Drugs For Leprosy And Leishmania

Leishmaniasis :

Caused by three *Leishmania species:*

- *L.tropica* causes:

Cutaneous leishmaniasis or oriental sore

- *L. brazeliensis* causes: Mucocutaneous leishmaniasis
- *L. Donovani* causes: Visceral leishmaniasis

Drugs used to treat leishmaniasis:

1. **Sodium Stibogluconate (Pentostam):**

Drug of choice for all forms of leishmaniasis (imp)

It is a pentavalent antimonial (antimony is a metallic element)

Mechanism of action : unknown but they say that this drug produces oxygen radicals and by doing this they affect the respiration of the microorganisms .

This drug is not absorbed orally so it's given either IV or IM

It's partially metabolized and excreted in the urine .

The distinct side effect of this drug is QT prolongation and Hemolytic anemia ..

2. **Amphotericin**

- Antifungal agent.
- alternative therapy for visceral leishmaniasis, especially in areas with high resistance.

Side effects :

- **Distinctive side effects include : anaemia, hypokalaemia, liver damage, thrombocytopenia and anaphylatic reactions. Nephrotoxicity is the most common and the most serious long-term toxicity of amphotericin B administration so it is a very toxic drug.**

3Miltefosine

- **An alkylphosphocholine analog**
- **For visceral leishmaniasis.**

- **Given orally, for 28 days.**
- **Causes V & D, hepatotoxicity, nephrotoxicity, and it is teratogenic.**

4

- **Inhibits DNA replication.(mechanism of action)**
- **Also, DHF reductase inhibitor**
- **Not absorbed orally**
- **Given IV/ IM.**
- **Accumulative drug & eliminated slowly in urine (elimination half-life 12 days).**
- **Not effectively cross blood brain barrier**

Can be inhaled as a nebulized powder.

Used in the treatment of the following :

Leishmaniasis:

Alternative to sodium stibogluconate for visceral leishmaniasis

Pneumocystis jiroveci:

Treatment and prophylaxis of patients who cannot tolerate or fail other drugs.

Trypanosomiasis:

For early hemolymphatic stage.

Adverse Effects: Pancreatic, Renal, and Hepatic toxicity.(distinctive)

LEPROSY:

- **A chronic disease caused by the bacteria Mycobacterium leprae and Mycobacterium lepromatosis**
- **a granulomatous disease of the peripheral nerves and mucosa of the upper respiratory tract, skin lesions are the primary external sign**
- **the first drug discovered for the treatment of leprosy was dapsone and its mechanism of action is : Targets dihydropteroate synthase (DHPS)**

- **Inhibits nucleic acid synthesis**

Drugs for the treatment of leprosy:

- **<u>1.Dapsone and Sulphones:</u>**
  - **Related to sulphonamides.**
  - **Inhibit folate synthesis.**
  - **Resistance develops.**
  - **Combined with Rifampin and Clofazimine.**
  - **Also used for *Pn. Jeroveci* in AIDS patients.**
  - **Well absorbed and distributed.**

Retained in the skin, muscle, liver and kidney

The most distinctive side effect is : Hemolysis, particularly in G-6-PD deficiency

The doctor mentioned here a condition that can be either produced by the disease itself or as a side effect of the drugs used to treat it and this condition is :

Erythema Nodosum Leprosum : Inflammation of the fat cells under the skin (panniculitis)

suppressed by :

- **Steroids**
- **Thalidomide**
- **Chochicine**

2. Rifampicin and Clofazimine:

- **Rifampicin (Rifampin): Inhibit RNA synthesis**
- **Clofazimine: Anti-inflammatory**

Rifampin:

- ***Used against Stretomyces miditerranei.***
- **Mycobacteria, enterococci and chlamydia**
- **Binds to the beta subunit of bacterial DNA-dependant RNA polymerase and therefore inhibits RNA synthesis.**

- **Rifampin does not affect mammalian polymerases**
- **Bactericidal**
- **Well distributed.**
- **Well absorbed, highly bound to proteins**
- **Hepatic metabolism and exhibits enterohepatic recirculation.**

Uses of rifampin:

- **TB**
- **Leprosy**
- **Meningococcal Carrier State**
- **Prophylaxis in *H.influenzae.***
- **Serious Staph osteomyelitis and valve endocarditis.**

Major side effects :

- **Hepatitis is a major adverse effect, and the risk is highest in patients with underlying liver diseases and in slow isoniazid acetylators; the rate of hepatotoxicity is increased if isoniazid and rifampin are combined**
- **Induce hepatic cytochrome P-450 enzymes, leading to an increased metabolism of many drugs**
- **An immune-mediated systemic flu-like syndrome with thrombocytopenia also has been described.**
- **Rifampin imparts a harmless red-orange color to urine, feces, saliva, sweat, tears, and contact lenses.**

This is an important not about this drug : Absorption is impaired if rifampin is given concurrently with aminosalicylic acid or is taken immediately after a meal

<u>clofazimine:</u>

- **Binds to DNA.**
- **Stored widely in RES and skin.**
- **Released slowly from storage sites, $t_{1/2}$ = 2 months.**
- **Given for sulphone- resistant or intolerant cases.**
- **Causes skin discoloration (red-brown to black) and GI intolerance .**