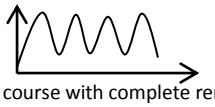
Rheumatoid Arthritis (RA)

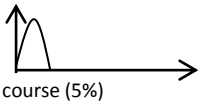
- Epidemiology
  - Adult females, 1% of the world's population, rare in AA, higher in American Indians
- Mechanism
  - 1° Synovial 2° Extra-Articular Inflammation
    - Early: typical S/S of inflammation
    - Chronic: manifests uniquely with destructive changes (below) & pannus formation (inflammatory, vascularized, synovial hyperplasia that acts like a locally invasive tumor that erodes into bone, cartilage, ligament, and tendons), NB these findings are becoming less common b/c more effective medicines are being developed against B-Cells (Ag: CD-20), Macrophages (Cytokine: TNF, IL-1), T-Cells (?)
- S/S
  - Variable severity with some capable of performing activities of daily living (today b/c of new Tx) to some confined to a bed (20yrs ago)
  - Constitutional Symptoms
    - Morning Stiffness which improves as the day progresses
    - General Constitutional Symptoms: fatigue, low grade fever, weight loss, anorexia
  - Skeletal Involvement
    - Arthritis: Gradual Onset (wks-mos, however 15% can present acutely) Chronic (however 10% can have just one attack) Symmetrical Polyarthritis (appendicular sparing axial except cervical, begins at a few joints and then evolves in an additive fashion) joints are inflamed and feel warm/spongy/tender, etc
      - Hand: NO DIP (rare unless severe) but instead Carpal/MCP/PIP w/ ulnar deviation at MCP, Swan Neck Deformity (flexed DIP, hyperextended PIP), Boutenniere Deformity (hyperextended DIP, flexed PIP)
      - Cervical Spine: 60% have atlantoaxial subluxation (surgical emergency requiring decompression and fusion), 20% have subaxial subluxation, 20% have basilar invagination into Foramen Magnum, p/w neck pain, occipital HA, paresthesia, etc, life threatening problem, NB remainder of the spine is spared
      - Other: Foot, Ankle, Knee, Hips, Elbows, Shoulders
  - Cardiac Involvement
    - Pericardial Effusions (50%)
    - M/AR (35%)
    - Conduction Abnormalities 2/2 Rheumatic Nodules in the Heart (very rare)
  - Pleural Involvement
    - Interstitial Fibrosis (50%)
    - Changes 2/2 Tx (gold, methotrexate, et al) (25%)
    - Pleural Effusions (characteristic low glucose and low complement) (25%)
    - Lung Rheumatic Nodules which can become infected and cavitate often mistaken for cancer (rare)
  - CNS Involvement
    - "Mononeuritic Multiplex"
  - Heme Involvement
    - AOCD
    - Thrombocytosis
    - Vasculitis
    - Felty's Syndrome (1%, SM resulting in pancytopenia, high RF titers, extra-articular disease is common, occurs late in the disease, + Rheumatic Nodules, + Sjogren's, serious infections, leg ulcers, mononeuritis multiplex, +ANCA)
    - Increased NH Lymphoma (esp if taking methotrexate) and Lung Cancer
    - Decreased Colorectal and Stomach Cancer 2/2 NSAID use
    - Large Granular Lymphocytes (LGLs) – unique lymphocytes which often clonally proliferates resulting in LGL Syndrome and neutropenia and splenomegaly (Psuedo-Felty Syndrome)
  - Ocular Involvement
    - Dry Eyes
    - Scleromalacia (softening of sclera which can perforate and lead to blindness)
    - Episcleritis/Scleritis
  - GI Involvement
    - Sjogren's like symptoms
    - Esophageal dysmotility
    - Liver Infiltration w/ Nodules
  - Cutaneous Involvement
    - Subcutaneous Rheumatic Nodules (30%) on extensor surfaces of joint (esp elbow, sacrum, occiput), bony prominences, and in viscera, nodules portend worse prognosis
    - Thin/Atrophic Skin
    - Ulcerations of fingers
    - Dry MM
    - Raynaud's
  - Clinical Course

        - chronic undulating course with incomplete remissions (65%)



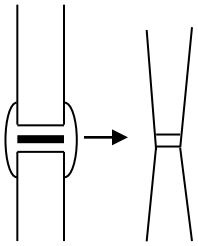
        - chronic undulating course with complete remissions (20%)

        - one acute episode that subsides and pt never has an attack again (10%)



        - chronic progressive course (5%)

        - 50% stop working w/in 10yrs of disease onset
        - 80% become disabled w/in 20yrs of disease onset
        - 3-18yr decreased life expectancy primarily due to premature vascular disease including MI (leading cause of death) and stroke, infection, and GI Bleed b/c of prior heavy NSAID use
- Diagnosis
    - Lab
        - Rheumatoid Factor (RF)
            - RF is an IgM, G, A, et al against IgG (its role in the pathogenesis of RA is unclear)
            - Sensitivity (70%)
                - lower sensitivity earlier in the disease
                - higher sensitivity later in the disease
                - thus the strength of titer correlates with severity of disease
            - Specific (80%)
                - positive titers seen in 3% of the general healthy population
                - rheumatologic disorders (Sjogren's 90%, Cryo 90%, SLE 20%)
                - lung dz (ILD)
                - infections (HCV 70%, TB, endocarditis, syphilis, any acute viral infection)
                - miscellaneous (sarcoid, cancer esp L/L, old women)
        - Anti-Cyclic Citrullinated Peptide (anti-CCP)
            - Anti-CCP is an IgG against synovial membrane peptides that have become citrullinated
            - Sensitivity (40%)
            - Specificity (~100%) NB this test should be a reflex test to a + RF to confirm a diagnosis of RA
        - Inflammatory Markers: ESR, CRP, Increased Globulins
        - NB these proteins are seen in serum of RA pts sometimes 10yrs!!! before RA becomes clinically apparent suggesting subclinical inflammation
    - Inflammatory Synovial Fluid Analysis
    - Imaging
        - X-Ray
            - Loss of Juxtaarticular Bone Mass aka Periarticular Osteopenia esp at finger joints
            - Symmetric Narrowing of the Joint Space 2/2 thinning of the articular cartilage
            - Fusiform periarticular inflammation
        - MRI/US
            - able to pick up erosions in pts with normal x-ray, this is important b/c more aggressive treatment is warranted when damage is present, however MRI is still too expensive to warrant to common use
    - 1987 ACR $\geq$4/7 Criteria for RA – really used to define homogenous cohorts for research purposes not for clinical dx
        - Morning Join Stiffness $\geq$6wks for $\geq$1hr
        - Poly ($\geq$3 joints) Arthritis $\geq$6wks
        - Symmetric Arthritis $\geq$6wks (does not have to be actually symmetric just roughly bilateral)
        - Hand Arthritis $\geq$6wks
        - SC Nodules
        - +RF
        - Rheumatoid Radiographic Changes of Hands/Wrist
        - Thinning of cartilage resulting in decreased joint space
        - b/c of the synovitis there is loss of corners of bones



- Poor Prognostic Indicators
  - High RF/anti-CCP Titers
  - The More Joints and the more erosive they are
  - The More Severe the Inflammation (increased APR)
  - SC Nodules
  - Lower Socioeconomic/Educational Level
  - Decreased Functional Status
  - CV Co-Morbidities
  - Increased Age
  - Extra-Articular Dz

- Treatment
  - Short Term Symptomatic Treatment for pain
    - 1° NSAIDs/Tylenol (do not stop progression they just provide palliation)
    - 2° Low Dose Corticosteroids (good for bridging while DMARDs take effect, unlike NSAIDs steroids have been shown to slow progression)
  - Long Term Disease Modifying Anti-Rheumatic Drugs (DMARDs) (50% respond to MTX, 40% respond to MTX + anti-TNF, 10% need more, begin as soon as diagnosis is made)
    - First Line
      - Slow Disease: hydroxychloroquine (Plaquenil) (SEs: retinopathy therefore get yearly eye exam) or sulfasalizine (Azulfidine) (SEs: myelosuppression, discoloration of body fluids, hepatitis, reversible oligospermia)
      - Aggressive Disease: methotrexate or leflunomide (Arava) (SEs: similar to MTX)
    - If refractory to above
      - Anti-TNF: many (refer)
      - Anti-IL-1: anakinra (Kineret) (NB does not really work)
      - cyclosporine
    - If refractory to above
      - Anti-T-Cell: abatacept (Orencia)
      - Anti-C-Cell: rituximab (Rituxan)
    - If refractory to above
      - gold salts (SEs: myelosuppression and proteinuria)
      - D-penicillamine (SEs: myelosuppression and proteinuria)
      - AZA/6MP
  - Exercise to maintain range of motion
  - Joint Replacement / Fusion Surgery