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**BMFS : Aplastic Anemia**

★ 4.7 | 12 Min

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**Myeloproliferative Neoplasms: PV**

Continue

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**Myeloproliferative Neoplasms: PMF & ET**

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RHUPUS

Rheumatoid Arthritis

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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 : and 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 reticulohistiocytosis

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
<p>↓</p> <p>Synovial hypertrophy</p> <p>↓</p> <p>Pannus</p> <p>↓</p> <p>marginal erosions</p>	<ul style="list-style-type: none"> • Non-inflammatory arthritis • Involves articular cartilage • X ray features : <ul style="list-style-type: none"> a. Loss of joint space. b. Subchondral sclerosis. c. Osteophytes.

Rheumatoid arthritis	Osteoarthritis
Joints involved	
5th MTP	PIP
MCP	DIP
Wrist	1st CMC
PIP	
CI-Ca	
TMJ	
Cricothytenoid	
Joints spared	
DIP	Wrist
1st CMC	MCP
1st MTP	
Lumbar, thoracic, sacral spine.	

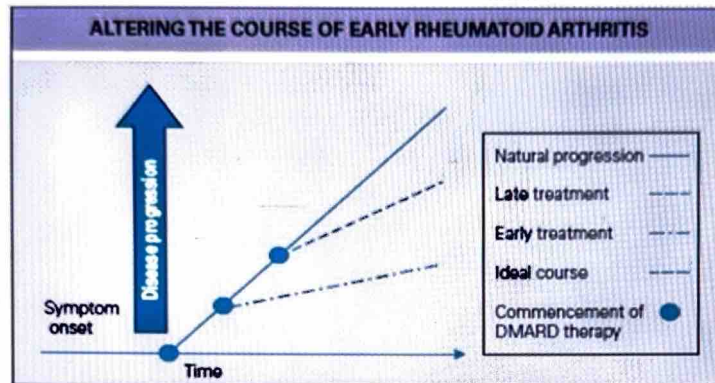
Note :

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

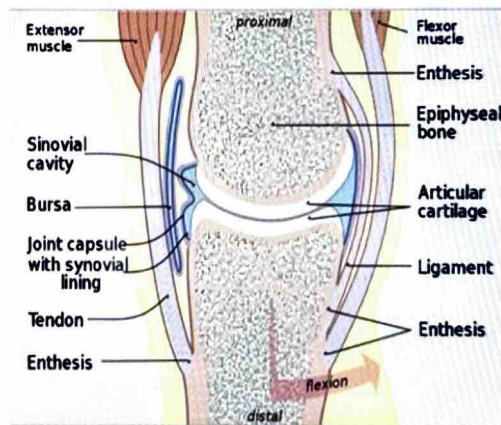
Disease progression :

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 stabilized 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

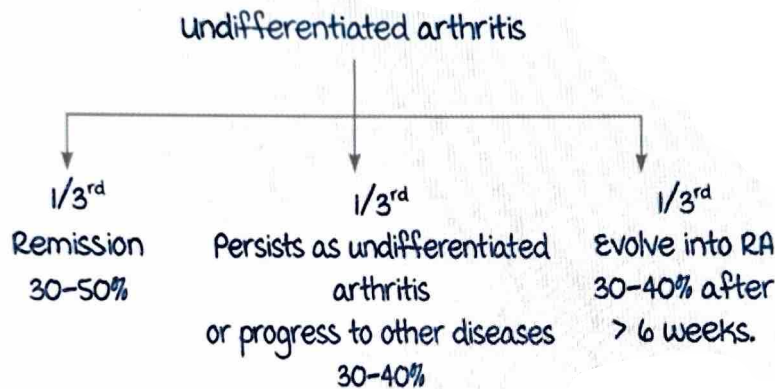
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Clinical features :

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

2 possibilities :

- Post viral arthritis (Parvo B19).
- 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.

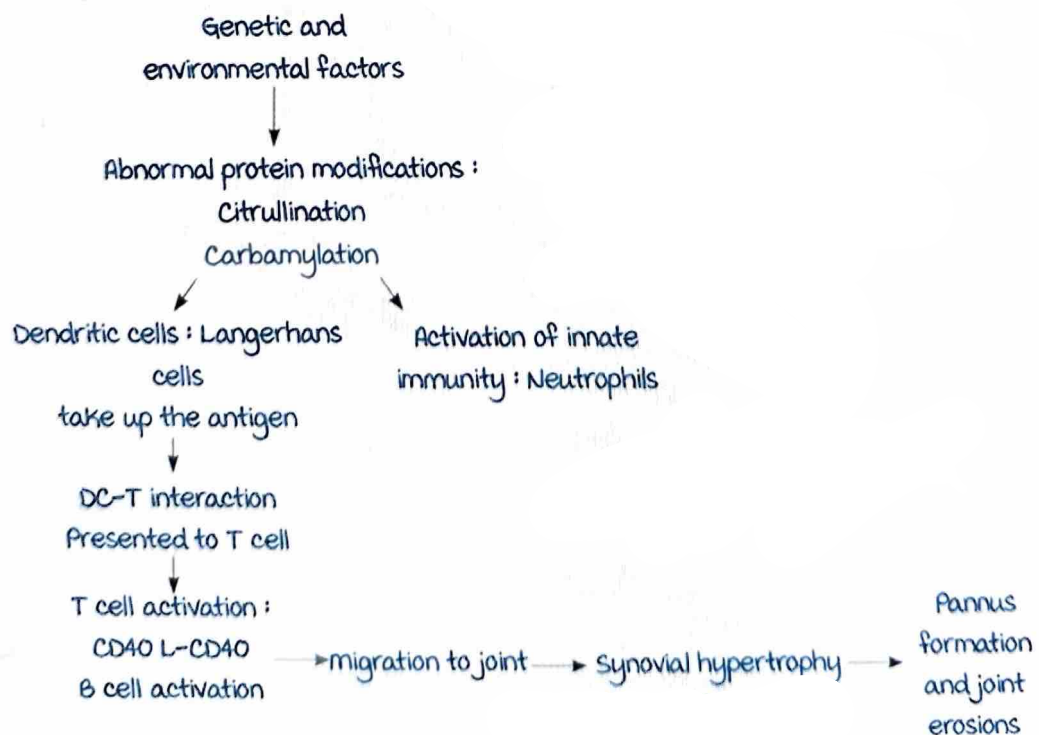
2. Anti CAR peptide (Anti carbamylated peptide) : To diagnose palindromic rheumatism.

3. Anti PADI antibodies.

4. Rheumatoid factor (RF) :

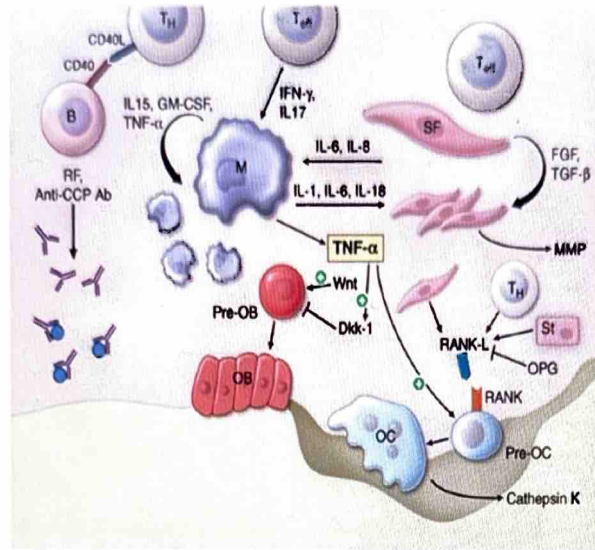
- IgM antibody against Fc portion of IgG vH3.
- Specificity : 75-80 % (Poor).
- Predicts prognosis, not used in relapse.
- RF is positive in other conditions :
 - a. Sjogren syndrome.
 - b. Cryoglobulinemia 2/3.
 - c. JIA (10 % : RF positive).
 - d. Infective endocarditis/leprosy/Parasitic infestation/PBC/Sarcoidosis/ HBV/HCV.

Pathogenesis :



T cells activation :

- TH1 produce Interferon $\gamma \rightarrow \uparrow$ macrophages : $\text{TNF-}\alpha \rightarrow$ Activation of osteoclasts (RANKL-RANK) and inhibition of osteoblasts (Dkk-1 pathway).
- TH17 : IL-17.

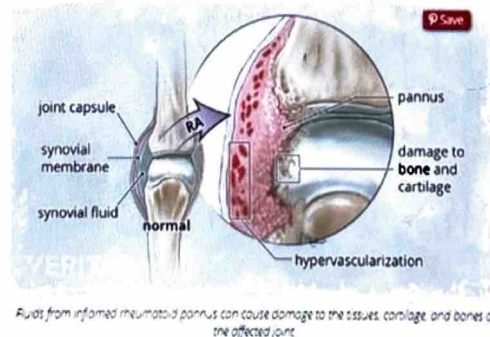


Rheumatological conditions producing osteoporosis :

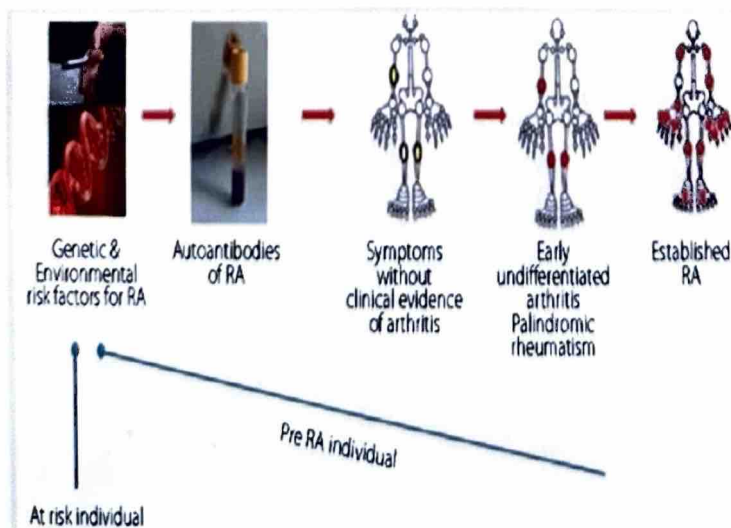
- Rheumatoid arthritis.
- Ankylosing spondylitis.

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^a

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^{g,h}	(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%) :

- Symmetrical small joint inflammatory polyarthritis.
- Elderly RA can mimic palindromic rheumatism.

Acute(10-15 %) :

Explosive painful small + Large polyarthritis in elderly.

Palindromic rheumatism :

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

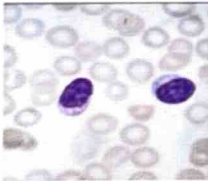
Elderly RA :

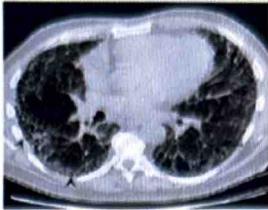
- Can mimic PMR.
- Acute explosive polyarthritis.
- Arthritis robustus : Erosive arthritis but patient is unaware.

Deformities in RA :

Reversible 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 	<ul style="list-style-type: none"> • 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. • methotrexate : 10 % cases can have ↑ size of nodules.

<p>Ocular features</p>	<ul style="list-style-type: none"> • Keratoconjunctivitis sicca (a° 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.
<p>Neurological manifestations</p> 	<ul style="list-style-type: none"> • Acute quadripareisis : C1-C2 subluxation d/t erosion of odontoid process. • Entrapment neuropathy : Carpel tunnel syndrome (m/c). • Peripheral nervous system : Small fibre neuropathy. • CNS/brain parenchyma : Not involved.
<p>Hematological manifestations</p> 	<ul style="list-style-type: none"> • Anemia of chronic disease (m/c). • WBC count : Normal. • Thrombocytosis/a° ITP. • Rapidly progressive anemia : AIHA d/t warm antibody IgG. <p>Felty's syndrome :</p> <ul style="list-style-type: none"> • Rheumatoid arthritis + Neutropenia + Splenomegaly. • A/w : <ul style="list-style-type: none"> a. HLA DRB1-04. b. Long standing RA. c. RF positive. d. Nodules/deformities ++. e. Antibody against citrullinated histones. • Peripheral blood smear : Large granular lymphocytes (LGL Leukemia). • RA increases risk of diffuse large B-cell lymphoma (DLBCL).

<p>Pulmonary manifestations</p>	<p>Pleuritis +/- exudative pleural effusion (m/c) :</p> <ul style="list-style-type: none"> • u/L > B/L, lymphocytic/exudative (Lite's criteria). • Protein content > 4g/dL, low glucose < 30 g/dL, high LDH. <p>Interstitial lung disease (ILD) :</p> <ul style="list-style-type: none"> • 30 % patients. • males, smoker, RF/Anti CCP ++. • usual interstitial pneumonia (UIP) : <ul style="list-style-type: none"> a. Honey comb pattern. b. Cysts. c. Traction bronchiectasis. • Parenchymal destruction : Poor prognosis. • Screening : Pulmonary function tests, DLCO ↓, HRCT.  <p>Caplan's Syndrome :</p> <ul style="list-style-type: none"> • Nodules + Cavitation + Pneumoconiosis. • RF positive active synovitis. • Coal dust exposure. • D/D : <ul style="list-style-type: none"> a. Wegener's granulomatosis b. Silicosis
<p>CVS manifestations</p>	<ul style="list-style-type: none"> • m/c/c of death in RA : Acute coronary syndrome. • RA : MI equivalent (Accelerated atherosclerosis). • m/c cardiac manifestation : Pericarditis without tamponade. • m/c valvular heart disease : MR > AR. <p>Vasculitis in RA :</p> <p>Small vessel vasculitis :</p> <ul style="list-style-type: none"> • Immune complex mediated. • Leukocytoclastic vasculitis. • C/F : Purpura, urticaria. <p>medium vessel vasculitis :</p> <ul style="list-style-type: none"> • Long standing disease with RF +ve. • males, smoker. • ↓ Complement C3, C4. • C/F : Nodules, ulcers, gangrene. <p>mononeuritis multiplex</p> <p>Dangerous forms of vasculitis in RA (Indication for treatment with Rituximab) :</p> <ul style="list-style-type: none"> a. Digital gangrene. b. Intestinal infarcts. c. mononeuritis multiplex.

Renal manifestations	<ul style="list-style-type: none"> • Secondary amyloidosis. • membranous nephropathy.
Endocrine manifestations	Hypoandrogenism.
Skin manifestations	<ul style="list-style-type: none"> • Rheumatoid nodules. • Purpura. • Pyoderma gangrenosum.

