

Rheumatoid Arthritis

- 3 ways to give DMARDs
 - sequential monotherapy : not used anymore
 - step-up combination therapy
 - initial combination (induction) therapy
- aggressive treatment to rapidly achieve a low level of disease activity using a combination of agents has superior efficacy to approaches that involve sequential low-dose monotherapy
- pyramid of treatment : salicylates & NSAIDS - antimalarials, Gold and sulfasalazine - MTX, azathioprine, penicillamine - biological drugs - surgery
- Conventional DMARDs
 - MTX : inhibits purine synthesis, cytokines and induction of monocytes apoptosis
 - Sulfasalazine : inhibits cytokines and neutrophil migration
 - Leflunomide : inhibits pyrimidine synthesis, cytokines and neutrophil migration
 - Hydroxychloroquine HCC : unknown mechanism
 - Azathioprine : interferes with adenine and guanine synthesis
 - Cyclosporine and Cyclophosphamide
- Biologic DMARDs
 - Etanercept : TNF inhibitor
 - Infliximab : chimeric anti TNF antibody and lysis of TNF cells
 - Adalimumab : human anti TNF antibody
 - Anakinra : IL1 agonist to inhibit it
 - Rituximab : chimeric Anti CD20 antibody (anti B cells) : given IV
 - Abatacept : inhibits T cells by binding to CD80/86
 - Tocilizumab : antibodies against IL6
- DAS-28 interpretation for RA activity
 - < 2.6 : remission
 - 2.6-3.2 : low disease activity
 - 3.2-5.1 : moderate disease activity
 - > 5.1 : high disease activity
- Initial therapy
 - MTX is the first DMARD of choice
 - MTX needs 4-6 weeks to start its action and we need 3 months to evaluate the initial response
 - patients who had an inadequate response to 20-25 weeks of oral MTX must change to SC or IM MTX may be more efficacious

- alternative initial therapy : Leflunomide / Sulfasalazine / HCQ
- Screening before DMARDs : LFT KFT CBC / CXR for MTX / biologics : CXR and hepatitis B & C and PPD / HCQ : ophthalmology
- During therapy we have to monitor CBC LFT KFT after 2 weeks, 1 month, 3 months or 6 months if stable

DMARDs

- NSAIDs
 - PGE2 produces fever
 - PGE2 and PGI2 increases blood flow causing erythema
 - coxibs are selective COX2 inhibitors
 - side effects : GI / salt and water retention / closure of ductus arteriosus / high LFT / erythema multiform / urticaria / toxic epidermal necrolysis
- Corticosteroids
 - decreases IL1 IL2 IFN IL6 TNFA
 - low doses prevent radiographic joint destruction
 - not given subcutaneously
 - side effects : osteoporosis / myopathy / HTN / dyslipidemia / atherosclerosis / skin thinning / Ecchymoses / cushingoid moon face / Acne / Hirsutism / impaired wound healing / pancreatitis / GI bleeding / hyperglycemia / insomnia / depression / memory impairment / cataract and glaucoma
- HCQ
 - limited efficacy when used alone
 - leads to retinopathy with cumulative dose
 - safe in pregnancy and has low toxicity profile
 - least likely to slow radiographic progression
- Sulfasalazine
 - broken down to Sulfapyridine + 5-ASA
 - given to patients with MTX contraindications
 - adverse effects : anorexia / NVD / leucopenia / rash / hepatotoxicity
- MTX
 - structurally similar to folic acid
 - deprives cells of tetrahydrofolate
 - side effects : anorexia / NVD / bone marrow suppression mostly leukopenia /

hepatotoxic / lung toxicity : pulmonary fibrosis and acute interstitial pneumonitis

- ◆ must give folic acid to prevent them
- ◆ do not use antifolate drugs like trimethoprim
- small rheumatoid nodules may increase in size
- contraindications : liver cirrhosis / hepatitis B and C / alcohol abuse / pregnancy and breast feeding
- Leflunomide
 - very teratogenic and contraindicated in pregnancy
 - as effective as methotrexate and sulfasalazine
 - causes GI symptoms and hepatotoxic
 - high hepatotoxicity when combined with MTX
 - should be stopped 4 months before pregnancy
 - cholestyramine can be given for 11 days while stopping
- Azathioprine : reserved for those patients who are intolerant of other agents
- anti-TNFs
 - TNF causes adhesions expression / synthesis of IL1&6 / activation of T cells / up regulation of RANKL / induction apoptosis
 - contraindications for anti-TNFs
 - ◆ SLE
 - ◆ demyelination diseases : optic neuritis and MS
 - ◆ pregnancy
 - ◆ active serious infections like HEPB and TB
 - ◆ congestive heart failure

Osteoarthritis

- non pharmacological treatment
 - aerobic exercises and water based exercises
 - Insoles
 - Braces
 - Cane or stick
 - Local heat or ice
 - Acupuncture
 - Transcutaneous electrical nerve stimulation
 - Yoga

- Ultrasound
- pharmacological treatment
 - paracetamol and NSAIDs
 - topical capsaicin
 - Glucosamine sulfate
 - Chondroitin sulfate
 - Intra-articular corticosteroids
 - Intra-articular hyaluronic acid preparations
- Surgical intervention
 - Joint lavage
 - Arthroscopic debridement
 - Osteotomy
 - Joint replacement
 - Joint fusion