PHARMATEAM 430

مهند شريفي - رحاب الرشيدي

سعود الموسى - أنفال الشايع

مهند العميل - نوف الحماد

عبدالله الموسى - حنان الشعلان

Disease Modifying Antirheumatic drugs

(Slow Acting Anti-inflammatory Drugs)

ملاحظات التيم:

اللون الأزرق للشرح والفهم

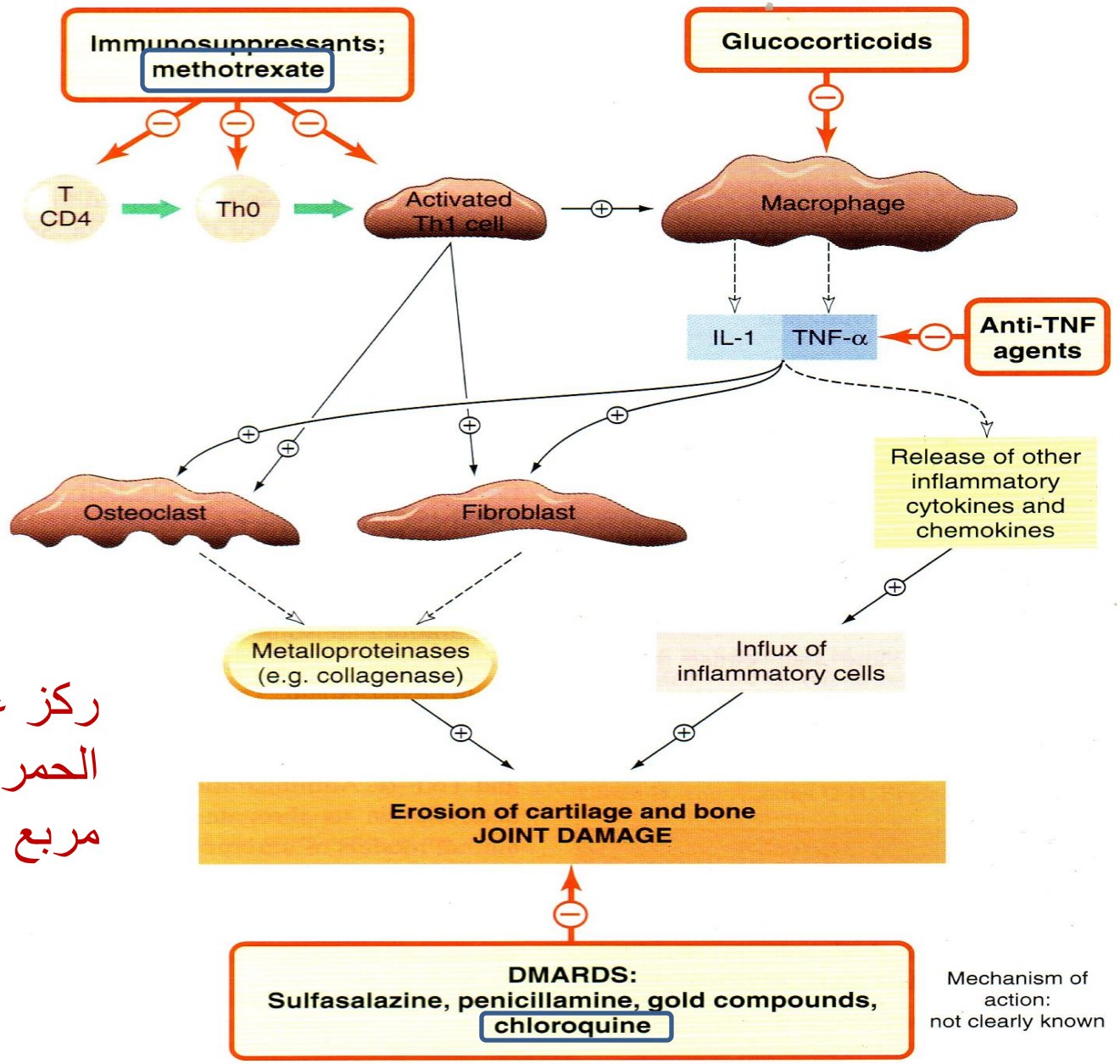
واللون الاحمر الغامق يعني ركز عليه

General Features

- **Low doses are commonly used early in the course of the disease**
- **Used when the disease is progressing & causing deformities**
- **Can NOT repair the existing damage , but prevent further deformity**
- **Have NO analgesic effects (That's why we give NSAIDs).**
- **Their effects take from 6 weeks up to 6 months to be evident (That's why we give NSAIDs-DMARDs combination)**

General Clinical Uses

- **Treatment of rheumatoid arthritis**



ركز على المربعات الحمراء واربط كل مربع بالدواء حقه

Fig. 16.5 **A schematic diagram of the cells and mediators involved in the pathogenesis of rheumatoid joint damage indicating the action of antirheumatoid drugs.** The anti-TNF agents are etanercept and infliximab. (IL-1, interleukin-1, TNF-α, tumour necrosis factor-α; DMARDs, disease-modifying antirheumatoid drugs.)

Hydroxychloroquine

Mechanism of action (MOA)	Adverse effects
Stabilization of lysosomal enzyme activity (the enzymes that released from osteoclast, revise the previous picture)	Nausea & vomiting
Eliminates free radicals	Irreversible retinal damage
Suppression of T-cells (Because it is autoimmune disease)	Corneal deposits

Methotrexate

Mechanism of action (MOA)	Adverse effects
Inhibition of neutrophils (polymorphoneuclear) chemotaxis	Bone marrow depression
Inhibition of T-cells	Mucosal ulcers
	Hepatotoxicity

Biologicals

Tumor necrosis factor–α(TNF-α) is an inflammatory mediator, and this type of drugs inhibit this factor

Biological drugs = blocking agents (antagonists) for TNF-α

Infliximab

A chimeric antibody (25% mouse, 75% human)

Chimeric: prepared from 2 components

Infliximab

Mechanism of action (MOA)	Pharmacokinetics	Adverse effects
Binds to human TNF-α resulting in inhibition of macrophage & T cell function	Given by IV infusion	Upper respiratory tract infections
		Cough
		Infusion site reaction
	Half-life 8-12 days	Activation of latent tuberculosis (Because it's immune suppression drug)
		Headache

Concurrent therapy with methotrexate decreases the prevalence of human antichimeric antibodies (because our immunity may create antibodies against the drug (chimeric) itself due to its origin)

يعني بالعربي: نديه methotrexate ليمنع تكوين antibodies ضد الـ Chimeric

patient with history of TB **never (contraindicated)** given Infliximab

Comparison between NSAIDs & DMARDs

DMARDs

- Slow onset of action
- Arrest progression of the disease.
- 6 weeks – 6 months
- Prevent formation of new deformity
- Used in chronic cases when deformity is exciting

NSAIDs

- Rapid onset of action
- No effect on the disease (for analgesic effect).
- Minutes - hours
- Can NOT stop formation of new deformity
- Used in acute cases to relief inflammation & pain

SUMMARY

- DMARDs are used mainly in chronic cases of rheumatoid arthritis , when the disease is progressing and forming deformities.
- They do NOT remove the existing damage but prevent further formation of deformities.
- They have NO analgesic effect.
- They are slow in onset needs weeks to manifest their effects .
- Hydroxychloroquine acts mainly through suppression of the activity of lysosomal enzymes and trapping (eliminating) free radicals .
- Its main adverse effects is irreversible retinal damage.

CONTINUE…

- Methotrexate acts mainly through suppression of phagocytic cells & T cells
- Its adverse effects are bone marrow depression & mucosal ulceration
- Infliximab is a chimeric TNF-α blocking agent.
- Given with methotrexate to reduce antichimeric effect
- Its main adverse effects are upper respiratory tract infections & reactivation of latent TB