

# 'HLS'3"Immunosuppressive'Drugs

## Introduction

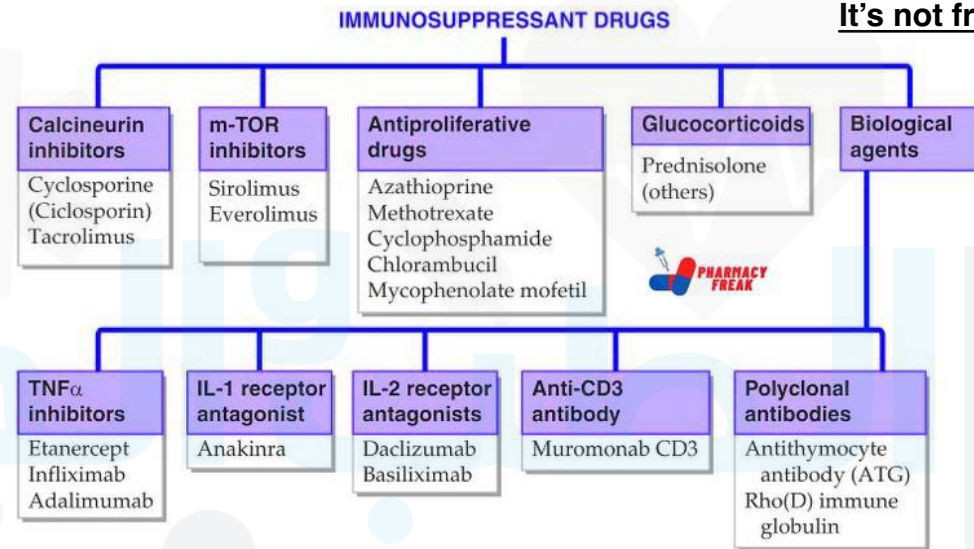
• Immunosuppressive drugs inhibit the immune response.

- Used for:
- Preventing organ transplant rejection
- Treating autoimmune diseases
- Long-term use → ↑ risk of:
- Infections
- Cancers

• Mechanism:

- Inhibit cytokine release
- Inhibit immune cell signaling
- Inhibit cell proliferation

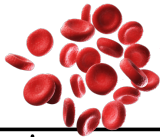
- Main classes:
- Glucocorticoids
- Calcineurin inhibitors
- mTOR inhibitors
- Antimetabolites
- Biological agents & antibodies



It's not from the lecture



It may look like the font is small, but it is very useful. The entire lecture is on one page—I think it's worth it. Good luck to everyone.



# Immunosuppressive Drugs



## 2 Calcineurin Inhibitors

## 3 Antimetabolites & Cytotoxic Drugs

## 4 mTOR Inhibitors

## 5 Biological Immunosuppressive Drugs

## 1 Glucocorticoids (Corticosteroids)

**Mechanism**

- ↓ lymphocytes (lysis + redistribution)
- ↓ cytokines (IL-1, IL-6)
- ↓ T-cell activity + ↓ IL-2
- ↓ neutrophil & monocyte chemotaxis

**Examples**

- Prednisone**
- Methylprednisolone**

**Adverse effects (long-term)**

- Hyperglycemia
- Hypertension
- Edema
- Osteoporosis
- Cushing features
- Peptic ulcer
- Recurrent infections

**Uses**

- Autoimmune diseases:
- ITP, RA, SLE, pemphigus, Crohn's disease
- Graft-versus-host disease (GVHD)
- Organ transplantation (early use)
- Acute lymphoblastic leukemia

**Cyclosporine**

**Mechanism**

- Inhibits calcineurin → ↓ T-cell activation → ↓ IL-2

**Uses**

- Drug of choice in organ transplantation
- Autoimmune diseases (RA, psoriasis)

**Side effects**

- Nephrotoxicity (MOST important)**
- Hypertension
- Hyperlipidemia
- Hyperkalemia
- Hyperuricemia
- Hirsutism
- Gum hyperplasia
- ↑ infections & lymphoma

**Drug interactions**

- ↑ level: verapamil, ketoconazole, erythromycin and glucocorticoids (CYP3A4 inhibitors)
- ↓ level: phenytoin, rifampin, induce CYP3A4
- Needs therapeutic drug monitoring**

**Pregnancy**

- Category C (relatively safe)

Cyclosporine is the drug of choice for organ or tissue transplantation to prevent rejection reactions. It may be used with or without other immunosuppressive drugs (e.g. = mycophenolate, +/- steroids, +/- cytotoxic drugs)

**Tacrolimus**

**Mechanism**

- Same as cyclosporine (calcineurin inhibitor)
- BUT 10-100x more potent**

**Uses**

- Prevent transplant rejection
- Topical** → vitiligo & atopic dermatitis

**Side effects**

- Nephrotoxicity
- Hypertension
- Hyperkalemia
- Neurotoxicity (tremor, seizures)**
- Hyperglycemia & diabetes**
- ↑ infections & tumors
- Diarrhea, alopecia (with mycophenolate)



**Siroliimus & Everolimus**

**Mechanism**

- Not** calcineurin inhibitors
- Block mTOR** → ↓ T & B cell proliferation
- ↓ immunoglobulin production

**Pharmacokinetics**

- Oral
- Long half-life (~60 hrs)
- CYP450 metabolism
- Need monitoring**

**Toxicity**

- Myelosuppression (especially thrombocytopenia)
- Hepatotoxicity
- Diarrhea
- Hypertriglyceridemia
- Pneumonitis, headache

**Uses**

- Prevent organ rejection
- Topical dermatologic uses**
- Drug-eluting stents → ↓ restenosis

3. Recently, sirolimus eluting coronary stents have been shown to reduce restenosis (due to antiproliferative effects) in patients with severe coronary artery disease

4. Sirolimus eluting stents (SES) for **Endothelial tube dysfunction** to suppress stent-induced tissue hyperplasia

**T-cell inhibitors**

- Basiliximab** → anti-IL-2 receptor → prevent rejection

**B-cell depletion**

- Rituximab** (anti-CD20):
- Lymphoma
- CLL
- Autoimmune diseases

T-cell inhibitors: Basiliximab (anti-IL-2 receptor antibodies) to prevent acute rejection of transplanted organs

B-cell depleting agents: Rituximab (Anti CD 20) treats certain cancers (Non-Hodgkin Lymphoma, Chronic Lymphocytic Leukemia) and autoimmune diseases (rheumatoid arthritis, pemphigus vulgaris)

## 6 Polyclonal Antibodies

- Antithymocyte globulin (ATG)**
- From rabbits
- Directly toxic to lymphocytes

- Thymoglobulin**
- polyclonal Ab. Targets T & B cells → apoptosis

**Uses**

- Acute renal transplant rejection**

1- Antithymocyte globulin (ATG or ATGAM). ATG is a purified  $\gamma$ -globulin from serum of rabbits immunized with human thymocytes. ATG has a **direct cytotoxicity** to lymphocytes

2- Thymoglobulin  
Polyclonal antibodies targeting B & T lymphocyte, natural killer cell & plasma cell surface antigens. It induces rapid apoptosis of CD3+ T cells present in the bloodstream.

**Lefunomide**

**Mechanism**

- Inhibits pyrimidine synthesis

**Uses**

- Autoimmune diseases

**Side effects**

- Diarrhea (common)
- Hepatotoxicity

**Contraindicated in pregnancy**

**Mycophenolate mofetil**

**Mechanism**

- Inhibits IMP dehydrogenase → ↓ purine synthesis
- ↓ T & B cell proliferation

**Uses**

- Organ transplantation
- Autoimmune diseases
- Adjunct** → ↓ cyclosporine dose

**Side effects**

- Hepatotoxicity
- Infections
- Bone marrow suppression

**Contraindicated in pregnancy**

**Cyclophosphamide**

**Mechanism**

- Alkylating agent → DNA damage
- ↓ lymphocytes → ↓ autoantibodies

**Side effect**

- Bone marrow suppression**

**Contraindicated in pregnancy**

**Azathioprine**

**Mechanism**

- Prodrug → 6-mercaptopurine (6-MP)
- Inhibits purine synthesis → ↓ lymphocytes

**Uses**

- Organ transplant
- RA, IBD, autoimmune diseases
- 6-MP → used in childhood ALL

## Abbreviations

- Diseases & Conditions**
- ITP → Immune Thrombocytopenic Purpura
  - RA → Rheumatoid Arthritis
  - SLE → Systemic Lupus Erythematosus
  - GVHD (GvHD) → Graft Versus Host Disease
  - ALL → Acute Lymphoblastic Leukemia
  - CLL → Chronic Lymphocytic Leukemia
- Drugs & Drug Groups**
- ATG / ATGAM → Anti-Thymocyte Globulin
  - 6-MP → 6-Mercaptopurine
  - TNF- $\alpha$  → Tumor Necrosis Factor alpha



## 🔥 High-yield Summary

- Calcineurin inhibitors → ↓ IL-2 → ↓ T-cells
- mTOR inhibitors → ↓ proliferation
- Antimetabolites → ↓ DNA synthesis
- Steroids → broad suppression
- Biologics → targeted therapy

- IgG ضد Rh antigen
- يُعطى للأم Rh- خلال 24-72 ساعة بعد ولادة +Rh
- يمنع:
  - Hemolytic disease of newborn

## 8 IVIG (Intravenous Immunoglobulin)

### 🧬 Mechanism

- ↓ T helper cells
- ↓ antibody production
- Fc receptor blockade
- ↑ antibody breakdown

### 👤 Uses

- Immunodeficiency (after BM transplant and HIV , low dose 400 - 600 mg/kg/month)
- Autoimmune diseases:
  - Kawasaki
  - ITP
  - Guillain-Barré
  - SLE
  - Dermatomyositis
  - Myasthenia gravis
  - Multiple sclerosis
  - Toxic epidermal necrolysis
- as hyper immune therapy against specific infectious agents

### ⚠️ Side effects

- Common:
  - Headache, fever, vomiting, myalgia, erythema
- Rare:
  - Anaphylaxis
  - Aseptic meningitis
  - Renal failure
  - Arrhythmias , lung injury, dermatological problems

✓ Adverse effects are preventable with certain pre-medications, including non-steroidal anti-inflammatory drugs, antihistamines, corticosteroids, or saline for pre-hydration.

### ✅ Important

- Does NOT ↑ infection risk
- Safe in pregnancy & breastfeeding



لَا حَوْلَ وَلَا قُوَّةَ إِلَّا بِاللَّهِ

"من كنوز الجنة"

