NEET SS MEDICINE HIGH YIELD TOPICS

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RHUPUS

Rheumatoid Arthritis

00:00:28

Rhupus : SLE + RA.

SLE (Systemic lupus erythematosus) :

Symmetrical small joint non-erosive peripheral polyarthritis.

Rhupus : Erosive arthritis in SLE

Note : Renal involvement is less in rhupus.

Rheumatoid Arthritis :

- m/ multisystem autoimmune inflammatory connective tissue disease (CTD).
- Model for study of inflammatory and immune mediated disease.
- Primary target is synovium : Proliferative synovitis with synovial hypertrophy.
- Chronic (> 6 weeks) Inflammatory, multisystem, erosive arthritis.
- B/L, symmetrical, upper limb predominant, small joint polyarthritis of UL (>4 joints).
- Disease process starts at DRUJ (Distal radioulnar joint).

Note : 2nd m/C multisystem autoimmune inflammatory CTD : Sjogren syndrome.

Features of inflammatory arthritis
Synovial fluid WBC >2000/microL (BEST)
Raised inflammatory markers
X ray : Erosive arthritis
Early morning joint stiffness

Erosive arthritis
Rheumatoid arthritis
Rhupus
Chronic crystal arthropathy (Gout and pseudogout)
Psoriatic arthritis
Multicentric reticulohistocytosis

Non-erosive arthritis/ Jaccoud arthropathy
SLE
SLE like arthritis : • Sjogren • Scleroderma • Cryoglobulinemia • Polymyositis • Dermatomyositis
Acute rheumatic fever
Acute crystal arthropathy
Relapsing polychondritis

Arthritis involving small joints of hand :

- Rheumatoid arthritis.
- Psoriatic arthritis.
- SLE.
- SLE like arthritis.
- Osteoarthritis.
- Crystal arthropathy.

Rheumatoid arthritis	Osteoarthritis
Synovial hypertrophy ↓ Pannus ↓ marginal erosions	• Non-inflammatory arthritis • Involves articular cartilage • X ray features : a. Loss of joint space. b. Subchondral sclerosis. c. Osteophytes.

Rheumatoid arthtitis	Osteoarthitis
Joints involved	
5th MTP	PIP
MCP	DIP
Wrist	1st CMC
PIP	
C1-C2	
TMJ	
Cricoarytenoid	
Joints spared	
DIP	Wrist
1st CMC	MCP
1st MTP	
Lumbar, thoracic, sacral spine.	

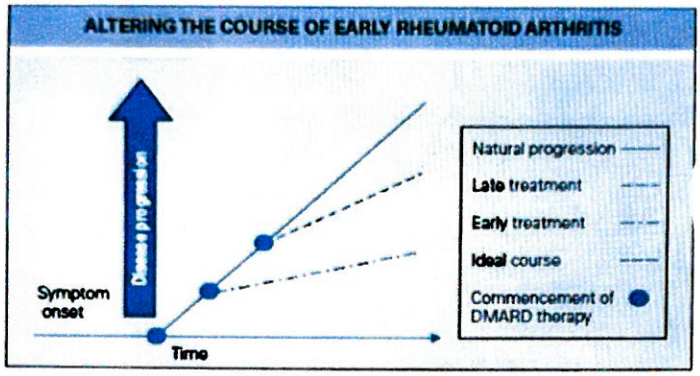
Note :

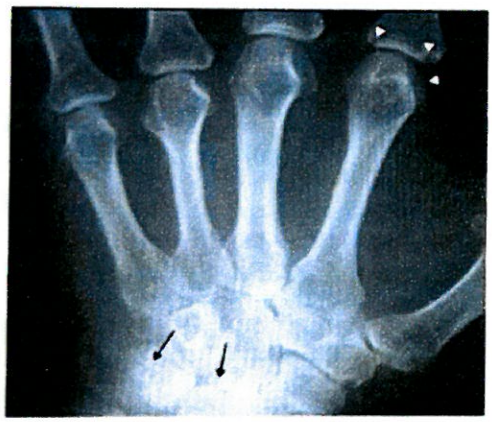
Non erosive arthritis such as SLE, acute rheumatic fever can be deforming d/t laxity of ligaments (Jaccoud arthropathy).

Disease progression :

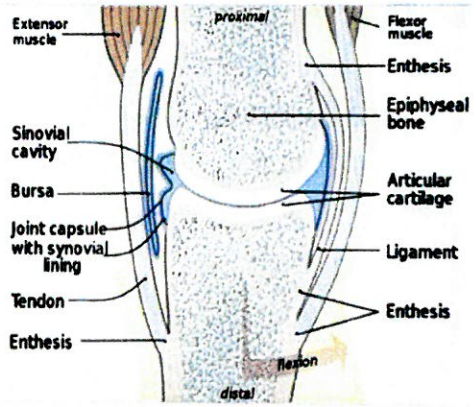
Treatment started as early as possible.

- very early rheumatoid arthritis (VERA) : < 3 months, best prognosis.
- Early established RA : 3-12 months.
- Late established RA : 1-2 years.
- Chronic stablized RA : > 2 years.





X ray hand : Rhupus
SLE with erosive arthritis



RA : Synovitis + Tendinitis + Bursitis.
Synovitis → Synovial hypertrophy → marginal erosions of bone (Not covered with articular cartilage).

Note :

Tenosynovitis : Lofgren syndrome (Ankle joint).
Polymyalgia rheumatica.

Etiopathogenesis :

Genetic factors : HLA

- HLA DRB1-04 in 70 % → 5 fold risk.
- Shared epitope : QKRAA motif on the third hypervariable region of DR β chains on DR4/DR14 (Amino acids 70-74).
- DR1/14 is causative.
- DR 1301 is protective.

Genetic factors : Non HLA

- PADI-4 : Post translational modification of arginine to citrulline. common in asian population.
- PTPN22 (Also in SLE).

Environmental factors

- Smoking :
  a. Strongest environmental risk factor.
  b. ↑PADI expression on the airway, promotes citrullination.
  c. ↑Risk for Interstitial lung disease (M > F).
  d. A/w bad prognosis (↑ Extra-articular manifestations).
- Silica : Scleroderma, SLE, RA.
- Alcohol/OCPs : Mild protection.

Note : Smoking associated ILD :

a. Desquamative interstitial pneumonia (DIP).
b. Langerhans cell histiocytosis (LCH).
c. Respiratory bronchiolitis associated ILD.
d. Rheumatoid arthritis associated ILD.

Epidemiology :

- F>M 3 : 1, ILD : M > F.
- 40-60 years.
- Pregnancy induces remission d/t IL-10 (Anti-inflammatory).
- No etiological link with infections (EBV/Parvo/mycoplasma).
- A/w oral periodontitis : Porphyromonas gingivalis.

F > M ratios :

3 : 1	9 : 1	15 : 1
Rheumatoid arthritis Polymyositis Dermatomyositis Scleroderma	SLE Takayasu arteritis Sjogren syndrome Primary biliary cirrhosis Fibromyalgia Chronic fatigue syndrome	MCTD

CLINICAL CRUX OF RA

Rheumatoid arthritis

00:00:25

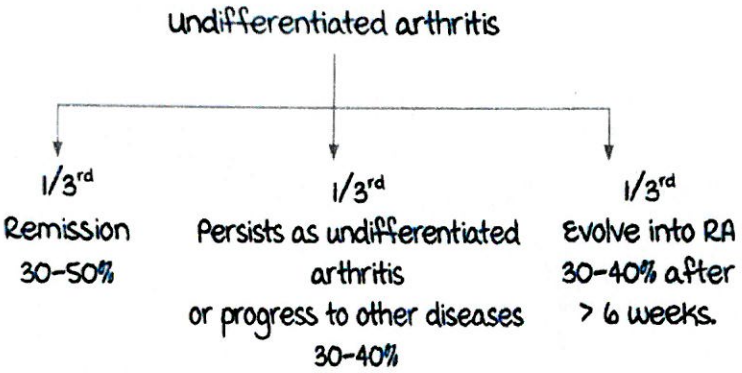
Clinical features :

Acute onset, symmetrical peripheral polyarthritis, involving small joints of upper limb.

2 possibilities :

a. Post viral arthritis (Parvo B19).

b. Undifferentiated arthritis.



Note :

- Rheumatoid arthritis is chronic (> 6 weeks).
- Wait till 6 weeks by which post viral arthritis should subside.

Scoring to predict progression into rheumatoid arthritis :

Epidemiological factors	Clinical factors	Serological factors
Age Female sex	Joint distribution Morning stiffness No. of swollen joints No. of tender joints	CRP RF CCP

Score > 8 : Start treatment.

Serological markers

1. Anti-CCP (Cyclical citrullinated polypeptide) antibodies :

- Aka ACPA (Anti-citrullinated polypeptide antibody)/mutated citrullinated vimentin (MCV).

- Specificity : 80-90% (Very high).
- Predictor for preclinical infection.
- High titres predict extra-articular manifestations.
- Test is not repeated in case of relapse.

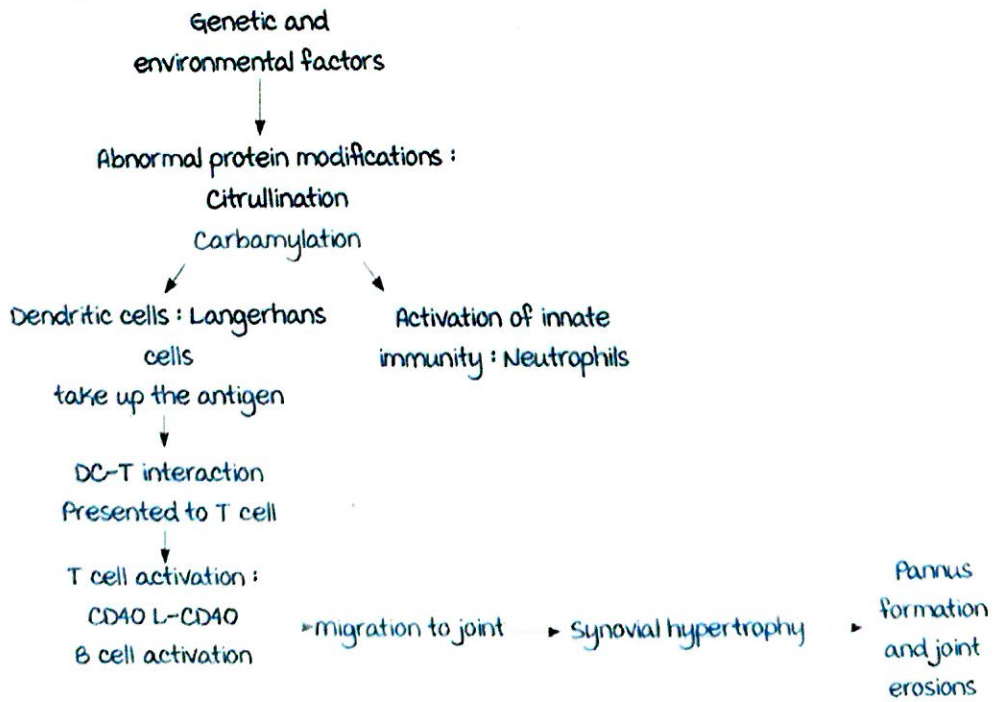
2. Anti CAR peptide (Anti carbamylated peptide) : To diagnose palindromic rheumatism.

3. Anti PADI antibodies.

4. Rheumatoid factor (RF) :

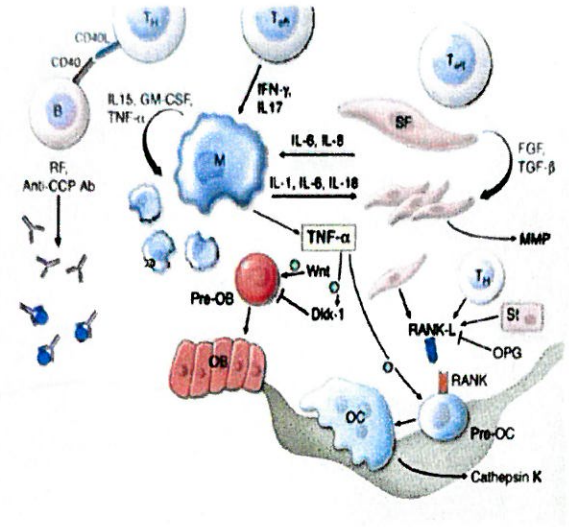
- IgM antibody against Fc portion of IgG VH3.
- Specificity : 75-80 % (Poor).
- Predicts prognosis, not used in relapse.
- RF is positive in other conditions :
  a. Sjogren syndrome.
  b. Cryoglobinemia 2/3.
  c. JIA (10 % : RF positive).
  d. Infective endocarditis/leprosy/Parasitic infestation/PBC/Sacoidosis/ HBV/HCV.

Pathogenesis :



T cells activation :

- TH 1 produce interferon γ → ↑ macropages : TNF α → Activation of osteoclasts (RANKL-RANK) and inhibition of osteoblasts (DKK-1 pathway).
- TH 17 : IL-17.



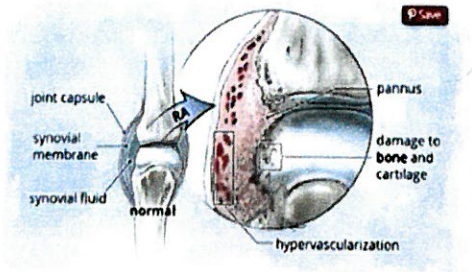
Rheumatological conditions producing osteoporosis :

a. Rheumatoid arthritis.

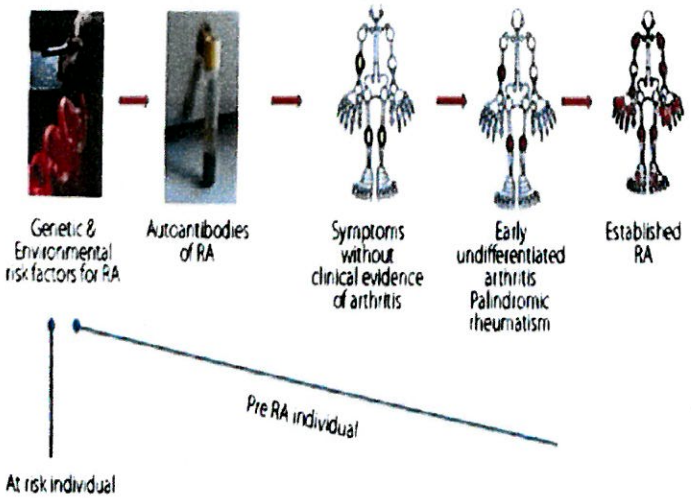
b. Ankylosing spondylitis.

Hallmarks of synovitis :

- Soft tissue swelling.
- Warmth.
- Tenderness on the joint line.
- Joint effusion.
- Loss of motion.



Pre-clinical RA : All stages before established RA :



Classification criteria for rheumatoid arthritis :

TABLE 76.4 2010 American College of Rheumatology/ European League Against Rheumatism Classification Criteria for Rheumatoid Arthritis

Joint Involvement[a]	(0-5)
1 medium to large[b] joint	0
2-10 medium to large joints	1
1-3 small[c] joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
>10 joints[d] (at least one small joint)	5
Serology[e,f]	(0-3)
Negative RF AND negative ACPA	0
Low-positive RF OR low-positive ACPA	2
High-positive RF OR high-positive ACPA	3
Acute Phase Reactants[e,g]	(0-1)
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1
Duration of Symptoms[h]	(0-1)
<6 weeks	0
≥6 weeks	1
The sum of scores needs to be >X to classify as RA	

Patterns of presentation

Insidious (55-65%) :

a. Symmetrical small joint inflammatory polyarthritis.
b. Elderly RA can mimic palandromic rheumatism.

Acute(10-15 %) :

Explosive painful small + Large polyarthritis in elderly.

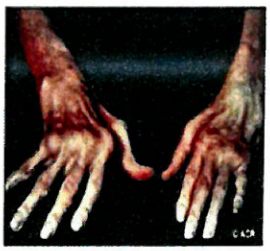
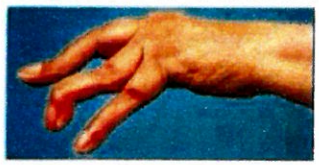
Palindromic rheumatism :

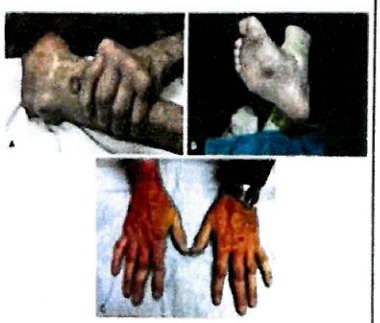
a. Acute monoarthritis of the knee/fingers.
b. Acute brief episodes of pain.
c. mimic septic arthritis/crystal arthropathy.
d. After subsequent episodes, reaches to baseline completely.
e. A/w Anti Car P antibody.

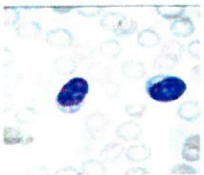
Elderly RA :

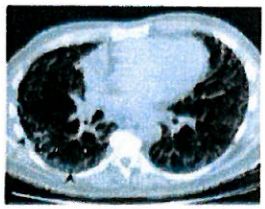
1. Can mimic PMR.
2. Acute explosive polyarthritis.
3. Arthritis robustus : Erosive arthritis but patient is unaware.

Deformities in RA :

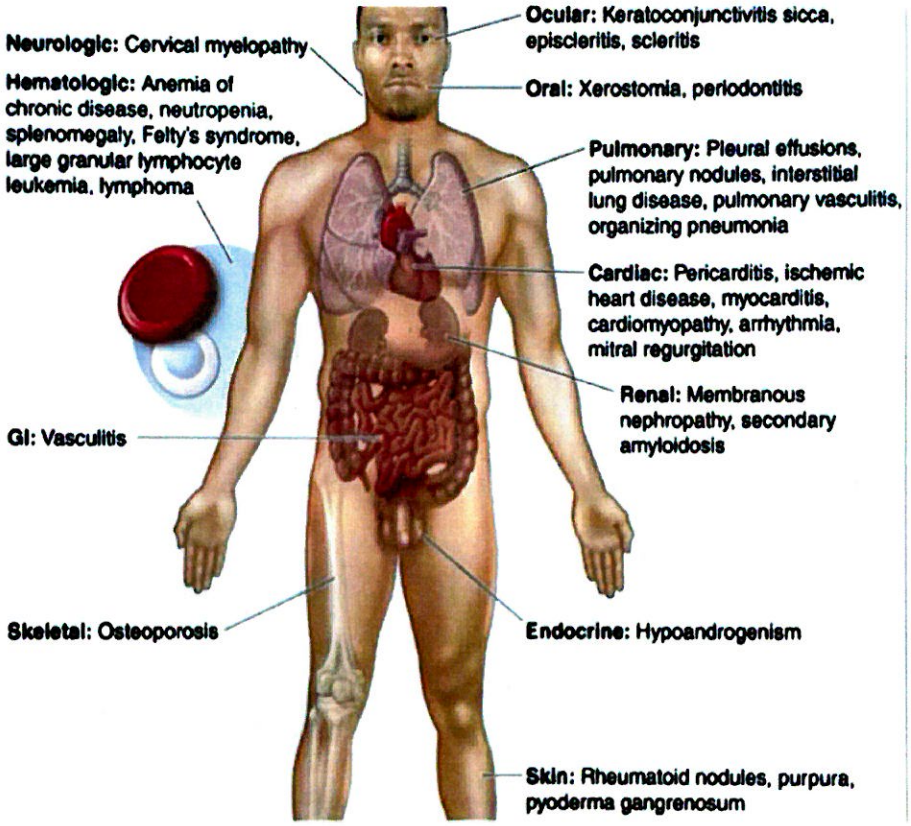
Resversible deformities	
Zig - Zag deformity	Radial deviation at wrist and ulnar deviation at MCP with extension at interphalangeal joints.
Piano key deformity of ulnar styloid	D/t rupture of ulnar collateral ligament. 
Hitch hiker's thumb	Abducted and hyperextended thumb.
True deformities (Irreversible)	
Boutonniere's deformity	Flexion at PIP and hyperextension at DIP. 
Swan neck deformity	Hyperextension at PIP and flexion at DIP. 
Opera glass hand	Complete destruction of hand.
Vaughan Jackson deformity	Involvement of extensor tendons, only index finger is spared.
Pes planus	

Extra-articular manifestations (40%)	
Rheumatoid nodules 	• m/c extra-articular manifestation (40 %). • Associated with high titres of RF +ve. • A/w smoking. • Painless nodules present at sites of friction (Olecranon). • Risk of early onset disease, long duration disease. • Bad prognostic feature. • Pathology : Granuloma (Type IV hypersensitivity). • Responds to treatment. • methotrextate : 10 % cases can have ↑ size of nodules.

Ocular features	• Keratoconjunctivitis sicca (2° Sjogren) : m/c manifestation is dry eye. • Episcleritis : more common, seen in high disease activity, not a/w vision loss. • Scleritis : Less common, recurrent episodes can lead to scleromalacia perforans. • Retinal vasculitis/uveitis : Not seen.
Neurological manifestations 	• Acute quadriparesis : C1-C2 subluxation d/t erosion of odontoid process. • Entrapment neuropathy : Carpel tunnel syndrome (m/c). • Perpheral nervous system : Small fibre neuropathy. • CNS/brain parenchyma : Not involved.
Hematological manifestations 	• Anemia of chronic disease (m/c). • WBC count : Normal. • Thrombocytosis/2°ITP. • Rapidly progressive anemia : AIHA d/t warm antibody IgG. Felty's syndrome : • Rheumatoid arthritis + Neutropenia + Splenomegaly. • A/w : a. HLA DRB1-04. b. Long standing RA. c. RF positive. d. Nodules/deformities ++. e. Antibody against citrullinated histones. • Perpheral blood smear : Large granular lymphocytes (LGL Leukemia). • RA increases risk of diffuse large B-cell lymphoma (DLBCL).

Pulmonary manifestations	Pleuritis +/- exudative pleural effusion (m/c) : • U/L > B/L, lymphocytic/exudative (Lite's criteria). • Protein content > 4g/dL, low glucose < 30 g/dL, high LDH. Interstitial lung disease (ILD) : • 30 % patients. • Males, smoker, RF/Anti CCP ++. • Usual interstitial pneumonia (UIP) : a. Honey comb pattern. b. Cysts. c. Traction bronchiectasis. • Parenchymal destruction : Poor prognosis. • Screening : Pulmonary function tests, DLCO ↓, HRCT.  Caplan's Syndrome : • Nodules + Cavitation + Pneumoconiosis. • RF positive active synovitis. • Coal dust exposure. • D/D : a. Wegener's granulomatosis b. Silicosis
CVS manifestations	• m/c/c of death in RA : Acute coronary syndrome. • RA : MI equivalent (Acclereated atheroscleosis). • m/c cardiac manifestation : Pericarditis without tamponade. • m/c valvular heart disease : MR > AR. Vasculitis in RA : Small vessel vasculitis : • Immune complex mediated. • Leukocytoplastic vasculitis. • C/F : Purpura, urticaria. Medium vessel vasculitis : • Long standing disease with RF +ve. • Males, smoker. • ↓ Complement C3, C4. • C/F : Nodules, ulcers, gangrene. Mononeuritis multiplex. Dangerous forms of vasculitis in RA (Indication for treatment with Rituximab) : a. Digital gangrene. b. Intestinal infarcts. c. Mononeuritis multiplex.

Renal manifestations	• Secondary amyloidosis. • membranous nephropathy.
Endocrine manifestations	Hypoandrogenism.
Skin manifestations	• Rheumatoid nodules. • Purpura. • Pyoderma gangrenosum.



MANAGEMENT OF RA

Drugs used in RA

00:02:47

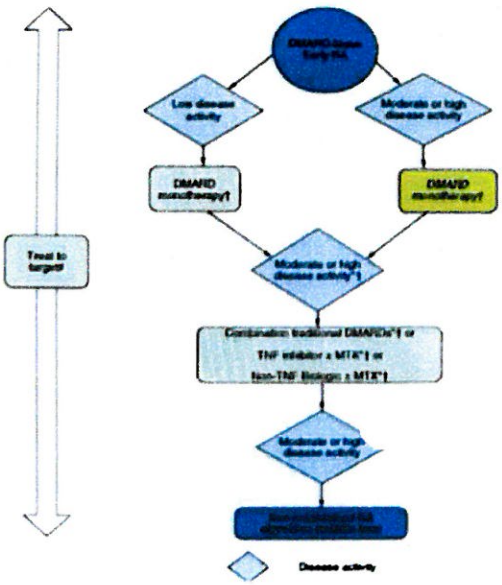
Drugs used in RA :

DMARDs (Oral)	Biological (IV)	Small molecules (Oral)
1. methotrexate 2. Leflunomide 3. Hydroxychloroquine 4. Sulfasalazine	1. Anti TNF α : • Infliximab • Adalimumab • Etanercept • Certolizumab • Golimumab 1. Anti CD20 : Rituximab 2. Anti IL-1 : Anakinra 3. Anti IL-6 : Tocilizumab 4. CTLA4-FcIgG : Abatacept	1. JAK 1/3 inhibitor : Tofacitinib 2. JAK 1/2 inhibitor : Baricitinib

Least imunogenic : Etanacept (Fusion protein).

most immunogenic : Infliximab.

Treatment on presentation :



DMARD monotherapy : methetrexate

Anti-metabolite drug.

MOA : Increases adenosine .

Dose : Start with 5mg weekly, increase to 20-25mg weekly.

Side effects :

- Bone marrow suppression (monitor CBC).
- Increase in liver enzymes (monitor LFT).
- mucositis (m/c toxicity).
- Increase in size of nodule (Does not produce ILD).

Assessment :

Done after 3 months.

Based on Boolean classification :

- No. of tender joints ≤ 1.
- No. of swollen joints ≤ 1.
- CRP ≤ 1.
- Patient global assessment ≤ 1.

If target not achieved, combination therapy must be started

Combination Therapy 00:07:38

1. MTX + Sulfasalazine + HCQ

Hydroxychloroquine (HCQ) :

- Dose : 4-7 mg/kg.
- Side effects :
    a. Corneal opacities (Reversible).
    b. Bull's eye maculopathy (< 1 %, irreversible).
    c. Screening must be done with Optical coherence tomogram (OCT).

Sulfasalazine :

- Dose : 500mg TID.
- Side effects :
    a. Dose dependent bone marrow suppression.
    b. Hemolytic anemia in G6PD deficiency patients.

HCQ only drug safe in pregnancy :

1. MTX + Biologics :

- Anti TNF α is most commonly used.
- Etanecept is used (Least immunogenic).
- Problems with Anti TNF α:
    a. Reactivation of TB → IGRA test must be done (Not practical).
    b. Drug induced lupus erythamatosus (DILE).
    c. Reactivation of Hepatitis-B.
    d. Risk of malignancy.

2. MTX + Small molecule:
    - most commonly used combination therapy now.
    - JAK 1/3 inhibitor is used (Tofacitinib).
    - JAK 1/2 inhibitor (Baricitinib) is also used currently.

Important points:

Never diagnose RA if:

- monoarthritis is present.
- Hands are involved.
- DIP joint is involved (Consider alternate diagnosis).
- Lumbar spine is involved.

RF never repeated as it correlates poorly with treatment.

SLE : INTRODUCTION

Introduction

00:02:47

SLE :

Usuallly diagnosed at 15-45 years.

F : M ration : 9 : 1.

Strong family history.

Positive concordance with more 40% of identical twins seen.

Other variants of SLE :

1. Male lupus : more aggressive, poor prognosis.
2. Child lupus : 100 % renal involvement seen.
3. Elderly lupus :
   - Also known as, post-menopausal lupus.
   - F : M ratio comparitively less.
   - Renal sparing is seen.
   - Polyserositis.
   - Anti-dsDNA -ve.
   - Complements are normal.
4. Drug induced lupus erythamatosus (DILE) :
   - F : M ratio is 1 : 1.
   - Good prognsois.
   - Caused by (CHIMP) :
     a. Carbamezepine.
     b. Hydralazine.
     c. Isoniazid.
     d. Infliximab.
     e. methyl dopa.
     f. Procainamide.
     g. Propylthiouracil.
   - 100% are ANA positive.
   - Homogenous pattern :
     Anti-histone antibody.
     Anti-dsDNA is negative.
   - Systems always involved : Skin & joint.
   - Systems never involved : Renal & CNS.

Conditions with 100 % ANA positivity
1. Autoimminue hemolytic anemia type I
2. Mixed connective tissue disorder (MCTD)
3. DILE

- Complements are normal.

Genetic Factors :

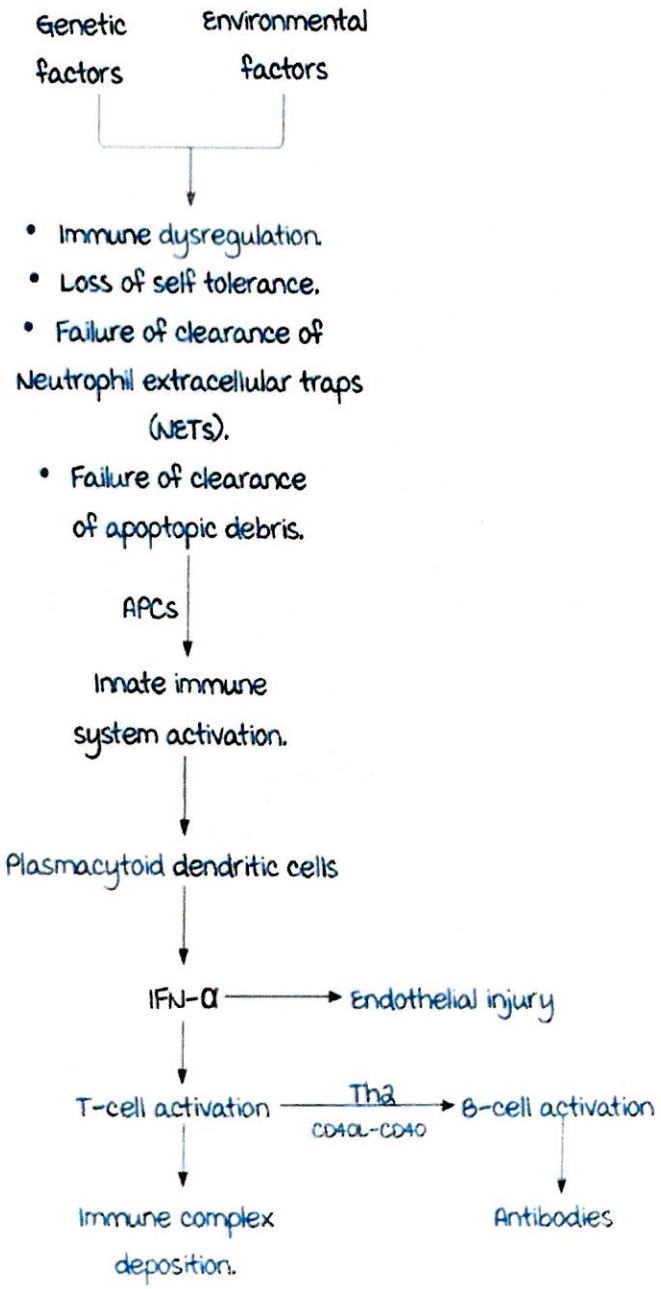
Early compliment deficiencies (C1q > C2, C4) :

- HLA related : DR-2 (C2), DR-3 (C4).
- Non HLA related : C1q (most important).
- TREX gene : Located on chromosome 3.
- X chromosome : Toll-like receptors (TLRs), IRAK4.

Environmental Factors :

- OCPs and estrogen.
- UV-B rays.
- Infections : Epstein-Barr virus.
- Vitamin-D deficiency, smoking (minor role).

Pathogenesis :



Types of T-cell activation		
Th 1	Th 2	Th 17
Seen in RA • IL-2 • IFN γ	Seen in SLE • IL-4 • IL-5 • IL-13	Seen in Ankylosing Spondylitis • IL-17/23

Important points :

- Central key pathogenic cytokine : IFN-α.
- Defective clearance of apoptotic debris.
- Inefficients degradation of NETs.
- Innate system activation.
- ↓ Clearance of dead cells → Exposure of autoantigens → Breaks self tolerance.
- Interferons are genetic signature.
- DR2 > DR3 association.
- A/w silica exposure (more commonly with scleroderma).
- Hyperactivation of T-cell/B-cell.
- T-cell activates B-cell by :
  1. IL-4.
  2. CD40L-CD40 interaction.
  3. B lymphocyte stimulator (BLYS).
  4. IL-12/21 pathway.

SLE : ANTIBODIES

Antinuclear Antibody (ANA)

00:00:59

It is the Screening test for CTD (Except in RA) :

- Positivity in SLE : 97 %.
- Positivity in Scleroderma : 95 %.
- Positivity in IMD : 93-95 %.
- Positivity in Sjogren's syndrome : 85 %.

Detected by indirect immunofluorescence (ELISA has no value).

Positivity detected by titres and pattern.

Titer > 1/80 is clinically significant.

Classification of types of patterns :

Types of patterns	Clinical significance
Homogenous	• dsDNA (SLE). • Antihistone (DILE).
Fine speckled	• Anti Ro/La. • Anti Mi-2 (Dermatomyositis).
Coarse speckled	• Anti UIRNP (MCTD). • Anti Smith (SLE). • RNA polymerase 3 (Scleroderma).
Centromere	• CREST syndrome (Limited scleroderma).
Dense fine speckled	• Rules out CTD.
Cytoplasmic	• Anti Jo-1 (Polymyositis, dermatomyositis).
Nucleolar	• Anti PM/Scl-70 (Polymyositis/ scleroderma overlap).

Types of profiling :

1. Extractable nuclear antigen (ENA) : 6 antibodies present.
2. ANA profile by Immunoblot : 14 antibodies present.

Reading an ANA report :

Method : Indirect immunofluorescence.

Dilution : Standard dilution 1 : 80, end dilution positivity 1 : 80.

Pattern : Fine, coarse or dense fine speckled, homogenous, cytoplasmic.

Anti Ro/La Antibody

00:09:47

Seen in (ANA negative SLE patients) :

Anti Ro : SS-A.

Anti La : SS-B.

Anti La usually not seen without Anti-Ro (Ro-52).

Importance of anti Ro/La in SLE :

- Positive incase of ANA negative.
- Can indicate secondary Sjogren's syndrome.
- Decreased risk of nephritis and vasculitis (Good prognosis).
- Tested in pregnancy : Seen in neonatal lupus with congenital heart block.
- Seen in SCLE (Subacute cutaneous lupus erythematosus) with HLA-DR3 association.
- Associated with shrinking lung syndrome (Diaphragmatic palsy).

Anti Ro/La positivity in Sjogren's syndrome indicates :

- Early disease onset, long duration (Bad prognosis).
- Increased risk for extraglandular manifestation.
- Increased risk for lymphoma (marginal zone B-cell lymphoma).

Anti dsDNA & Anti Smith Antibody

00:14:21

Comparison between Anti dsDNA & Anti Smith antibody :

	Anti dsDNA	Anti Smith
Specificity	Specific for SLE.	more specific for SLE.
Clinical significance	more	Less
Nephritis/vasculitis	Higher titers a/w increased risk.	No effect on prognosis.
Pattern on ANA	Homogenous	Fine speckled

Anti dsDNA methodology :

- Crithidiae Luciliae : Immunofluorescence (Qualitative).
- Immunoblot : Semi quantitative.
- ELISA : Quantitative.

No point in repeating ANA (Not prognostic marker).

Other antibodies of clinical significance :

Antibody	Features
Anti U1 RNP	Seen in MCTD
Anti-phospholipid	One third of SLE patients are positive.
Anti-RBC antibody	Warm antibody in AIHA in SLE.
Anti-platelet antibody	Seen in secondary ITP in SLE.
Anti-glutamate antibody	CNS manifestations in SLE (m/c : Decline in cognitive function).
Anti-ribosomal antibody	Depression/psychosis in SLE.

Biomarkers in SLE

00:21:19

Biomarkers in clinical utility :

- Increased disease activity implied by :
  - Low C3, C4.
  - Increased dsDNA titers.
  - Increased ESR.
- Repeating ANA, ENA is not useful.
- Anti C1q antibodies useful only in nephritis.
- CRP has no value.

Biomarkers in research setting :

- BAFF/BLyS.
- APRIL.
- IFN-α.
- Soluble IL-7 receptor.

SLE : CLINICAL CRUX

Clinical Manifestations in SLE

00:02:47

Clincal features seen in SLE can be grouped into :

1. Constitutional symptoms :

   Frequency : 90-95 %.

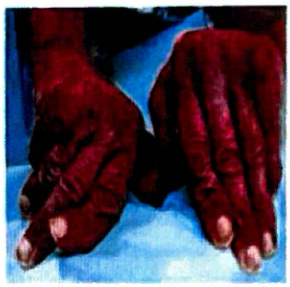
   Fatigue, fever, weight loss.

2. Musculoskeletal involvement :

   Frequency : 90 %.

   Inflammatory arthritis/arthralgia :

   - Inflammatory synovitis.
   - Polyarticular.
   - Peripheral
   - Small joint.
   - UL predominant.
   - Non-erosive (Difference from RA).
   - Deforming.

   Jaccoud arthropathy

   SLE- like arthritis : Jaccoud arthropathy.

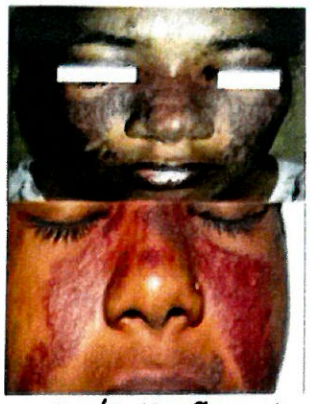
3. Mucocutaneous involvement :

Type	Involvement
Acute cutaneous lupus erythematosus (ACLE)	• Localized : malar/butterfly rash (90-95 %) • Generalized ACLE. • TEN-like ACLE.
Subacute cutaneous lupus erythematosus (SCLE)	• Annular SCLE : 42 %. • Psoriasiform SCLE : 39 %.
Chronic cutaneous lupus erythematosus (CCLE)	• Discoid lupus erythematosus. • Chillblain LE. • LE profundus.

Localized rash :

- Malar/Butterfly rash.
- m/c lupus specific rash.
- Highly photosensitive erythematous rash.
- Tendency for scaling present.

- Non-scarring rash.
- Nasolabial fold spared.
- A/w oral ulcers & non-scarring alopecia.
- No risk for malignancy.



Malar/Butterfly rash

Discoid LE :

5 %-20 % rule :

- 5 % of discoid rash patients have SLE.
- 20 % of SLE patients have discoid rash.

Scarring rash.

A/w scarring alopecia : Cicatricial alopecia.

Premalignant : Risk factor for SCC.

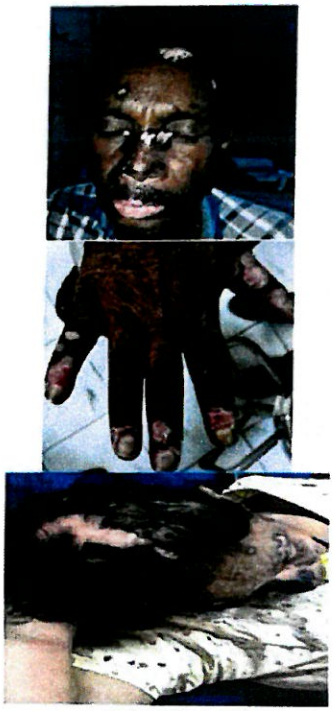
A/w follicular plugging, dermal atrophy.

Circular erythematous lesions :

- Face, scalp and neck.
- Centre : Hypopigmentation.
- Periphery : Hyperpigmentation.

Carpet track appearance on back.

Keratotic scaling.



Discoid LE

Subacute Cutaneous LE (SCLE) :

Types :

- Annular SCLE (m/c).
- Psoriasiform SCLE.

Photosensitive.

Non-scarring.

A/w anti Ro/La antibodies, HLA DR3.

m : F ratio is 1 : 4.

Seen on sun exposed parts :

- Sparing of mid facial region

SCLE rash

Organ system involvement :

Neuro-Ocular :

Brain parenchyma involved : Cognitive dysfunction.

CNS vasculitis : Rx → Plasmapheresis.

PNS : Small fiber neuropathy.

Dry eye (m/C ocular manifestation).

(Uveitis, episcleritis, scleritis, retinal vasculitis not seen).

Hematological :

m/C of anemia : Anemia of chronic disease.

Leukopenia present.

Platelet count decreased (High chance for 2° ITP).

Rapidly progressive anemia : Warm antibody AIHA (IgG subtype).

Increased risk for DLBCL.

Cardiovascular :

Vascular	Cardiac
m/C cause death in SLE : ACS (After 5 yrs). Small vessel vasculitis : • Immune complex mediated. • Leukocytoclastic vasculitis (LCV). Dangerous forms of vasculitis affects : • GIT. • CNS.	• Pericarditis without tamponade (m/C). • Libman-Sacks endocarditis : vegetations on the undersurface of th leaflet. • m/C valvular disease : MR.

Liver :

Type I autoimmune hepatitis (Lupoid Hepatitis).

100 % patients are ANA positive.

Lungs :

Pleuritis ± secretions (Normal sugars).

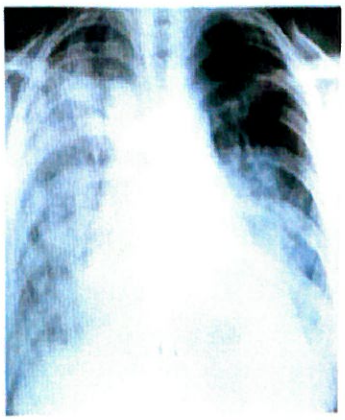
Diffuse alveolar hemorrhage :

- Indicates high disease activity.
- Rx : Plasmapheresis.

Shrinking lung syndrome :

- Diaphragmatic palsy, a/w anti-Ro/La.

ILD not seen



Diffuse alveolar hemorrhage

Renal :

Biopsy done if : Proteinuria > 1g/dl or > 500mg/dl with RBCs

Class 1 : Minimal mesangial. } Good prognosis
Class 2 : mesangio-proliferative. } No Rx required

Class 5 :

- Membranous lupus.
- Presents as nephrotic syndrome.
- Resistant to steroids.
- Decreased risk of CKD.
- CNI + MMF regimen used for treatment.

Class 3 : Focal proliferative. } Bad prognosis.
Class 4 : Diffuse proliferative. } Aggressive immunosuppression required.

In class 3,4 :

Immunofluroscence : Full house pattern (C1q, C2, C4 IgG, IgM).

Electron microscopy : Hematoxylin bodies of gross.
Subendothelial deposits (wire-loop lesions).

SLICC criteria :

Requirements :

- ≥ 4 criteria (At least 1 clinical & 1 laboratory criteria).
- Biopsy-proven lupus nephritis with positive ANA or Anti-DNA.

Clinical criteria	Immunologic criteria
1. Acute Cutaneous Lupus.	1. ANA.
2. Chronic Cutaneous Lupus.	2. Anti-DNA.
3. Oral or nasal ulcers.	3. Anti-Sm.
4. Non-scarring alopecia.	4. Antiphospholipid Ab.
5. Arthritis.	5. Low complement (C3, C4, CH50).
6. Serositis.	6. Direct Coomb's test.
7. Renal.	
8. Neurologic.	
9. Hemolytic anemia.	
10. Leukopenia.	
11. Thrombocytopenia.	

Management of SLE

00:22:08

Treatment of non-renal SLE :

Condition	Drugs used
Non life threatening lupus	• Low dose steroids + methotrexate.
moderate to severe non-renal lupus.	• CNI or MMF • Belimumab
Severe non renal lupus.	• Rituximab
Drugs used in all patients.	• Hydroxychloroquine • Low dose steroids • Topical photoprotection
Arthritis.	• methotrexate
CNS vasculitis or DAH.	• Plasmapheresis

Treatment of renal SLE (Class 3,4) :

- Pulse methyl prednisolone 500mg - 1g for 3days, continue with oral steroids.
- Low dose cyclophosphamide euro lupus regime : 500mg IV cyclophosphamide in 6 doses, every 2 weeks.
- MMF if condition does not improve in 3 months.
- Rituximab if condition does not improve in 6 months.
  (Resistant lupus)

Criteria for complete remission :

Criteria	Requirements
ACR criteria	• GFR > 60 ml • PCR < 0.2 • Inactive sediment
EULAR criteria	• Normal or stable RFT • Proteinuria < 0.2 gm/d • Inactive sediment
KDIGO 2012	• Return of S. Cr to previous baseline • Decline in uPCR to < 0.5

Resistant lupus : No improvement after 6 months of treatment.

Treatment options :

- Rituximab.
- Extended course of Cyclophosphamide x 3 more months.
- Multitarget therapy.
- IVIG.
- Therapeutic plasma exchange.
- Immuno-ablation Cyclophosphamide with or without Stem Cell.
- Hematopoietic stem cell transplantation (HSCT).

Maintenance Rx :

- Mycophenolate mofetyl (1000mg BID).
- Azathioprine (2mg/kg/day).
- Cyclophosphamide.
- Cyclosporine/Tacrolimus (Intolerant to other agents).

SPONDYLO ARTHROPATHIES

Spondylo Arthropathies (SpA)

00:00:14

Previously called : Seronegative arthropathies (RF -ve).

Forms of SpA :

Axial predominant
Radiographic axial SpA.
Non-radiographic axial SpA.
Juvenile onset AS.

Peripheral predominant
Reactive arthritis.
IBD associated arthritis/ Enteropathic arthritis.
Psoriatic arthritis.

Axial predominant SpA

- **Non- Radiographic axial SpA** — Clinical evidence of Axial SpA with/without Sacroiliitis in STIR MRI.
  - Followed for 15-20 yrs
  - Only 5-10 % develop into AS
- **Radiographic Axial SpA/Ankylosing spondylitis (AS).** B/L Sacroiliitis in X-ray.

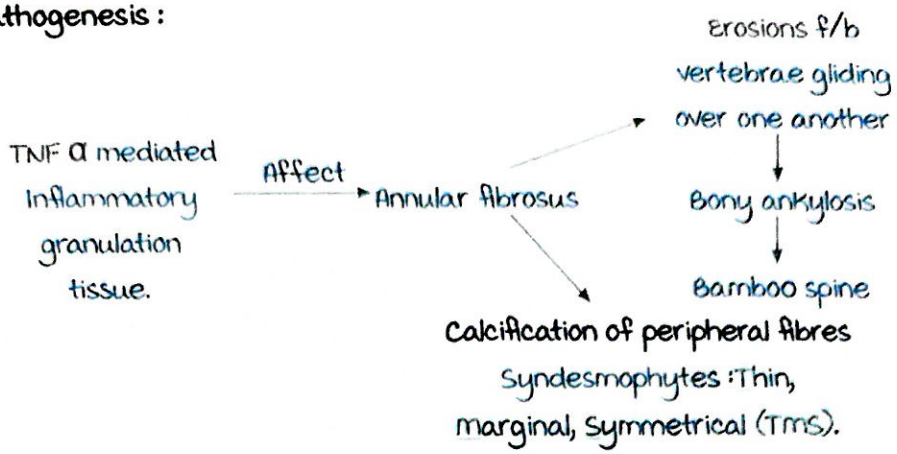
- Inflammatory back pain for > 3months.
- In males (M : F = 3 : 1) < 40 yrs of age.
- Early morning pain & stiffness lasting for 30 minutes relieving with activity. and NSAIDS.

Severe nocturnal pain over buttocks in alternating pattern + Enthesitis (Achilles tendonitis/ plantar Fasciitis) + Root Joint involvement (Shoulders and Hip).

Note :

- Key pathogenic cytokine : TNF α , IL-17/23, IL-12/23.
- In appendicular skeleton : 45 minutes stiffness.
- In axial skeleton : 30 minutes stiffness.

Pathogenesis :



- Single most important cause of death in SpA : Spinal fracture with trivial trauma.
- m/C site of fracture in AS is seen in C5-C6.
- Root joint early involvement : Poor prognosis.
- m/C Extra articular feature : 4A uveitis (Acute anterior alternating asymmetrical).

Lungs	B/L upper lobe fibrosis NSIP (Like Sarcoidosis).
Heart	Aortitis and AR. Note : In SLE and RA : MR.
Kidney	2° Ig A nephropathy.

Clinical characteristics of SpA :

1. RF -ve.
2. Absence of nodules & other extraarticular features of RA.
3. Overlapping extra articular features of the group (Eg : Uveitis).
4. Familial aggregation.
5. Associated with HLA B27 (90 % in AS).

Rx :

1. NSAIDS : Reverse natural history of disease.
   a. Indomethacin 50mg TDS for 2-3 wks.
   b. Naproxen 550 mg BD.
   c. Ibuprofen 800 mg TDS.
2. Anti-TNF α (DOC).
3. Anti-IL 17 : Secukinumab (In future replace TNF α as DOC).

Ankylosing Spondylitis :

Hallmark : Radiographic Sacroiliitis.

M : F = 3 : 1.

HLA B 27 (90 %).

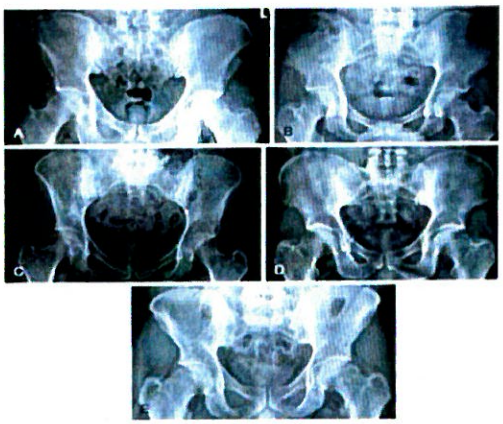
5-10 % of non-radiographic axial SpA develops into AS after 15-20 yrs.

Differentiating factor from RA is IL-17.

C/F :

- Inflammatory back pain.
- Bony ankylosis/bamboo spine.
- Enthesitis (Extra-articular tenderness) : Key factor.
- Syndesmophyte formation (Calcified annulus, vertical osteophyte).
- Ascending thoracic spine + Enthesitis at costo/manubriosternal Joint : Chest pain.
- Alternating acute anterior uveitis.
- Osteoporosis.

Slight blurring of cortical margin
↓
Erosion with Sclerosis
↓
Widening of Joint space
↓
Ankylosis



- Schober's test : +ve for Ankylosing Spondylitis (If expansion < 5cm).

Signs of AS :

- Dagger sign : Interspinous calcification.
- Trolley tract sign : Apophyseal Joint capsule calcification.
- Shiny corner sign (Sclerosis)/ Romano sign (Erosion) : In corners of vertebra.
- Square wave vertebra.

Note : DISH : In elderly with metabolic syndrome, no sacroiliitis, IVD space preserved (Flowing candle appearance).

Rx :

- Exercise.
- NSAIDS : 1st line of Rx for 2-4 wks.
- No benefits with DMARDS.

Reactive Arthritis :

Predominantly peripheral SpA.

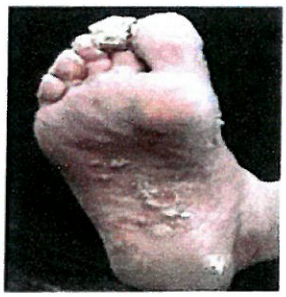
- Acute onset non-purulent arthritis after 2-4 wks in young adult male.
- M : F = 9 : 1 following urethritis & 1 : 1 following GIT.
- If HLA B27 association : 15-20 % chronicity.
- Causes :

Infective causes	GIT	Shigella flexneri (m/c cause in India).
	Genito urinary tract.	Chlamydia trachomatis (Worldwide m/c cause).
	Upper respiratory tract.	• Chlamydia pneumoniae • β Hemolytic streptococci

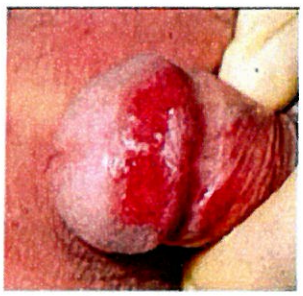
Asymmetrical additive painful arthritis with LL Knee predominance + Enthesitis & Dactylitis (Sausage digits) +

Muco-cutaneous involvement

1. Oral ulcer
2. Keratoderma blenorrhagicum
   Hyperkeratotic painless lesions over palms and soles
   D/d : Pustular psoriasis.
3. Circinate balanitis
   Painless shallow erythematous lesion on Glans penis.

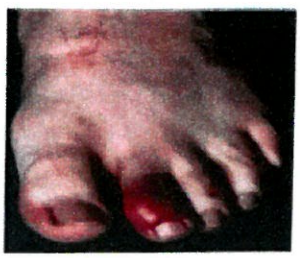


Keratoderma Blenorrhagicum



Circinate balanitis

- 1/3rd Pts have axial asymmetric sacroiliitis : Large, fluffy, non-marginal, asymmetric syndesmophytes d/t paravertebral ossification.
- Sterile arthritis : On biopsy organisms persist inside the monocytes of synovium, hence synovial fluid PCR can be done.
- Synovitis + Enthesitis + Dactylitis.



Dactylitis

Rx :

- NSAIDS : Indomethacin 50 mg TDS, reverse the natural history of the disease.
- DMARD approved for chronic cases.

Axial arthropathy in reactive arthritis :

- Asymmetrical sacroiliitis.
- Coarse asymmetric non-marginal syndesmophytes.
- HLA B27 +ve.

Enteropathic arthritis /IBD associated arthritis :

- M : F = 1 : 1
- M/C in Crohn's diseas > Ulcerative colitis.
- 10 % axial/25 % peripheral arthropathy.
    a. Axial : HLA B27 +ve (50 %).
    b. Peripheral : HLA- B27 -ve .
- B/L symmetrical sacroiliitis.
- Enthesitis/dactylitis rare.

Periphera arthropathy :

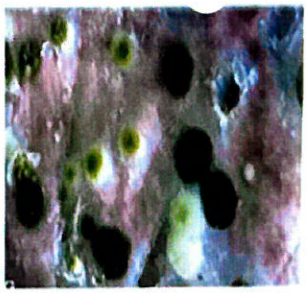
Types :

Type 1	Type 2
LMAP : Large Joint. migratory. Asymmetrical. Pauci articular arthritis. Pedominantly involving Knee joint.	SMAP-U : Small Joint (MCP). Symmetrical. Migratory. Aggressive. Polyarticular arthritis with Uveitis.
M/C type and limited	Persistent
Correlates with flares.	Not associated with flares.

Rx : Anti-TNF α.

Psoriatic Arthritis :

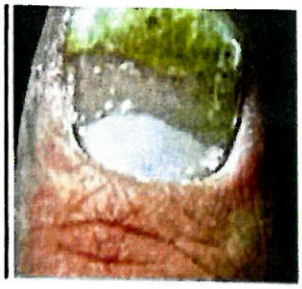
- > 40yrs, M = F.
- Seen in 7-40 % with psoriasis.
- Gene : HLA CW0602.
- B27 for axial arthritis alone.
- 90 % associated with nail changes :
    a. Pitting.

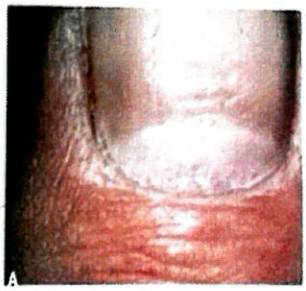


Pustular psoriasis

b. Onycholysis.
c. Yellow colour discoloration.
d. Hyperkeratosis.

- 60-70 % psoriasis f/b arthritis.
- 15-20% psoriasis with arthritis.
- 15-20% arthritis f/b psoriasis.
- most destructive arthritis is pustular psoriasis (Always rule out HIV).
- Dactylitis > enthesitis are very prominent.


Onycholysis

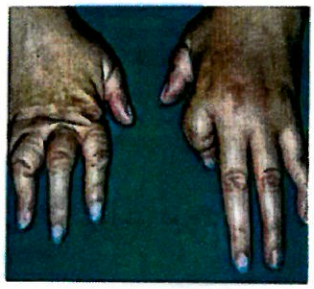

Nail pitting

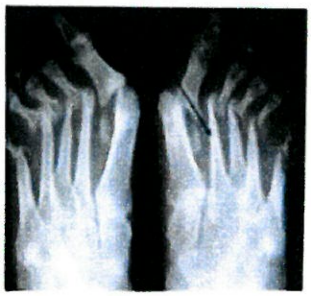
Wright and moll classification of Psoriatic arthritis :

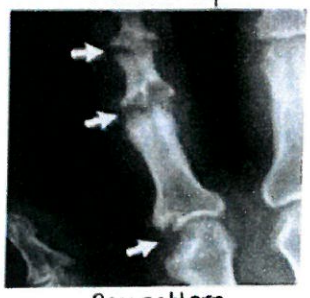
1. Symmetrical polyarthritis (m/c) : Small Joints.
2. Asymmetrical oligoarthritis : LL predominant.
3. Predominant DIP arthritis.
4. Predominant spondyloarthritis : Cervical spine.
5. Destructive arthritis mutilans in pustular psoriasis.

Other features of Psoriatic arthritis :

- Rapid tendency for ankylosis.
- CASPAR criteria.
- X-ray findings :
  a. Periostitis.
  b. Ankylosis.
  c. Pencil in cup deformity.
  d. Telescoping of fingers.
  e. marginal erosion with adjacent bone proliferation (Whiskering).
  f. Ray pattern (Virtual diagnostic of psoriasis).


Arthritis mutilans


Pencil in cup


Ray pattern

RX :

- Anti TNF (DOC).
- methotrexate.
- Anti IL-17 : Secukinumab.
- Anti IL-12/23 : Ustekinumab.
- PDE4 inhibitor : Apremilast.
- JAK 1/3 inhibitor : Tofacitinib.

Extra articular manifestations :

	lung	Heart	Eye	Kidney
Ankylosing spondylitis	B/L upper lobe fibrosis.	AR	4A uveitis.	2° IgA nephropathy.
Reactive arthritis	-	AR with conduction abnormality.	4A uveitis.	2° IgA nephropathy.
Psoriatic arthritis	-	Rare	B/L chronic Posterior uveitis.	2° IgA nephropathy.

ARRHYTHMIAS

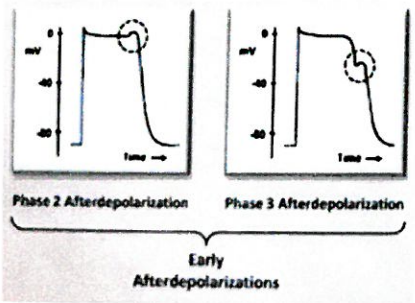
Mechanism of arrhythmias

00:00:30

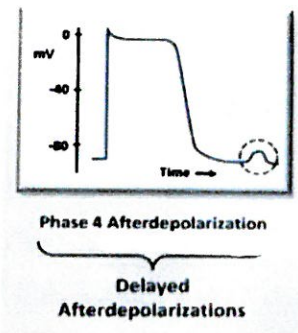
mechanisms of arrhythmias

- Automaticity
- Triggered activity
- Re-entry

Automaticity		Triggered activity		Re-entry
Enhanced normal automaticity	Sinus tachycardia	Initiated by after depolarisation upon the previous action potential		Majority of clinically relevant tachyarrhythmias
Abnormal automaticity	• Left atrial rhythms • Junctional rhythms • Atrial tachycardia • Digitoxicity • Accelerated Idioventricular Rhythm (AIVR) • Parasystole	Early after depolarisation (EAD)	Long QT syndrome (LQT)	• Sino Atrial Re-entry Tachycardia (SART) • Inter Atrial Re-entry Tachycardia (IART) • AV Nodal Re-entry Tachycardia (AVNRT) • Atrio Ventricular re-entry Tachycardia (AVRT) • Atrial Fibrillation (AF)/ atrial flutter • Brugada • Most Ventricular Tachycardias (VT) • Ventricular Fibrillation (VF)
		Delayed after depolarisation (DAD)	• Catecholaminergic polymorphic ventricular tachycardia (CPVT) • Right ventricular outflow tract VT (RVOT VT) • Left ventricular outflow tract VT (LVOT VT)	
Automatic tachycardia has a gradual onset and offset.		-		Maximum benefit with electrical cardioversion
Least benefit with electrical cardioversion				



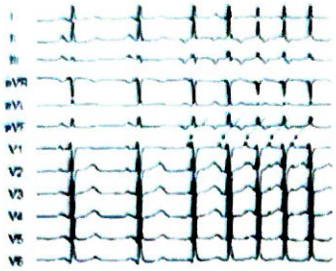
Early after depolarisations



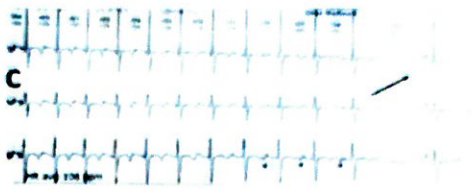
Delayed after depolarisations

Note :

- Atrial tachycardia : All 3 mechanisms.
- Polymorphic VT : Starts as triggered activity → maintained by re-entry.



Warm up phenomenon : QRS duration keeps on ↓, tachycardia picks up pace.



Cool down phenomenon : Tachycardia slows down as it ends.

Shown by automatic arrhythmias.

Re-entry tachycardias :

Short RP tachycardia	Long RP tachycardia
RP < PR	RP > PR
• Typical AVNRT • Typical AVRT	• Atypical AVNRT • Antidromic AVRT • Permanent Junctional Reciprocating Tachycardia (PJRT) • Atrial tachycardia • Sinus tachycardia • SA nodal re-entry tachycardia

Cardiac channelopathies

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Brugada syndrome :

- Loss of function of SCN5A gene.
- Sodium channelopathy.
- Autosomal dominant.
- Males : Female → 8 : 1.
- Peak age : 40 years.
- South east Asian population.
- Events occur during sleep/rest.
- Characteristic arrhythmia : Polymorphic VT.