: Lifestyle modifications, PPI, Treat Fe def anemia
- Small bowel > blind loop syndrome + bacterial overgrowth > diarrhea and malabsorption
  - Primary Treatment: Sequential antibiotics
  - Advanced cases: stomas and TPN can be offered
- Large bowel: chronic constipation, fish mouth diverticula (wide neck)
  - Treatment: Laxatives

◆ ***Renal crisis:***
- They usually have low BP, once you see a high reading suspect renal crisis
- Primary histopathological changes:
  - Localized small arcuate, interlobular arteries, and glomeruli

- Characteristic finding: intimal proliferation and thickening > narrowing and obliteration of the vascular lumen with concentric onion skin hypertrophy > activation of aldosterone- renin- angiotensin pathway
- Precipitating factors: high dose aldosterone, cyclosporine, and pregnancy
- Anemia is usually iron deficiency > microangiopathic hemolytic anemia
- Clinical findings:
  - New onset HTN > 150/85
    - 20 mmHg increase from baseline
    - can be normotensive
  - Proteinuria and hematuria > no RBC cast
  - High creatinine
  - Microangiopathic hemolytic anemia
- Treatment:
  - control BP (10 mmHg every 24 hours)
  - ACEI (best)

◆ ***Other manifestations:***

- Cardiac: myocardial fibrosis > conduction abnormalities, cardiomyopathies, and accelerated CAD
- Arthritis: RA with erosions and joint destruction
- Myositis: manifested by weakness with no pain and high muscle enzyme

Sjogren's syndrome:

- Characterized by lymphocytic infiltrates in exocrine organs
- Secondary to antibodies predominantly against lacrimal and salivary gland

❖ **Clinical feature:** *sicca* symptoms

- Xerophthalmia (dry eyes): feeling of sand in eyes
- Xerostomia (dry mouth)
  - ✓ Predisposes them to dental caries
- Vaginal dryness
- Parotid gland enlargement

❖ **Complications:**

- At risk for developing non Hodgkin's lymphoma (most dangerous complications)
- Look for persistent LAP or disappearance of PF
- Their LN come and go, but persistent or firm nodes would indicate malignancy

❖ **Criteria:** At least 4 (but criterion 5 or 6 have to be included)

- Ocular dryness
- Oral dryness
- Ocular signs (schirmer test)
- Oral signs
  - Sialogram
  - Scintigraphy
  - Sialometry findings
- +ve minor salivary gland biopsy findings (Lymphocytic infiltrate)
- Positive anti-SSA or anti-SSB antibody result

❖ **Extra articular manifestations:**

- Arthritis
- Palpable purpura
- Renal tubular acidosis
- Myositis
- ILD

- Interstitial nephritis
- Pancytopenia
- Demyelinating disease
- Fatigue

❖ **Diagnostic test:**
- *Best initial:* schirmer test
- *Most accurate:* lip or parotid gland biopsy shows lymphoid infiltration

❖ **Treatment** of glandular manifestations:
- Water the mouth
- Oral hygiene
- Avoid sugar to avoid cavities
  - ✓ Low saliva productions > helps fight against cavities
- Florid products
- Parasympathomimetics (pilocarpine)
  - ✓ Increase Ach > stimulate the production of saliva
- Artificial eye and mouth moisturizers
- Creams and lotions
- Vaginal lubricants

❖ **Treatment** of extraglandular manifestations:
- Steroids
- MTX (not in ILD)
- Azathioprine
- Cyclophosphamide
- Rituximab
- Renal tubular acidosis > $NaHCO_3$

Idiopathic inflammatory myopathies:

- Characterized by muscle weakness mainly in proximal muscles
- Insidious course and progressive
- Polymyositis: inflammation and necrosis of skeletal muscle fibers
  - With skin involvement dermatomyositis
- Pharyngeal muscles > dysphagia > aspiration pneumonia
- Chest wall > dyspnea > type II respiratory failure
- Heart > cardiomyopathy
- Antibody: anti Jo 1

❖ **Clinical features:**
- Symmetrical muscle weakness affecting proximal muscles (shoulder and pelvis)
- Increased incidence of underlying malignancy

❖ **Types**:
- Primary idiopathic (PM or DM)
- Associated with malignancy
- Childhood
- Associated with another CT disease
- Inclusion body myositis

❖ **Rashes:**
- Photosensitive
- Gattron's papules/ signs
- Erythroderma
- Heliotrope rash
- Shawl rash

Heliotropes and Gottron's papules are specific to this disease

- **Extramuscular manifestations:**
    - Arthiritis
    - RP
    - ILD
- **Investigations:**
    - Muscle enzymes
    - CK
    - AST and ALT
    - LD
    - Aldolase
    - MRI: biopsy > lymphocytic infiltrations
    - MRI muscle: edema
    - EMG: myopathic changes
- **Diagnostic tests:**
    - *Best initial*: CPK and aldolase
    - *Most accurate*: muscle biopsy
- **Treatment**:
    - Muscle strengthening
    - Steroids
    - MTX
    - Mycophenolate mofetil
    - Azathioprine
    - IV IG
    - RTX

3. Osteoarthritis:

- Normal articular surface of synovial joints:
    - Extra-cellular matrix includes: proteoglycans and collagen
    - If the surface wasn't smooth the body weight on weight bearing joints will cause pain
- Synoviocytes manufacture:
    - Synovial fluid
        - Provides nutrients to avascular cartilage
        - Provides viscosity needed to absorb shock from slow movement
        - Elasticity required to absorb shock from rapid movement
    - Hyaluronic acid: a glycosaminoglycans that is a major non cellular component of synovial fluid
- Cartilage homeostasis: balancing between synthesis and degradation
- Osteoarthritis: characterized by progressive destruction and loss of articular cartilage with an accompanying periarticular bone response
- Common in older individuals
- **Involved joints:**
    - Weight bearing like knees, hips, feet, cervical, and lumbosacral
    - Non weight bearing:
        - ★ DIP (unlike RA)
        - ★ PIP
        - ★ CMC
        - ★ First metapharyngeal joint of the foot

- **Risk factors:**
  - Age, obesity, trauma, hypogonadism, muscle weakness, infection (septic), crystal deposition, acromegaly, and prev. inflammatory arthritis (burnout RA)
  - Heritable metabolic causes: alkaptonuria, hemochromatosis, Wilson
  - Hemoglobinopathies: SCA and thalassemia
  - Neuropathic disorders > Charcot's joint: syringomyelia, tabes dorsalis, and uncontrolled diabetes, syphilis
  - Underlying morphologic risk factors: congenital hip dislocation and slipped femoral capital epiphysis
  - Disorders of bone: Paget's disease and avascular necrosis
  - Prev. surgery like meniscectomy
- **Pathogenesis:**
  - ➢ Inflammation: cytokines and metalloproteinase > released into the joint
    - Involved in excessive matrix degradation that characterizes cartilage degeneration on OA
  - ➢ Cartilage changes:
    - Swelling of the cartilage: proteoglycans drop and cartilage softens and loses elasticity > compromising joint surface integrity
    - Flaking and fibrillation:
      - loss of cartilage results in loss of joint space
      - Greater loss of joint space in areas with high loads
  - ➢ Bone change:
    - Bone denuded of its protective cartilage continues to articulate with the opposing surface > the increasing stresses exceed the biochemical yield strength of the bone
    - Subchondral bone undergoes cystic degeneration
      - Cysts also called: subchondral cysts, pseudocysts, geodes, or egger cysts if involved in acetabulum
      - 2-20 mm in diameter
  - ➢ joint changes:
    - vascularization of subchondral marrow
    - osseous metaplasia of synovial CT
    - ossifying cartilaginous protrusion lead to irregular outgrowth of new bone (osteophyte)
    - fragmentation of these osteophytes or the articular cartilage itself > presence of intraarticular loose bodies (joint mice)
  - ➢ Cartilage disruption:
    - High mobility B2 cells are responsible for production of chondrocytes
      - less chondrocytes > loss of cartilage
    - Cartilage specific precursor cell clump together and lose their function
- **Progression:**
  - Stage 1: breakdown of cartilage matrix occurs
  - Stage 2: involves the fibrillation and erosion of the cartilage surface
  - Stage 3: a chronic inflammatory response in the synovuim
  - Further progression alters joint architecture, compensatory bone overgrowth occurs, mechanical and inflammatory stress occurs in articular surfaces
- **Clinical features:**
  - Joint pain
  - Functional restriction
  - Pain made worse by movement, relieved by rest

- Stiffness occurs after rest and morning stiffness lasts less than 30 mins (transient)

❖ **Examination:**
- Periarticular tenderness
- Limited joint movement
- Muscle wasting
- Crepitus
- Synovitis

❖ **Deformities:**
- Heberdens nodes: DIP
- Bouchard's: PIP
- Varus: bone twist towards center of body
- Valgus: bone twist away from center of body

❖ **Subtypes:**
- Primary generalized:
  - Seen in combo with nodal OA
  - Onset is sudden and severe
  - Strong familial tendency
  - Hand joints commonly affected (symmetrical)
- Erosive: functional outcome is poor
  - MCPs are spared
- Chondromalacia patellae: cartilage under the surface of the patella deteriorates and softens

❖ **Ddx:**
- Crystalline arthropathies
- Inflammatory arthritis
- Seronegative spondyloarthropathies
- Septic arthritis or post infectious arthropathy
- Fibromyalgia
- Tendonitis

❖ **Investigations:**
- X ray is the most accurate diagnostic test (goldstone)
- MRI shows early cartilage changes
- Lab tests are normal
- CT and ultrasonography
- Bone scitigraphy
- Arthrocentesis: WBC (up to 200) is less compared to infections
  - ✓ Look for crystals

❖ **Treatment:**
- Lifestyle modification and rehab therapy
- Paracetamol and NSAIDs are initial choice for pain relief
- Intraarticular corticosteroids > short term improvement
- Muscle relaxants
- Surgical:
  - Arthroscopy
  - Osteotomy
  - Srthroplasty
  - Fusion and joint lavage
  - Stem cells

❖ **RA vs. OA:**
- Morning stiffness lasts less than 30 mins in OA

- DIP joints are affected in OA
- Wrist and elbow not effected in OA
- MTP joints not affected in OA
- OA is worse with activity better with rest
- Heat and warmth with significant synovial swelling in RA

4. Spondyloarthritis:

- +ve HLA B27:
  - Ankylosing spondylitis
  - Psoriatic arthritis
  - Reactive arthritis (sexually and Reiter's disease)
  - Enteropathic arthritis (IBD)

Ankylosing Spondylitis

- Most commonly affects sacroiliac joints and big joints like knees and ankles
- Takes 8 years from onset of disease to reach a diagnosis
- There is a familial predisposition in 1st, 2nd, 3rd degree relatives
  - 94%, 25%, and 4% respectively

❖ **Clinical features:**

- Young patient
- **Low back pain** (you can't have AS without back pain)
- Morning stiffness
- Radiates to the buttocks or posterior thighs
- Improves with exercise
- Progressive loss of spinal movement

■ 6 features to differentiate between Mechanical back pain and inflammatory back pain "I PAIN +M" I'M PAIN:

1. Insidious (slow progression).
2. Pain at night.
3. Age<45 (15-45).
4. Improved by exercise and movement.
5. Not improved with rest, it will make it worse.
6. Early Morning stiffness of more than 30 minutes.

Inflammatory back pain present if at least 4 out of 5 parameters are fulfilled,

- Inspection of the spine reveals:
  - Loss of lumbar lordosis
  - Increase in kyphosis
  - Limitation of lumbar spine mobility
    - ✓ demonstrated by +ve schober test
- Other features:
  - Enthesitis: Achilles tendonitis and plantar fasciitis
  - Tenderness around pelvis and chest wall
  - Transient peripheral arthritis of knees, hip, and shoulders
  - Reduction in chest expansion (due to costovertebral joint involvement)

- Non articular features:
    - **Acute anterior uveitis (the most common)**
        - Unilateral
        - Spontaneous remission
        - Most common
        - Does not correlate with disease severity
    - Psoriasis
        - Associated with all forms of Spondyloarthritis

❖ **Investigations:**

- *Best initial* test: X ray of SI joint
    - 2 years to show
- ESR and CRP (often raised)
- *Most accurate*: MRI
    - Detects before x ray
    - ✓ Shows sacroiliitis
- HLA B27 not tested because its positive in general population as well

❖ **Management:**

- Key: early diagnosis and treatment
    - To prevent irreversible syndesmophyte formation and progressive calcification
- Morning exercises to maintain posture and mobility
- First line treatment: NSAIDs
- Steroids are not effective
- Peripheral disease: second line is sulfasalazine or local steroids
- If failed or complications occur: TNF alpha blocker
- Axial disease: second line is TNF alpha blocker

Psoriatic arthritis:

- In 20% of patients with psoriasis, especially with nail disease and may precede skin disease
    - ✓ Effects the hands

❖ **Clinical features: (types/Patterns)**

- Asymmetrical: distal interphalangeal joints
    - Dactylitis and nail dystrophy (onycholysis, bridging, and pitting)
- Symmetrical: seronegative polyarthritis (resembling RA)
- Arthritis mutilans: severe form with destruction of the small bones in the hands and feet (telescope fingers)
- Sacroiliitis

- There is DIP involvement unlike RA

❖ **Investigations:**

- Initial: X ray (pencil in cup deformity in IPJs)

❖ **Treatment:**

- NSAIDs
- Local synovitis responds to intra articular steroids injections
- Severe: Methotrexate or TNF blockers, control both the arthritis and the skin lesions.

Reactive arthritis:

- Sterile synovitis secondary to:
    - GI infection: shigella, salmonella, Yersinia, campylobacter, or C diff
    - STD: chlamydia trachomatis or ureaplasma urealyticum
- Takes at least 10 days to appear
- ❖ **Clinical features:**
    - Young men
    - Acute arthritis
    - After infection (GI or STD)
    - LL joints asymmetrical pattern
    - Knees, ankle, and feet are the most common
- Additional features:
    - **Reiter's syndrome:** urethritis, Asymmetrical reactive arthritis and conjunctivitis
    - Enthesitis
    - Acute anterior uveitis
    - Few may develop sacroiliitis and spondylitis
- Skin lesions that resemble psoriasis:
    - **Keratoderma blennorrhagica:**Red plaques and pustules that resemble pustular psoriasis are found on the palms and soles of the feet.
    - **Circinate balanitis:** causes superficial ulcers around the penile meatus
    - Nail dystrophy may also occur.
- ❖ **Investigations:** *clinical diagnosis*
    - Progresses sequentially from one joint to the other
    - Aspirated fluid is sterile with high neutrophil count
    - ESR raised in acute stages
- ❖ **Management:**
    - NSAIDs and local corticosteroid injections
    - Infection > Abx
    - Relapsing cases treated with sulfasalazine or methotrexate
    - TNF blocking in severe cases

Enteropathic Arthritis

- Large mono or asymmetrical oligoarthritis
- With IBD (Crohn's or Ulcerative colitis)
- Parallels disease activity
- **Treatment**: with disease remission but DMARDs and bio treatment occasionally required

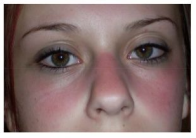
5. SLE:

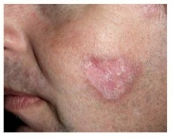
- Chronic, multisystem inflammatory disease characterized by autoantibodies directed against self antigens immune complex function and immune dysregulation resulting in damage to any organ.

❖ **Pathophysiology:**
- High ratio of CD4+ (T helper) to CD8+ (T cytotoxic)
- Defects in immune system leading to production of autoantibodies targeting antigens located in nuclei, cytoplasm, cell surfaces, and plasma proteins
- Autoantibodies leads to mostly immune complex function (kidney) and direct antibody mediated cytotoxicity (hemolytic anemia or thrombocytopenia)
- Cell mediated autoimmunity also plays a part
- Tissue damage follows

❖ **Risk factors:**
- Age: mostly between 16-55 years of age
- More common in females "especially at fertility years"
- **Hormonal: estrogen, also higher in males with Klinefelter XXY**
- Genetics:
  - **HLA DR2 and HLA DR3**
  - Deficiencies in the complement genes C4 and C2
  - **Increases risk if mother has SLE or other autoimmune disease**
- Racial: higher among African Americans and common in urban areas
- Environmental: UV rays, viruses, drugs, silica dust, cigarettes

❖ **Clinical features:** RASH OR PAIN: Rash(malar+discoid), Arthritis, Serositis, Hematologic, Oral, Renal, Photosensitivity, ANA,Immunologic disorder and Neurologic disorders


MALAR RASH


DISCOID RASH

- **Malar rash:**could be flat or raised over the malar eminence, tends to spare nasolabial fold
- **Discoid rash**: raised patches with adherent keratotic scaling and follicular plugging, may leave atrophic scarring
- **Photosensitivity**
- **Oral ulcer**: painless, could be nasopharyngeal ulcer
- **Arthritis:joint pain w/o deformity, non erosive**, involves >/= 2 peripheral joints. May be tender, swollen. Its first symptom patient present with 90%
- **Serositis:**pericarditis or pleuritis
- **Renal disorder**, Nephritic/nephrotic glomerulonephritis.
  - proteinuria > 0.5 grams a day
  - cellular cast: red, Hb, granular, tubular, mixed
- **neurologic disorder**: seizures or psychosis
- **hematologic disorder**: hemolytic normocytic normochromic anemia (anemia of chronic disease) , leukopenia, lymphopenia thrombocytopenia
- **immunologic disorder**:
  - anti DNA
  - anti smith (sm)
  - positive antiphospholipid antibodies
  - Anti-histones for drug induced lupus
- **ANA:**most important marker in SLE, if -ve exclude

- Organ involvement:
  - Joints (90%)
  - Skin: Raynaud's phenomenon, malar rash, discoid & alopecia
  - Pleuropericardium (serositis)
  - Mucous membrane
  - Kidney (50%)
  - CNS: Headache, meningismus, dementia, stroke, ataxia, GBS, MS, tremor, rigidity
- Diffuse alopecia is treated once you treat the disease (hair grows back)
- Discoid rash can leave hyperpigmentation
  - In hair leads to permanent alopecia
- Subacute cutaneous lupus associated with anti-SSA

❖ **Diagnosis:**

- Do CBC & Renal function test
- **Positive ANA:**sensitive but not specific
- **Anti-dsDNA and anti Sm Ab**: very specific but not sensitive
- **Anti SSA and SSB (a.Sjögren's syndrome | b. Subacute cutaneous Lupus) c. Pregnant woman with SLE and positive anti SSA and SSB > pass the antibodies to the child > neonatal lupus > congenital heart block**
- **Anti-histone:always +ve in drug induced lupus**
- Decreased complement level in flares

- Considerations:

★ Drug induced lupus:

- **hydralazine,isoniazid and methyldopa (HIM)**

❖ **Treatment:** HYDROXYCHLOROQUINE !!!

- Mild – mod:
  - Restricted to skin and joints :
    - ✓ Analgesics and hydroxychloroquine
    - ✓ May use steroids along with immunosuppressant
- Life threatening: renal, CNS, cardiac
  - ✓ High dose steroids and immunosuppression (cyclophosphamide)
- Maintenance therapy: oral immunosuppression
- **Hydroxychloroquine: 1st line**
- Treat co-morbidities: Hypertension & dyslipidemia
- Avoid UV light

- Poor prognostic factors:
  - Renal disease or CNS
  - Hypertension
  - Male sex
  - Young age
  - Presence of antiphospholipid antibodies

U finished ⅕ of medicine :)