Rheumatoid Arthritis

- It is a chronic (> 3 months) idiopathic systemic inflammatory autoimmune disorder that primarily affects the joints
- It occurs more in women
- Risk factors
    - Females
    - Genetics : HLA-DR4 and HLA-DR1
    - Smoking and alcohol
    - Hormones : premenopausal women are at highest risk and those using OCPs
    - Infections : EBV / parvovirus
    - Urban environment and socioeconomic status
    - Obesity
    - Family History
    - Age : 80% of cases are between 35-50
- CD4+ T cells migrate to synovial joints and release cytokines like IL1, IL6, TNFa, and GM-CSF causing inflammation
- Rheumatoid Factor
    - It is an IgM that binds to the Fc region of IgG and form complexes detected in serum
    - May take up to 2 years to become positive
    - It is not specific for rheumatoid arthritis and can be found in SLE, sjogren, sarcoidosis, malignancies and infections like endocarditis and HCV
    - Individuals with positive RF are more likely to develop extraarticular manifestations
    - High titers is indicative of a more aggressive disease but it is not used to monitor disease activity
    - anti-CCP (ACPA) is the most specific to RA : if positive with at least one swollen joint then that’s enough to diagnose
- Synovitis characterizes Rheumatoid Arthritis
- Articular Manifestations
    - Symmetrical polyarthritis starting with small joints of hands and feet
    - Most commonly affected joints are MCPs, PIPs, wrist joints, and the cervical spine (atlantoaxial)
    - The DIPs, rest of axial skeleton abdominal first carpometacarpal joints are usually spared
    - There is prolonged morning stiffness relieved by warm water and movement
    - Painful handshake is an early sign of arthritis
- Joint deformities
    - Ulnar deviation and volar subluxation at MCP joints
    - Swan neck : flexion contracture of DIP & hyperextended PIP
    - Boutonnière : flexion contracture of PIP & hyperextended DIP
    - Piano key sign : dorsal subluxation of the ulna
    - Carpal Tunnel Syndrome
    - Baker cyst : collection of synovial fluid in the popliteal fossa (it’s rupture mimics

DVT)
    - Hammer and claw toes
    - Atlantoaxial subluxation : early morning neck pain and stiffness / cervical radiculopathy / high risk for airway compression during surgeries
- Extraarticular Manifestations (more common in men)
    - Constitutional symptoms like fever and weight loss
    - Most common extraarticular manifestation is rheumatoid nodules (and secondary sjogren manifestations)
    - Rheumatoid Nodules : fibrinoid granulomatous necrosis
        - Associated with RF positivity and tobacco use
        - May occur as a result of small vessel vasculitis
        - Can be on skin, pleura, pericardium or sclera
        - Methotrexate can worsen them
        - The pulmonary nodules may be accompanied by fibrosis and pneumoconiosis (caplan syndrome)
    - Eyes : keratoconjunctivitis with sjogren / scleritis is the most aggressive / episcleritis / keratitis
    - Lung : nodules / ILD / exudative pleural effusion / pericarditis / pleuritis
    - Vascular : Raynaud
    - Rheumatoid small vessel vasculitis RSVV
        - Splinter hemorrhages
        - Periungual infarcts
        - Leg ulcers
        - Digital gangrene
        - These occur mostly in the lower limbs and where the skin is exposed to pressure like fingertips
    - Heart : pericarditis / myocarditis / increased risk for MI and strokes
    - Hematologic : anemia of chronic disease correlating with disease activity / non hodgkin lymphomas / splenomegaly
    - CNS : mononeuritis multicomplex (uncommon) due to RSVV of the vasa vasorum
    - Amyloidosis
    - Renal manifestations are rare
- Felty syndrome
    - SANTA : splenomegaly / anemia / neutropenia / thrombocytopenia / arthritis
    - Fever and Chest pain can be present
    - Positive RF and anti-CCP
    - Treatment : MTX / antibiotics due to pancytopenia / splenectomy / granulocyte-colony stimulating factor
- Diagnosis based on
    - Joint involvement (more in smaller joints) occurring ≥ 6 weeks
    - High ESR and CRP
    - ANA is elevated in 30-50% of cases

    - Positive RF and anti-CCP
    - Joints Xray : marginal erosions are the hallmark of RA most commonly seen in carpal bones, ulnar styloid, MCPs, and MTPs / joint space narrowing / osteopenia / subchondral cysts
- 30% of patients with RA are negative for ACPA and RF : Seronegative Rheumatoid Arthritis
- Treatment
    - When the damage begins early start aggressive treatment early
    - Temporary anti Inflammatories : NSAIDs and Glucocorticoids
    - Heat or cold packs for pain management
    - All patients regarding of baseline disease activity or duration should receive a conventional DMARD : MTX / Hydroxychloroquine / Sulfasalazine / Leflunomide / Azathioprine
    - Biologic DMARDs : TNF-α inhibitors like infliximab and etanercept / rituximab (anti-CD20) / anakinra (IL-1 receptor antagonist)
        - Side effects : infections / allergic reactions / lymphomas / hepatotoxicity / demyelinating disorders / Vasculitis / GI perforation
    - Double or triple therapy can be used
    - Surgical Management : Total joint replacement or Synovectomy
- MTX is the drug of choice for RA
    - Side effects : liver toxicity / teratogenicity / stomatitis / pancytopenia / ILD
    - Administer folic acid to prevent side effects
    - Avoid administering NSAIDs on the same day as MTX
    - Contraindicated in hepatitis B, alcoholic hepatitis and liver failure
    - Avoid combining it with azathioprine
- Compared to the general population women with RA lose 10 years while men lose 4 years of life