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Hallmarks of rheumatoid arthritis are inflammation, altered immune response, and the Synovial hyperplasia. Although the cause of this disease remained elusive, considerable advances have been made in characterization of certain factors involved in its pathogenesis.

The association of HLA-DR4 or other HLA-DRB1 alleles has now been established in nearly every population. The presence and gene dosage of HLA-DRB1 alleles affect the course and outcome of disease. Family studies are making it increasingly clear that other genes are involved in the pathogenesis of rheumatoid arthritis, both within and outside of the major histocompatibility complex with the TNF locus showing perhaps the most promise as a second MHC influence.

T cells play a critical role in rheumatoid arthritis. They are probably continuously involved in pathogenesis, from the initiation to the chronic stage. The part they play in rheumatoid arthritis is closely linked to the roles of macrophages and mesenchymal cells. Recent studies come to the conclusion that therapeutic approaches should target the pannus fibroblast rather then T cells themselves. It could be hypothesized that aggressively growing Synovial fibroblasts not only mediate matrix destruction, but also induce the migration of CD4+ T cell to the joints.

Infectious agents have been repeatedly suspected to be the cause or at least a major factor in the pathogenesis of rheumatoid arthritis. Two possible infection-related pathways were described: persist infection versus infection-triggered induction of autoimmunity. Human T cell lymphotrophic virus type –1 is a prototype for an arthritis-inducing retrovirus, but definite evidence is lacking that known retrovirus are involved in the pathogenesis of RA. Bacteria have been involved in the etiology of rheumatoid arthritis based on different lines of evidence, including the efficacy of some antimicrobial agents in rheumatoid arthritis, alternations in the intestinal flora of RA patients, and the detection of humoral and cellular immune responses against certain bacteria in RA. Proteus mirabilis, Chlamydia, Samonella and mycobacterium tuberculosis had been implicated. Although there was ample indirect evidence for involvement of infections in the pathogenesis of this autoimmune disease, direct proof is still missing.

Lastly, the role of neuropeptide and hormone in animal model and RA were discussed. In RA, a first report on the circadian relationship between interleukin-6 and the hypothalamus-pituitary-adrenal axis hormones, demonstrates that the overall activity of this axis remains inappropriately normal and appears insufficient to inhibit inflammation in untreated patients.