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 anaphylactic reactions. Nephrotoxicity is the most common and the most serious long-term toxicity of amphotericin B administration so it is a very toxic drug.

3. Miltefosine
- An alkylphosphocholine analog
- For visceral leishmaniasis.
• Given orally, for 28 days.
• Causes V & D, hepatotoxicity, nephrotoxicity, and it is teratogenic.

• 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:

• **1. Dapsone and Sulphones:**
  – 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 clofazimine:

  – 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.