DMARDs

Terminology
DMARDs stands for disease-modifying antirheumatic drugs. The term is given because of the ability of the members of this heterogeneous group of drugs to reverse joint damage, an effect never seen with nonsteroidal anti-inflammatory drugs- NSAIDs-. This group is also called SAARDs which stands for slow acting antirheumatic drugs because it takes 6 weeks to 6 months for their benefit to be apparent.

DMARDs agents
1- Methotrexate
2- Sulfasalazine
3- Cyclosporine
4- Infliximab & adalimumab
5- Etanercept
6- Leflunomide
7- Gold compounds
8- Hydroxychloroquine
9- Penicillamine

DMARDs mechanisms of action
1- Methotrexate
   It reduces the number of immune cells required to the inflammatory response.
2- Sulfasalazine
   The sulfapyridine moiety appears to be more important than the 5-aminosalicylic acid component as antirheumatic.
3- Cyclosporine
   It binds to T-lymphocyte`s immunophylline which leads finally to inhibition of certain cytokines important in
inflammation.

4-Infliximab & adalimomab
   They are monoclonal antibodies that bind to and prevent the action of TNF-alpha, a cytokine which plays a key role in inflammation.

5-Etanercept
   A recombinant protein composed of two TNF receptors and acts as a decoy decreasing the cellular actions of TNF-alfa.

6-Leflunomide
   It inhibits dihydroorotate dehydrogenase, an enzyme required by activated lymphocytes for the synthesis of the pyrimidines needed for RNA synthesis.

7-Gold compounds
   Gold compounds as auranofine (oral) and aurothioglucose (injectable) alter the activity of macrophages, cells which play a central role in inflammation. They also suppress the phagocytic activity by neutrophils (microphages).

8-Hydroxychloroquine
   It may interfere with activity of T-lymphocytes, decrease leucocyte chemotaxis and other mechanisms.

9-Penicillamine
   Its mechanisms of action is similar to that of hydroxychloroquine.

Clinical indications of DMARDs
1-Rheumatoid arthritis (RA) not responding to other agents.
2-Lupus erythematosus
3-Juvenile RA
4-Sjögren syndrome
5-Other immunological diseases

Kinetics of DMARDs
-Oral
Toxicity of DMARDs (side effects)
DMARDs can cause severe or fatal toxicities
1-Methotrexate
.....Gastric irritation.....Hematotoxicity.....Teratogenicity
2-Sulfasalazine
.....GIT disturbances.....Leukopenia.....skin rash
3-Cyclosporine
.....Nephrotoxicity.....Peripheral neuropathy.....Hypertension
4-Infliximab & adalimumab
.....Activation of latent TB.....Upper respiratory tract infection.
5-Etanercept
.....Injection site reactions
6-Leflunomide
.....Teratogenicity.....GIT disturbances.....Hepatotoxicity.....Skin reactions.
7-Gold compounds
.....Diarhoea.....Hematologic abnormalities.....Dermatitis.
8-Hydroxychloroquine
.....GIT disturbances.....Rash.....Myopathy.....Neuropathy.....ototoxicity.
9-Penicillamine
.....GIT disturbances.....Dermatitis.....Hematological abnormalities.....Proteinuria.