Rheumatoid Arthritis

Rheumatoid Arthritis

- Multisystem disease of unknown etiology
- Persistent Inflammatory synovitis of Peripheral joints in Symmetric distribution
- Variable course but potential for cartilage damage n bone erosions

Epidemiology

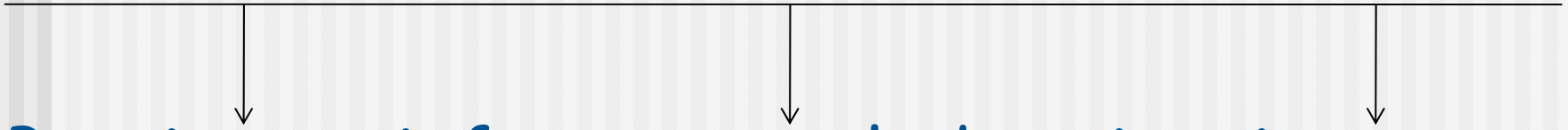
- Women : Men = 3 : 1
- Onset → 4th decade (35 – 50 yrs)

- Genetic pred. → in first-degree relatives n monozygotic twins
  role of HLA – DR 1, DR 4, DRB1 alleles

- ? Environ. Factors → Smoking, Urbanizations

Etio-pathogenesis

- Infectious agent in genetically susceptible host
- ? Mycoplasma ? EBV / CMV / Rubella / Parvo



- Persistent infxn Or retention of microbial prodcts
- revealed antigenic peptides (collagen, heat-shock protein
- cross-reactv

Etio-pathogenesis

- RA synovitis→ Hyperplasia (Pannus) + Microvascular Injury (CD4+)
  (edema, thrombosis, neovascularisation)

- IL-1, TNF-œ & IL-6 (also involved in systemic manifestations n potential anti-cytokine therapy)

- Ac. Inflam. process in synovial fluid overriding Chr. Inflam. in synovial tissue

Clinical Manifestations

- Non-sp. gradual onset (fatigue, anorexia) in 2/3rd of patients until overt synovitis
- 10% have acute presentation with polyarthritis, fever, lymphadenopathy n splenomegaly

Clinical Manifestations

- Articular manifestations :

  (arthritis n deformities)
  - Inflam. Arthritis with Morning Stiffness
  - Symm. Pattern
  - Joint swelling→ ↑ synovial fluid, synovial hypertrophy, thickened joint capsule
  - PIP, MCP, Wrist joint
  - DIP rarely involved
  - Baker's cyst
  - Upper cervical spine (never Lumbar spine)

Clinical Manifestations

- Articular manifestations :

  (arthritis n deformities)

  - Z deformity→ radial deviation at Wrist
    + ulnar dev. at MCP
    + palmar subluxation at PIP
  - Swan neck defomity → hyperext at PIP
    + flexion at DIP
  - Boutonniere deformity → flxn cont at PIP
    + Ext at DIP

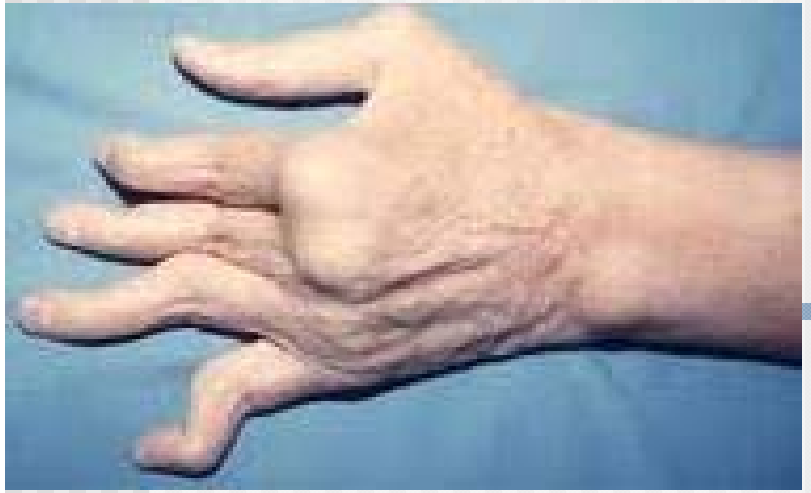
Clinical Manifestations

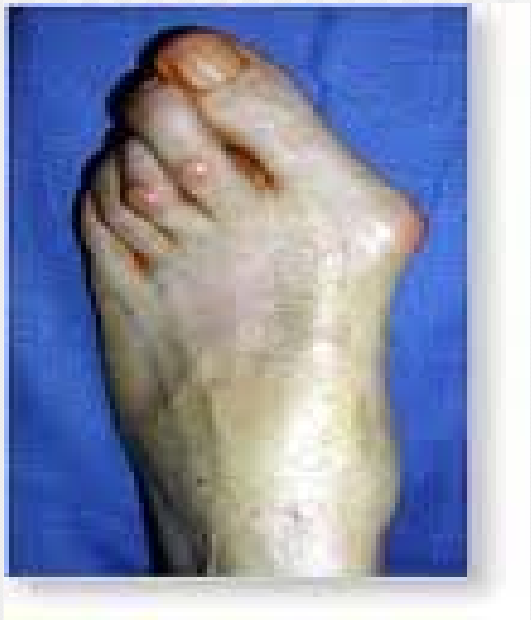
- Articular manifestations :

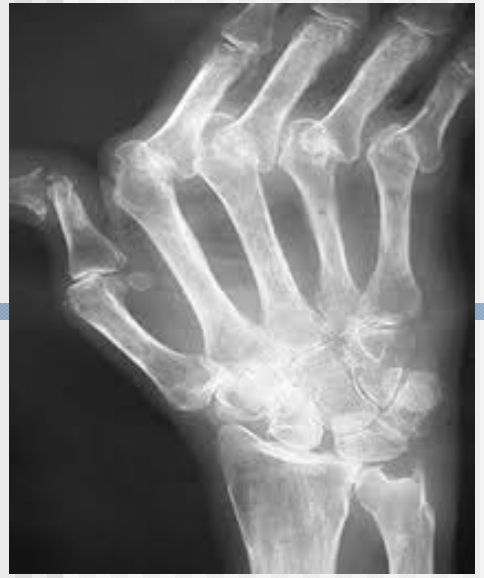
  (arthritis n deformities)

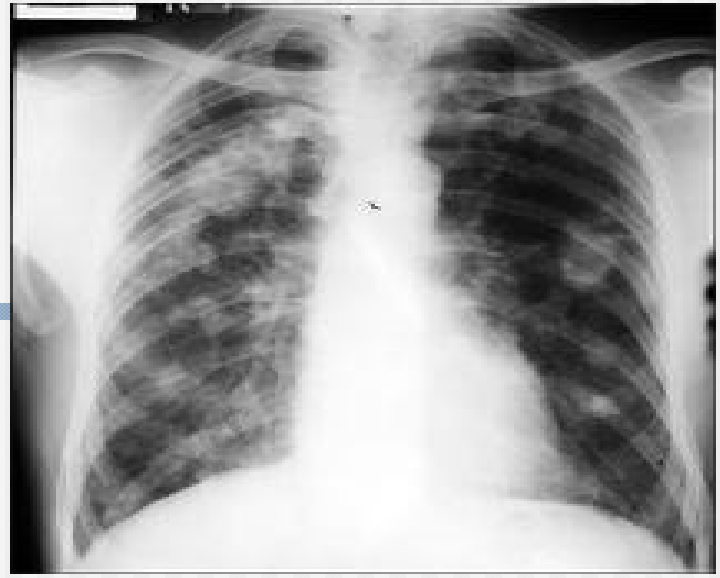
  - Hyperext at 1st (thumb) IP joint and Flexion at 1st MCP joint (loss of pinch)

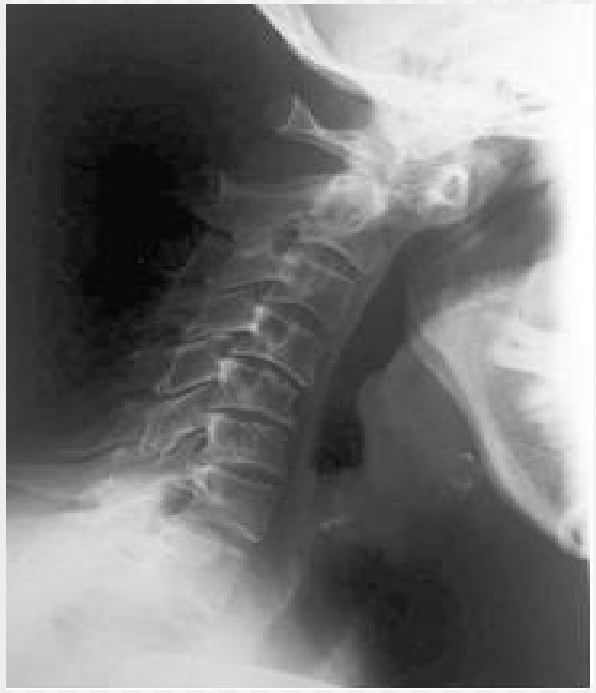
  - Foot deformities – hallux valgus
    - eversion (subtalar joint)
    - plantar subluxation of metatarsals











Clinical Manifestations

- Extra-Articular manifestations :

- Periarticular Rheumatoid nodules→ usually on extensor surfaces like olecronon bursa, achilles tendon, occiput (MTX îses number)

- Skeletal muscle atrophy (asa 3 weeks)

- Osteoporosis (often compounded by steroid therapy)

Clinical Manifestations

- Extra-Articular manifestations :

- Rheumatoid vasculitis – polyneuropathy, mononeuritis mutiplex, digital gangrene, visceral infarction
- Pleuro-pulmonary ds. – Pleural effusion, pleural fibrosis, ILD, pneumonitis, Caplan syndrome (Pulm Rh. nodule + Pneumoconiosis)
- Felty's syndrome – RA + Splenomegaly
  + Neutropenia (<1500/μL)

Clinical course and Prognosis

- Variable course, difficult to predict in an individual patient
- 15% have short-lived inflammatory process that remits without major disability
- Sustained ds activity for >1 yr portends poor outcome
- Most rapid rate of functional disability within first 2 yrs
- High RF titers, high ESR, > 20 joints involved Rh. Nodules→ progressive disease

Lab Investigations

- Rheumatoid Factor : Ig M against Fc portion of Ig G
  - also + in 5 % healthy population, CLD, Hep B SABE, Malaria, Syphilis, Leprosy, ILD
  - high titers → progressive disease
- ESR and Ac phase reactants (CRP, Cerulopl.)
- Radiolographic eval. → Juxta-articular osteopenia, bone erosions etc.

Diagnosis

- B/L Symm. Inflam. Polyarthritis involving small and large joints of both UL n LL with Sparing of axial skeleton (except for cervical spine)

Diagnosis

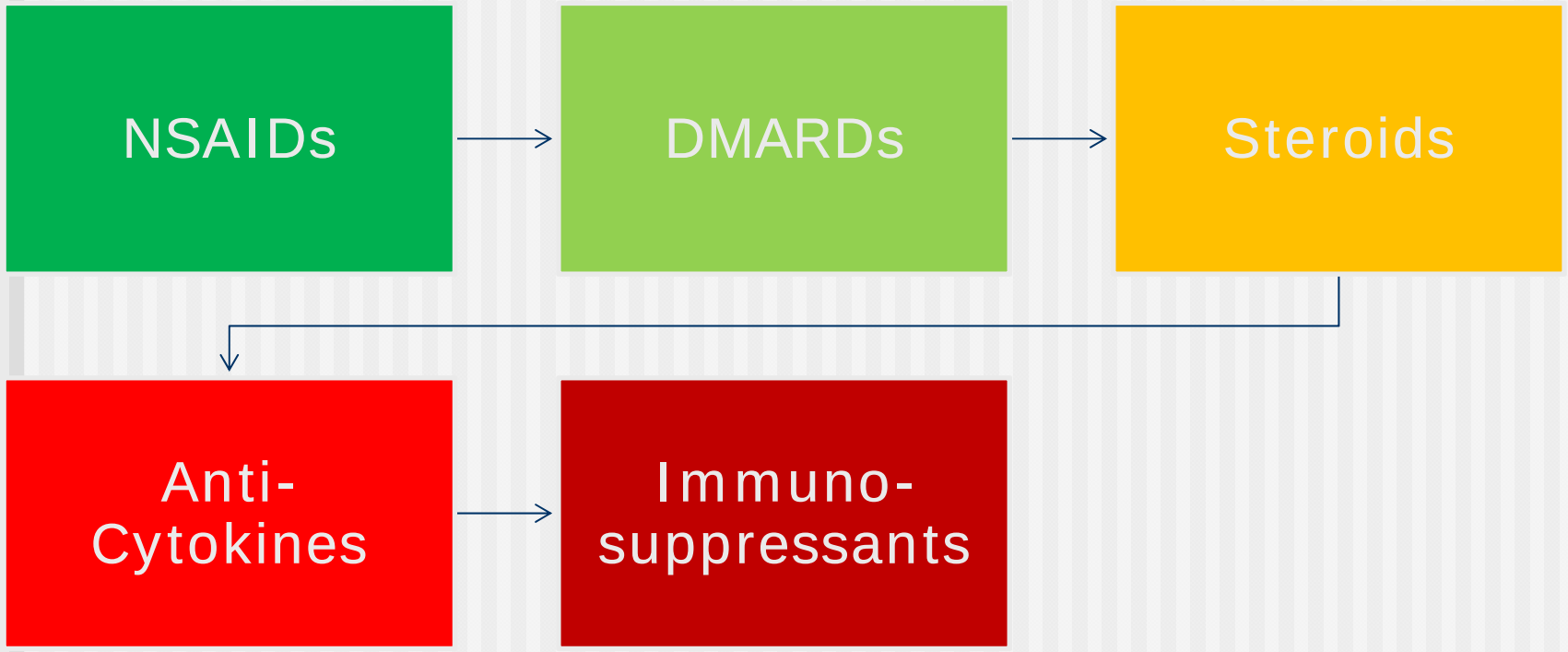
- ACR criteria, 1987 (4/7)
  - Morning stiffness (> 1 hr)
  - 3 or more joint area
  - Hand joints
  - Symmetric distribution
  - Rheumatoid nodules
  - RF
  - Radiographic changes

Treatment

- Treatment goals :
- Relief of Pain
- Reduction of Inflamm. N protection of articular surfaces
- Control of Systemic features
- Maintenance of functional status

- All therapeutic interventions are palliative and none is curative

Treatment


NSAIDs
DMARDs
Steroids
Anti-
Cytokines
Immuno-
suppressants

NSAIDs

- Relief of pain, reduces swelling
- Rest and splintage ameliorates symptoms
- Rapidly effective in mitigating sign n symptoms
- However, no effect on disease progression
- Coxibs n classical NSAIDs equally effective but lesser S/E like gastritis
- S/Es : gastritis, azotemia, platelet dysfunc.

DMARDs

- Reduce levels of Ac. phase reactants and can modify inflammatory process but….
- can not induce true remission and onset of action is delayed
- Options : -MTX
  -D-penicillamine
  -Antimalarials (HCQ)
  -Sulfasalzine
  -Gold compounds

DMARDs

- Methotraxate : DMARD of choice

  - relatively rapid onset of action n sustained improvement with ongoing therapy

  - 7.5 to 30 mg/week

  - maximal improvement by 6 months (thereafter negligible)

  - S/Es → hepatic dysfunction, oral ulcerations, gastritis….give Folic Acid

Glucocorticoids

- Additive therapy both for acute flare-ups as well as chr. low dose maintenance therapy (< 7.5 mg/day)
- Monthly pulse high dose glucocorticoids ?
- Intra-articular steroids when systemic medical therapy not effective
- S/Es → Osteoporosis, gastritis (++NSAIDs)

Anti-cytokine agents

- Anti-TNF œ therapy:
  - TNF receptor bound to Ig G (Etanercept)
  - Chimeric monoclonal Ab to TNF (Infliximab)
  - Humanised monoclonal Ab (Adalimumab, Gole)
- Effective in DMARD failure and DMARD naïve patients as well
- Issues → Cost, Parenteral admin., TB, AntiDNA Ab, CNS demyelination

Anti-cytokine agents

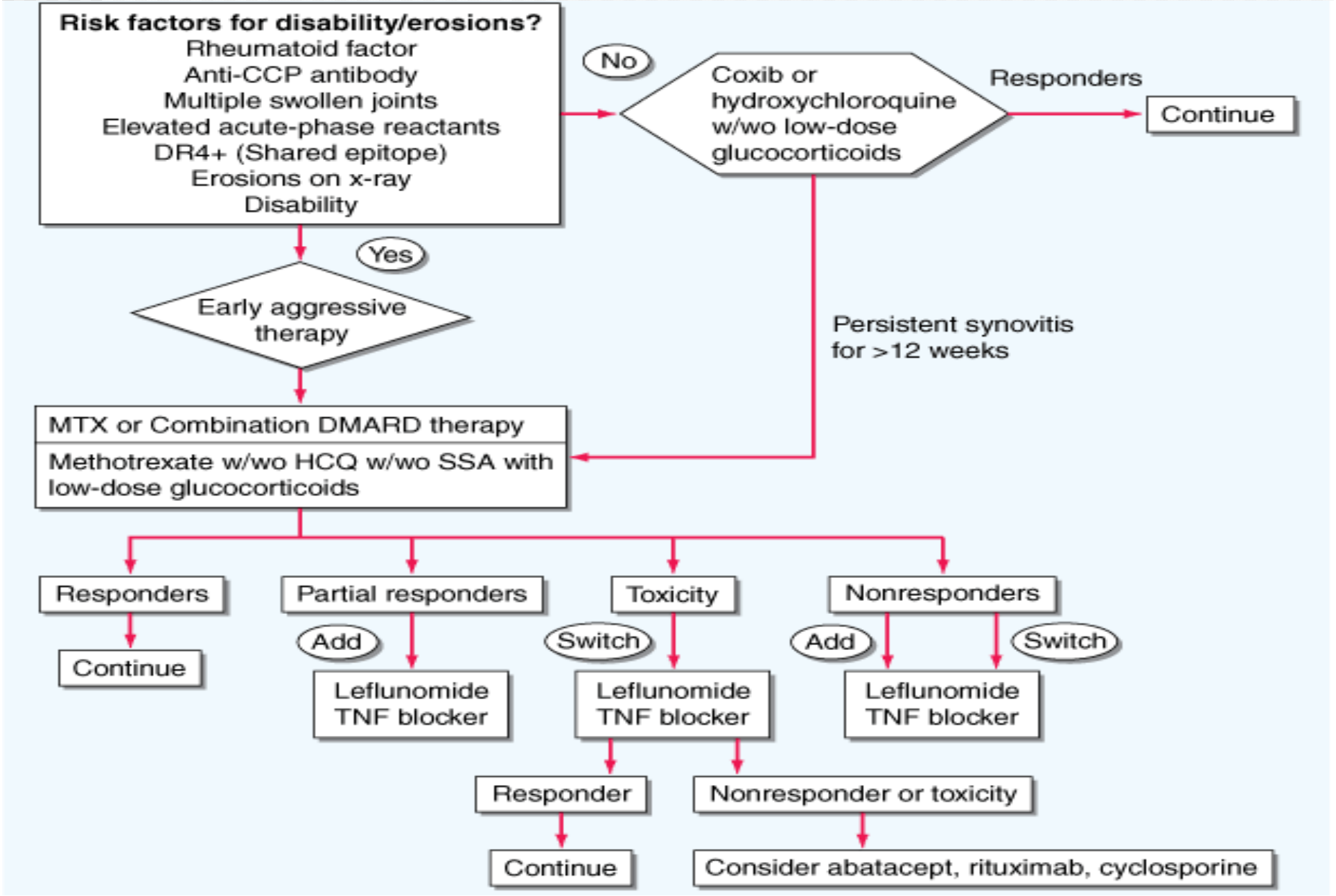
- IL-1 Receptor antagonist (Anakinra)
- Monotherapy or in combination with MTX
- Injection site reactions a major S/E

- CTLA4 bound to Ig G (Abatacept)
- Inhibits co-stimulation of T-cells by preventing surface receptor interaction CD28-CD80

Immunosuppressive therapy, Surgery and Rehabilitation

- Not more effective than DMARDs
- More serious S/E profile
- Reserved for clearly failed DMARD and Anti-cytokine therapy
- Options→ Azathioprine, leflunomide, cyclophosphamide
- Surgery → Arthroplasty, Joint Replacement, Synovectomy, Orhtotic and Assistive devices, Exercise

Approach to patient



The End
(Of RA1 &2)