

Transplantation:

1 Glucocorticoids

- first line immunosuppressive ($\downarrow \downarrow$ GVHD)
- anti-inflammatory → 1 suppress cell mediated immunity ($\downarrow \downarrow$ Cytokines genes $\rightarrow \downarrow \downarrow$ IL-2) (T cells > B cells \leftarrow αγ γ)
- 2 Suppress humoral immunity ($\downarrow \downarrow$ IL-2 + IL-2 R)
- modulate allergic + treating disease e.g.: asthma

→ side effects → hypertension, hyperglycemia, Gastric ulcers, Cataracts, Osteoporosis, adrenal gland & pituitary redistribution, immunodeficiency, growth failure + delayed puberty, excitatory effect on CNS

2 Calcineurin Inhibitors

↳ A) Cyclosporine

uses: → autoimmune disease (psoriasis, asthma, rheumatoid arthritis)
 → ophthalmic Solution
 → human organ transplantation + $\downarrow \downarrow$ GVHD
 ↗ allogeneic stem cells transplantation
 ↗ cyclosporine + methotrexate

→ side effects → **narrow therapeutic window** → low dose → transplantation rejection
 ↗ high dose → toxicity
 ↗ monitoring
 ↗ ↑ incidence of -lymphoma
 - Skin cancer
 - Kaposi's sarcoma
 etc
 ↗ gingival hyperplasia

↗ nephrotoxicity
 ↗ mental confusion
 ↗ hyperglycemia
 ↗ hypertension

↳ B) Tacrolimus uses: topical preparation → ointment → psoriasis
 ↗ atopic dermatitis
 ↗ side effects → D.M
 → cyclosporine ↓ nephrotoxicity
 Kidney (كلى) ↓

NOTE

→ Cyclosporine
 → Tacrolimus
 → Sirolimus

«أدوية تحدى جهاز المناعة»

3 Sirolimus - Rapamune -

→ inhibits → mTOR → $\downarrow \downarrow$ IL-2 → $\downarrow \downarrow$ growth of immune cells

target dose - long monitoring
 narrow therapeutic window → low dose → transplantation rejection
 ↗ high dose → toxicity
 ↗ mental confusion
 ↗ nephrotoxicity

4 Anti-metabolites → dose limiting factor (cancer → ↑ doses
 transplantation → ↓ doses)
 → $\downarrow \downarrow$ proliferation of: B, T cells

↳ A) Methotrexate → folic acid analogue (binds dihydrofolate reductase → \downarrow tetrahydrofolate)

uses: Mainly → autoimmune disease (rheumatoid arthritis, Behcet's disease)
 → transplantation (كلى، ملتحمة، ...)

↳ B) Azathioprin & mercaptopurine

uses: Mainly → control transplant rejection reaction

↳ C) Mycophenolate < IMPDH inhibitor >

mechanism: inhibits IMPDH → $\downarrow \downarrow$ G_{nucleotides} $\xrightarrow{\text{intrinsic monophosphate dehydrogenase}}$ antiproliferation of lymphocytes (T, B cells)

→ more effective than Azathioprine in preventing acute rejection in solid organ transplant patient

* mycophenolate + cyclosporine or tacrolimus
 renal transplants → low doses (جراحت)
 * mycophenolate + prednisone
 dont tolerate these drugs

