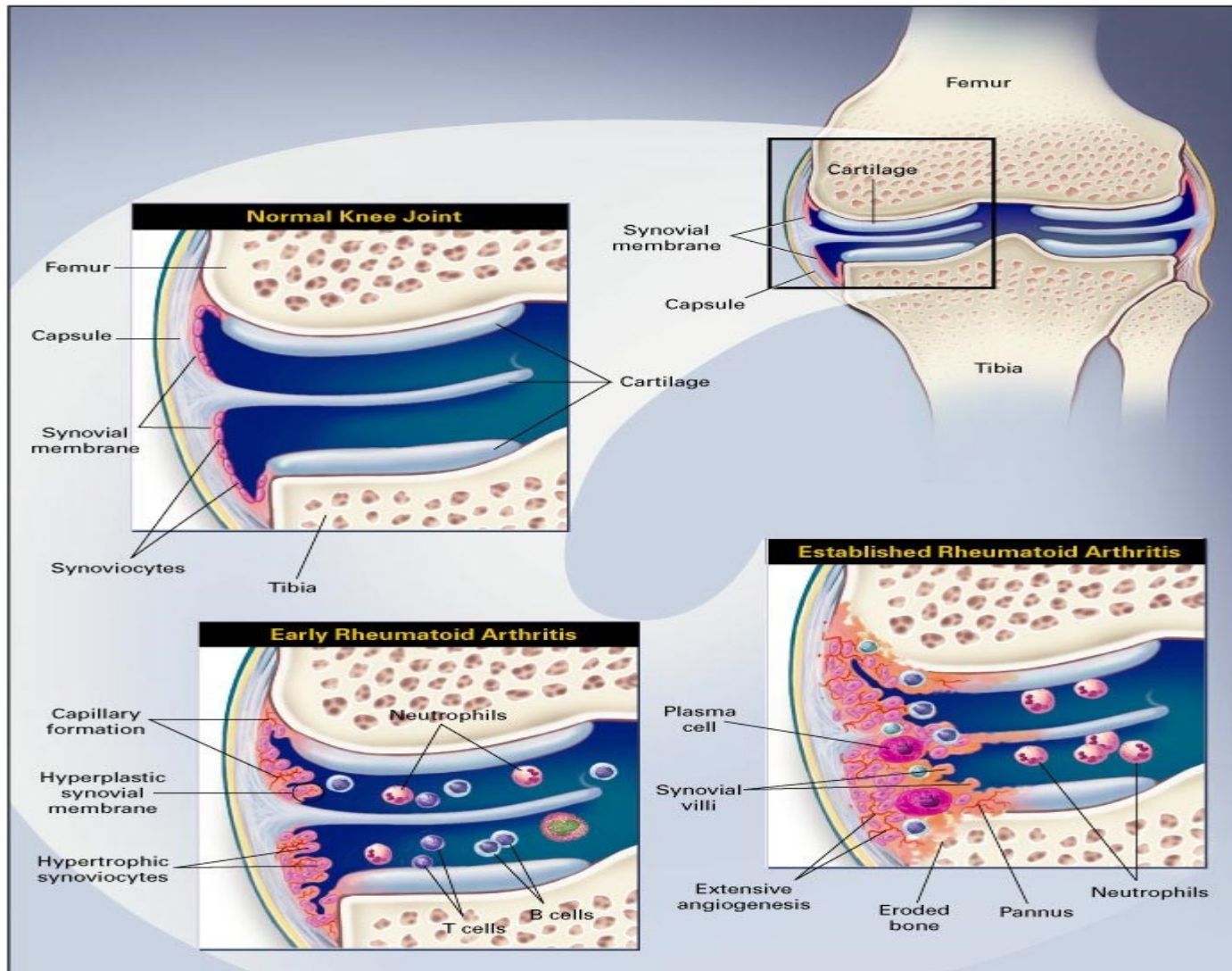


Rheumatoid Arthritis

RHEUMATOID ARTHRITIS

- ❑ RA is the most common autoimmune disease
- ❑ Affects approximately 1% of the world's population
- ❑ In patients <60 years, there is 3-5:1 female predominance
- ❑ Pathogenesis –
 - ❑ Autoimmune inflammatory destruction of the synovium (membrane that covers joints)
 - ❑ Can erode into bone and cartilage
- ❑ Symptoms
 - ❑ Morning stiffness around joints
 - ❑ Sometimes, subcutaneous nodules over bony prominences
- ❑ It is important to diagnose rheumatoid arthritis in the early stage as only an early diagnosis and its immediate treatment inhibits irreversible damages of the progressive disease.

PATHOGENESIS OF RHEUMATOID ARTHRITIS



RA – Laboratory tests

- ESR & CRP
- RF (usually IgM)
- ANA
- Anti-CCP (cyclic citrullinated peptide)

RHEUMATOID FACTOR (RF)

- ❑ RF is an **antibody** (auto-antibody) against the Fc portion of Immunoglobulin G (IgG), which itself is an antibody
- ❑ RF and IgG join to form immune complexes which contribute to the disease process
- ❑ Antibody prevalence
 - About **80% of people** with rheumatoid arthritis have detectable rheumatoid factor
 - In combination with signs and symptoms, RF can play a role in both diagnosis and disease prognosis

RHEUMATOID FACTOR (RF)

Specificity

- Specificity of RF is **low**
- RF are present **in patients with other autoimmune and infectious diseases**, and even in a noticeable proportion of normal healthy subjects, particularly in ageing individuals
- RF can also be detected at high titers in most patients with primary Sjögren's syndrome and may also be elevated in chronic hepatitis, any chronic viral infection, leukemia, dermatomyositis, infectious mononucleosis, systemic sclerosis and systemic lupus erythematosus

Antibody Isotypes – Predominantly IgM; sometimes IgA

RA cannot be definitively diagnosed by RF alone

ANTI CCP (CYCLIC CITRULLINATED PEPTIDE)

- ❑ Citrullination (deimination-amino acid arginine in a protein is converted to citrulline) of proteins is a chemical reaction which occurs when inflammatory cells release enzymes in local tissues
- ❑ Patients with RA form antibodies to citrullinated peptides
- ❑ The exact significance of citrullated peptides and antibodies to these proteins is uncertain, but evidence suggests that these antibodies may contribute to the pathogenesis of RA.

ANTI CCP (CYCLIC CITRULLINATED PEPTIDE)

□ Sensitivity and Specificity

- Studies have suggested similar sensitivities of anti-CCP and RF for RA (70- 80%). Some patients who have a negative RF test may be anti-CCP positive
- Anti-CCP appears to be **more specific for RA (approximately 98%) compared to RF**. Thus, anti-CCP results in fewer false positives compared to RF testing

□ Correlation with disease activity

- The presence of anti-CCP is associated with significantly higher levels of erosions compared to rheumatoid factor and other parameters. Anti-CCP is an independent predictor of radiological damage and progression.

Anti - CCP Ab : Death of the RF ??

- It is an enzyme-linked immunosorbent assay (ELISA) that tests for the presence of antibodies that recognize specific antigens containing citrulline

| | Specificity | Sensitivity |
|-----------------------------|--------------------|--------------------|
| Anti - CCP Antibody Test | 95% | 67% |
| Rheumatoid Factor (RF) Test | 85% | 69% |

Diagnostic Utility :

- Part of ACR- EULAR classification criteria for RA
- Positive in 40% patients who test negative for RF

Anti - CCP Ab : Death of the RF ??

Prediction of disease onset :

- antedates clinical arthritis by an average of 5 years
- Predict the eventual development into RA when found in undifferentiated arthritis (UA)

Prognostic Marker :

- Useful for monitoring treatment response
- In established disease, presence of anti- CCP is associated with more severe clinical outcomes, higher disease activity and worse radiographic progression