# Review Article – Pathogenesis of Rheumatoid Arthritis

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**Abstract—** Rheumatoid Arthritis,is a chronic inflammatory disease .Most common autoimmune disorder known to cause disability in less than 2 years.RA has unknown etiology.[1]It affects one percent of the word population.

The focus of the review is to understand pathogenesis of RA and throw light on all the chief pathways involved in the interplay causing the disease.

**Index Terms**— Pathogenesis, Rheumatoid, Arthritis , autoimmune disorder, etiology, cartilage erosion, synovitis, synovium, bone

## 1. INTRODUCTION

Rheumatoid Arthritis,is a chronic inflammatory disease .Most common autoimmune disorder known to cause disability in less than 2 years.RA has unknown etiology.[1]It affects one percent of the word population.The first structure to get affected is the synovial membrane of the joints causing synovitis.[2-3]After synovium is affected subsequently cartilage erosion follows and then finally bone is eroded.RA is a scavenger of synovium ,cartilage and bone.RA is characterized by articular inflammation and systemic inflammation both .Multiple organs get affected so comorbid conditions are common in RA.Most common symptoms of RA are joint pain ,fatigue and loss of joint function .CVD and atherosclerosis are the most common comorbid conditions responsible for mortality in RA patients.[4-6]

RA is a autoimmune disease with inflammatory origin and systemic manifestations.Three etiological factors interplay Genetic,environmental,and immunological leading to structural joint damage.The disease has socio-economic and emotional burden .The damage is irreversible ,so a cause of depression in the sufferers.[7]

**The diagnosis of RA** rests on clinical criteria .It is judged by physical examination findings.The classification criteria published in 1987 by the American College of Rheumatology (ACR) is used primarily to diagnose RA.The score of 4 out of 7 criteria is considered diagnostic of RA.Its a progressive disease with bilateral involvement.[8-9]

**Laboratory markers of consideration** are RF ( a high affinity autoantibody directed against the Fc portion of immunoglobulins),ACPA( Anti citrullinated protein antibody) .These 2 are markers of autoimmune dysfunction.Markers of inflammation are ESR and CRP.In the 2010 RA classification criteria ,a score of 6 out of 10 was considered indicative of RA and hence set on treatment regimen.These criteria help in early diagnosis of RA and are a useful tool to set the patient on RA treatment as early as possible and slow down the progression of the disease.[10]

**Epidemiology**-In the global scenario, RA world wide prevalence is 1 percent .Its more common in women because of the emotional labile nature of them.Regional and geographic variability of case prevalence indicates genetic factors contribute to RA.[11]

**Pathophysiology**-Environmental triggers in genetic susceptible patients result in RA.Increased incidence of RA in infertile women and in immediate postpartum period of after first pregnancy indicate role of female hormones in the interplay of pathogenesis.Infectious triggers of consideration are viral infections,EBV ,Parvovirus,Bacterial infections Proteus and Mycoplasma.Heat shock proteins create immune complexes that triggers RF .Gastrointestinal bacteria also trigger autoantibody production .Porphyromonasgingivalis causative organism for

periodontal disease and smokers are also prone to have RA.[12-14]

Genes HLA –DRB1 are linked to RA susceptibility .If patients with these genes are smokers it further aggravates the risk of RA.This gene affects disease susceptibility, disease severity and production of TNF.[15]

The cardinal features of RA synovial thickening, joint swelling and bone erosions underline the inflammatory and autoimmune processes.Genetic and environmental factors together cause self proteincitrullination early in the disease process.[16]

The end result of pathophysiology of RA is synovial hyperplasia,cartilage damage and bone erosions .Most of the patients are affected within one year of diagnosis.The aim of designed management plan should be to prevent bony erosions.Pain and immobility signals joint damage..Most of the patients are work disabled in 2 yrs hence earlt aggressive treatment is indicated as soon as RA is diagnosed.Disease severity can be scaled by pain score and joint mobility.[17-18] .(Fig 1,2,3)

**Fig. 1 Showing Disease Activity in the Joint**

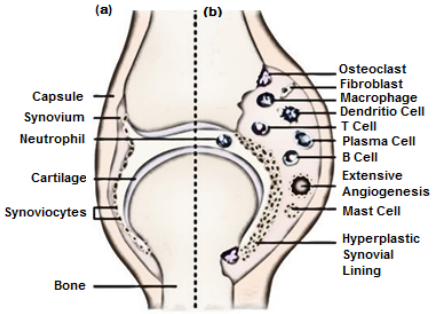


**Fig.2 Pathogenesis of RA**

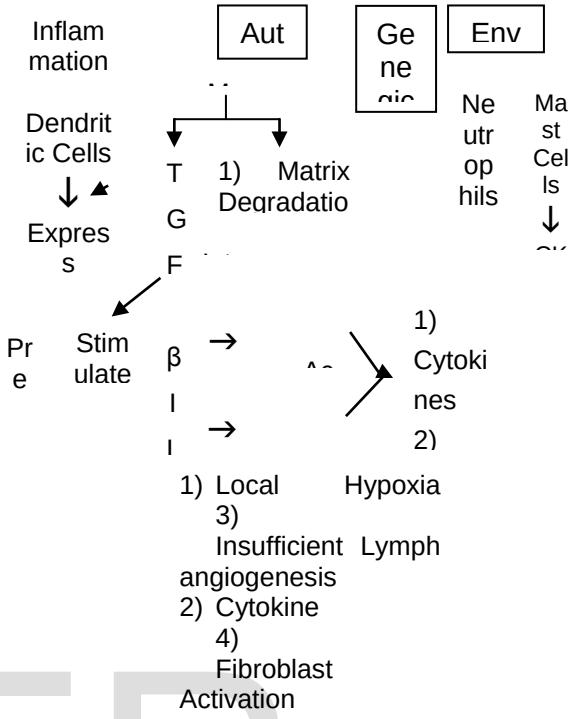


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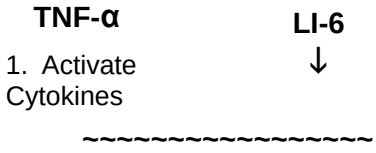
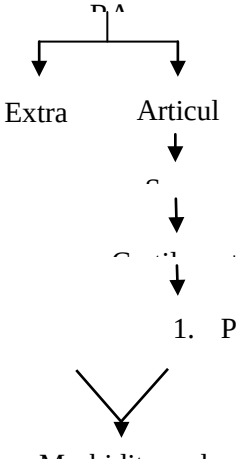
**Fig. 3 Prime Inflammatory Mediators & Their Role**




**Most common systemic manifestations in RA** are vasculitis,atherogenesis ,stroke ,osteoporosis,fractures,fatigue,depression ,stroke,neuropathy,pericarditis,myocardialinfarction,glomerulonephritis,Sjogrenssyndrome,metabolicsyndrome,Pleuritis,Felty'ssyndrome,amyloidosis ,rheumatoid nodules.[19](Fig-4)

Inflammatory mediators play vital role in systemic complications.These manifestations raise mortality in men more than women.Besides traditional risk factors involved in CVD in RA ,there are RA disease related factors also that play role in raised incidences of CVD.[20-21,27]

**Fig. 4 RA & MANIFESTATIONS**




The **prognosis of the disease** is affected by both severity of the disease and effectiveness of treatment.**Clinical remission** ,defined as absence of inflammatory signs and symptoms should be the aim of management plan of RA.Remission is monitored by low disease activity and also through monitoring of joint damage through MRI,Ultrasound .Radiological evidence of disease progression is a way to monitor both disease progression and effectiveness of treatment.[23]Disease activity is also scaled using various indices .These indices play vital role in office settings to guage the treatment effectiveness.[24]

Due consideration should also be made for Vitamin D deficiency in RA patients, since it's a key hormone responsible for immune regulation.[26, 28, 29]

**Poor prognostic factors are** –functional limitation, extraarticular disease, RF +,ACPA +,Bony erosions on X rays.[25]

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## 3. CONCLUSION

The focus of the review was to understand pathogenesis of RA and throw light on all the chief pathways involved in the interplay causing the disease.The review also considered the T Cell and B cell interaction in the mechanism.TNF alpha and IL-6 are chief inflammatory mediators in RA responsible for both articular and extraarticular manifestations in RA.

The review recommends early identification of the disease, before bone and joint damage becomes evident and this approach will further improvise management plans in RA.

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