

bone preventing bone ends being crushed. Joint (articular) cavity that contains synovial fluid. The joint cavity is enclosed by a two-layered articular capsule, the tough external fibrous layer is composed of dense irregular connective tissue that is continuous with the periosteum of the articular bones, this layer strengthens the joint so that the bones are not pulled apart, the inner layer of the joint capsule is a synovial membrane composed of loose connective tissue, besides lining the fibrous layer internally it covers all internal joint surfaces that are not hyaline cartilage, the synovial membranes function is to make synovial fluid. Synovial fluid occupies all free spaces within the joint capsule, this fluid is derived largely by filtration from blood flowing through the capillaries in the synovial membrane, synovial fluid reduces friction between the cartilages, the fluid is forced from the cartilages when a joint is compressed then as pressure on the joint is relieved synovial fluid seeps back into the articular cartilages, this process is termed weeping lubrication, and lubricates the free surfaces of the cartilages and nourishes their cells, synovial fluid also contains phagocytic cells that rid the joint cavity of microbes and cellular debris. Synovial joints are reinforced and strengthened by ligaments. Synovial joints are richly supplied with sensory nerve fibres that innervate the capsule. The inner layer of the synovial membrane is rich with supporting capillaries and is composed of; macrophage like synoviocytes (type A) which have migrated from the bone marrow, and fibroblast like synoviocytes (type B) which secrete hyaluronic acid and glycosaminoglycans and lubricin. The external layer is rich with lymphatic and blood vessels and is composed of macrophages and fibroblasts. Histologically, the intimal layer appears much rougher than a normal epithelial lining layer.

Pathogenesis

RA disease pathway; autoimmune component. The immune system attacks the joint lining, leading to inflammation of the joint lining. Untreated inflammation leads to joint damage, joints become hot, red, swollen and stiff, ultimately joint damage cannot be repaired.

80% of patients have serum immunoglobulin M (IgM) (and less frequently IgA) autoantibodies that bind to the Fc portions of their own self IgG. These autoantibodies are called rheumatoid factors. They may form complexes with self IgG that deposit in joints and other tissue, leading to inflammations and tissue damage. The incidence of rheumatoid factor increases with duration of disease. 20% of RA patients remain negative for rheumatoid factor- sero-negative RA. Rheumatoid factor can be found in joints affected by RA and can be detected before RA presents clinically.

Many RA patients produce antibodies against cyclic citrullinated peptides (CCPs) which may contribute to joint lesions. CCPs are derived from proteins in which arginine residues are converted to citrulline residues posttranslationally. In RA, antibodies to citrullinated fibrinogen, type II collagen, alpha-enolase, and vimentin form immune complexes that deposit in the joints. These antibodies are a diagnostic marker for the disease.

The strongest genetic association with seropositive RA is within the human leukocyte antigen (HLA) region. In particular, HLA-DRB1 molecules sharing a common sequence, R(Q)K(R)RAA, the so called shared epitope, are associated with both susceptibility and severity of RA, with some substitutions in the shared epitope conferring protection from RA, and some leading to severe RA. alleles encoding HLA-DRB1-SE molecules increase the risk