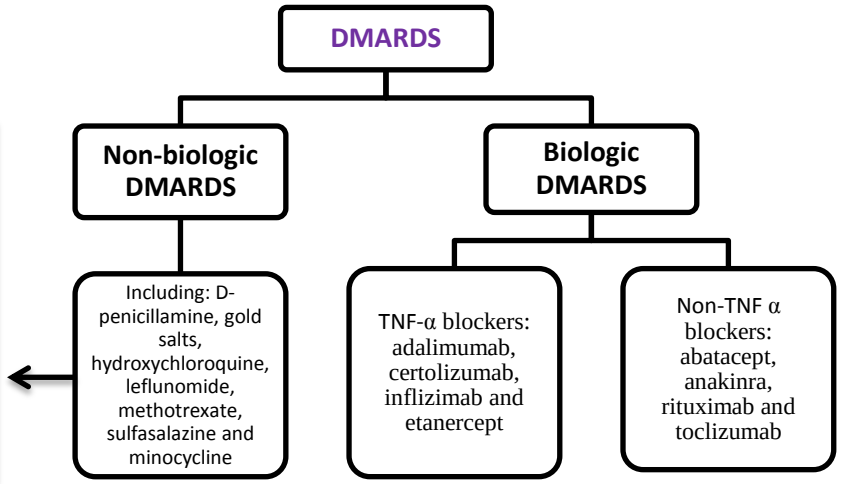
- **Goals for maintaining Rheumatoid arthritis:**
  - **Relieve pain and suppress inflammation**: this is achieved by using Non-Steroidal Anti-Inflammatory Drugs (NSAIDS). NSAIDS generally act by inhibiting the enzyme cyclooxygenase which is normally responsible for the breakdown of arachidonic acid to prostaglandins, thromboxane and prostacyclin. NSAIDS are classified to:
    - ✓ *Non-selective NSAIDS: COX-1 inhibitors.*
      - ❖ The most important drugs are ibuprofen (advil), indomethacin (indocin) and diclofenac (voltaren).
      - ❖ Non-selective NSAIDS have less GIT and renal safety profiles.
    - ✓ *Selective NSAIDS: COX-2 inhibitors.*
      - ❖ Drugs belonging to this group end with (-coxib).
      - ❖ Selective NSAIDS have more GIT and renal safety profiles but are associated with higher risks for cardiovascular thrombi events that's why they are contraindicated in patients with coronary artery disease/ by-pass graft surgery.
    - ✓ **Note**: COX-1 inhibitors decrease thromboxane production more effectively than prostacyclin production, tipping the balance away from thrombosis. In contrast, COX-2 inhibitors inhibit only prostacyclin production, decreasing inflammation but tipping the balance toward thrombosis.
  - **Prevent or control joint destruction: this is achieved by using Disease-Modifying Anti-Rheumatic Drugs (DMARDS). DMARDS are classified to:**



1. **D-penicillamine, gold salts & sulfasalazine:** they cause ulceration of the mouth.
2. **D-penicillamine & gold salts:** cause nephritic syndrome
3. **Sulfasalazine:** causes reversible male infertility & hemolysis in G6PD def.

- ✓ *Methotrexate (Non-biologic DMARD):*
  - ❖ It is the gold standard in treatment of Rheumatoid Arthritis.
  - ❖ **Dose**: starting dose is 7.5-10 mg a week (orally). The dose might be increased to 20-25 mg a week if needed.
  - ❖ **Mechanism of action**: inhibition of T-cell proliferation due to its effects on purine/pyrimidine synthesis (folate antagonist).
  - ❖ **Side effects**: pulmonary infiltrate/fibrosis and dose-related hepatotoxicity (which is rare). Side effects are reduced by leucovorin (rescue therapy) 24 hours after each weekly dose.
  - ❖ **Pregnancy category**: X (contraindicated).
- ✓ *Tumor Necrosis Factor-Alpha antagonists:*
  - ❖ **Etanercept**: binds to TNF-α to prevent its binding to cell-surface receptors.
  - ❖ **Adalimumab + inflizimab**: monoclonal anti-TNF-α antibodies binding to TNF-α and preventing its binding to its cell-surface receptors.
  - ❖ These drugs have additional effect when taken with methotrexate.
- ✓ *Mechanism of action of non-TNF α biologic DMARDS:*
  - ❖ **Abatacept**: T-cell co-stimulation modulator.

- ❖ **Anakinra**: interleukin-1 receptor antagonist.
- ❖ **Rituximab**: B-cell depleting (cytotoxic agent).
- ❖ **Toclizumab**: interleukin-6 receptor antagonist.

- **Preserve or improve patient's functional ability.**
- **Treatment of extra-articular manifestations.**

- **The inverted pyramidal approach of therapy in patients with rheumatoid arthritis (see the figure):**
  - **Why was the old pyramidal approach replaced by the new inverted one?**
    - ✓ Because DMARDS have significant benefits when used early. These benefits may be enhanced when the drugs are used in combination.