

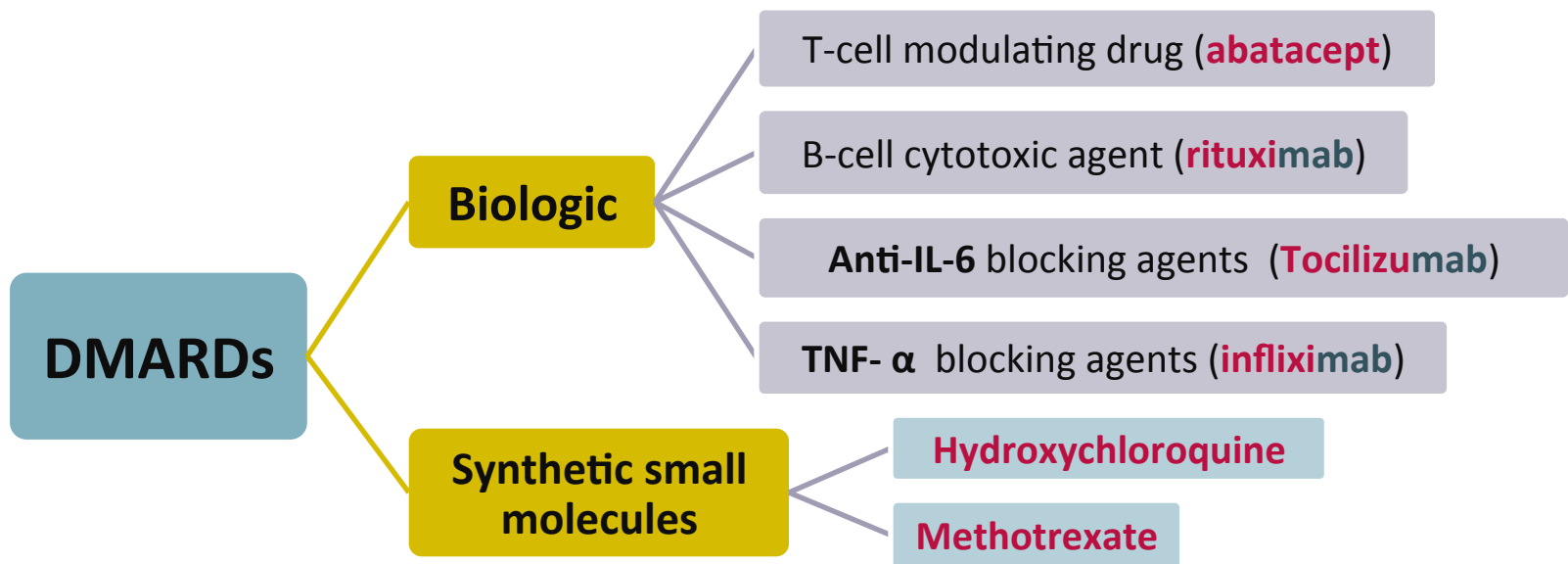


Lecture 3

Disease modified Anti-rheumatic drugs (DMARD)

- Additional Notes
- **Important**
- Explanation –Extra-

For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com



DMARD

General Features and Conditions to use

- Used when the inflammatory disease **is not responding** to NSAIDs
- Used when the disease is **progressing** & causing **deformities or damage** (used in chronic inflammation, while in acute inflammation NSAID's are used).
- **Low doses** are commonly used early in the course of the disease. (Because they have a lot of side effects)
- Can not **repair** the existing damage (not treating) , but **prevent** further deformity.
- Have **no analgesic** effects (not directly) but they reduce pain because they are anti-inflammatory (when inflammation is reduced the pain is reduced too).
- **Slow onset** their effects take from **6 weeks** up to **6 months** to be evident

General Clinical Uses

- Treatment of **rheumatic disorders** (mainly, but some of them treat other diseases)
- Combination therapies are both safe & effective. (Can prescribe them with other drugs in the same time)

When the disease begin to progress (damage happens to the body tissues) **NSAID's** are useless, so we start to give the patient **DMARD's** to prevent further damage.

Synthetic small molecules

Drug	Hydroxychloroquine	Methotrexate
Mechanism of action	<ul style="list-style-type: none"> - Trapping of free radicals. - Suppression of T lymphocytes. 	Immunosuppressant > inhibit T-Cells "Cell mediated immunity"
Side effects	GIT upset & irritation, Blurred vision or irreversible retinal damage , headaches, Discoloration of nail beds & mucous membranes (Becomes yellowish brown) and Pruritus "severe itching of skin" .	Cytopenia "deficiency in blood elements" (suppression of bone marrow), Nausea, liver cirrhosis, Acute Pneumonia, Mucosal ulceration
Metabolized by	Liver	-
Pharmacokinetics and other notes	Rapidly & completely absorbed following oral administration, penetrates CNS "Blood Brain Barrier" (Causes headaches) & cross placental barrier (This explains the large number of side effects).	Used in Chemotherapy for cancer treatment, doses as antirheumatics are lower than needed for chemotherapy, given once a week.

Biologic disease modifiers

Drug	Tocilizumab (Anti-IL-6 receptor antibody)	Infliximab (TNF- blocking agent)
Mechanism of action	<ul style="list-style-type: none"> IL-6 receptor inhibitor (IL-6 plays an important role in chronic inflammation) Blocks the activity of IL-6 mediated signaling Half-life is dose dependent (11-13 days) 	<ul style="list-style-type: none"> Binds to human TNF-α resulting in inhibition of macrophage & T cell function
Side effects	<ul style="list-style-type: none"> Severe infusion reactions (immune reaction) Serious infections (bacterial, tuberculosis ,fungal) Increase cholesterol level Increase liver enzymes Decrease in WBCs Blood tests will be used monthly for increase in cholesterol, liver enzymes & decrease in WBCs.	<ul style="list-style-type: none"> Activation of latent tuberculosis (because TNF plays an important role in immunity against infections including Mycobacterium tuberculosis) Upper respiratory tract infections Infections Infusion reactions Pancytopenia
Pharmacokinetic and other notes	<ul style="list-style-type: none"> Given as monthly IV infusion. Used as monotherapy in adult with rheumatoid arthritis or in children over 2 years with systemic juvenile arthritis In combination with methotrexate or other non biologic anti-rheumatic drugs in patients with active rheumatoid arthritis. 	<ul style="list-style-type: none"> A chimeric antibody (25% mouse, 75% human) \rightarrow 62% of patients reject it. Given as IV infusion over at least two hours Half-Life 8-12 days Given every 8 weeks regimen. Elicits up to 62% incidence of human antichimeric antibodies. Concurrent therapy with methotrexate decreases the incidence of human antichimeric antibodies. Contraindicated in patients with a history of tuberculosis.

- Biologic disease modifiers:** genetically engineered drugs that are used to modify imbalances of the immune system in autoimmune diseases:
 - Block**, or **modify** the activity of **selected cells** in the immune system.
 - Blocking action of certain mediators** that responsible for inflammatory conditions.

Comparison between NSAIDs & DMARDs

	DMARDs	NSAIDs
ONSET OF ACTION	Slow onset of action used in chronic cases when deformity or damage is exciting.	Rapid onset of action used in acute cases to relief inflammation & pain.
EFFECT ON PROGRESSION OF DISEASE	Arrest progression of the disease.	No effect.
EFFECT ON DEFORMARTIES	Prevent formation of new deformity	Can not stop formation of new deformity

★ Summary

	Synthetic small molecules		Biologic	
Drug	Hydroxychloroquine	Methotrexate	Tocilizumab	Infliximab
Mechanism of action	Trapping of free radicals	Immunosuppressant	anti-IL-6 receptor antibody	TNF- blocking agent
Side effects	irreversible retinal damage	- Cytopenia. - Mucosal ulceration.	↑ cholesterol and enzymes. ↓ WBC → serious infections.	- Tuberculosis - Upper respiratory tract infections
Administration	-	Once a week	Monthly (IV infusion)	8 weeks regimen (IV infusion) in 2 hours.
Notes	Crosses BBB and placenta	Chemotherapy	Monotherapy: systemic juvenile arthritis Combination: rheumatoid arthritis	Chimeric antibody

★ MCQs

Q1: During the early course of a disease which kind of dose of DMARD is used?

- A. High dose
- B. Low dose
- C. Medium dose

Q2: When's the time for DMARD to be used?

- A. When an inflammatory disease is not responding to NSAIDS
- B. When an inflammatory disease is not responding to Paracetamol
- C. When an inflammatory disease is not responding to Asprin

Q3: In what condition DMARD is NOT used?

- A. Treatment of Ulcer
- B. Treatment of Rheumatic disease
- C. Treatment of Joints and bones discomfort

Q4: Which of the following is an immunosuppressant drug and used in chemotherapy?

- A. Tocilizumab
- B. Methotrexate
- C. Infliximab

Q5: Slow onset of action used in chronic cases when deformity or damage is exciting, is related to..?

- A. DMARDs
- B. NSAIDs
- C. None of the above

Q6: Which of the following is incorrect about Infliximab?

- A. Given as IV infusion over at least two hours
- B. Half life 8-12 days
- C. Contraindicated in patients with no history of tuberculosis

Answers:
1- B
2- A
3- A
4- B
5- A
6- C

Good luck!

Done by Pharmacology team 434

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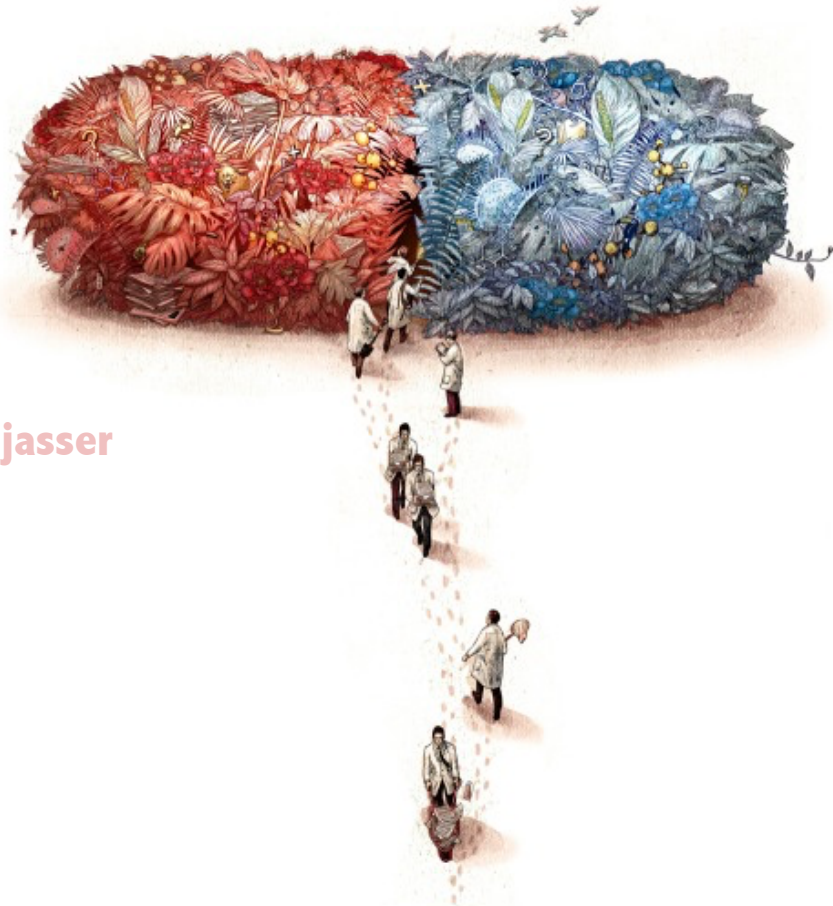
Rasha bassas

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