

# **ANTI-PROTOZOAL DRUGS**

Prepared By

**DOPPALAPUDI SANDEEP**

**M. Pharmacy,**

**Assistant Professor**

**Department of Physiology & Pharmacology**

**Chebrolu Hanumaiah Institute of**

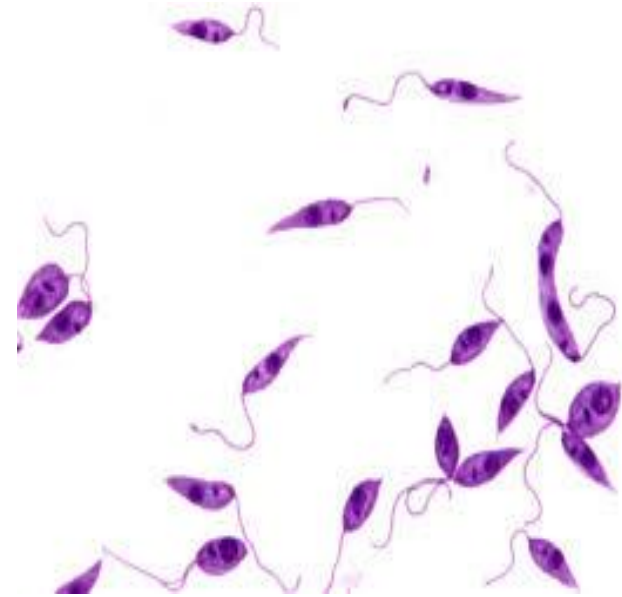
**Pharmaceutical Sciences,**

**Chandramoulipuram, Chowdavaram, Guntur,**

**Andhra Pradesh, India – 522019**

# PROTOZOAL INFECTIONS

- They include
  1. Giardiasis
  2. Trichomoniasis
  3. Leishmaniasis
  4. Trypanosomiasis



# GIARDIASIS

- Caused by *Giardia lamblia* – a flagellate protozoan which lives mostly as a commensal in intestine.
- Invades mucosa and causes diarrhoea.
- **DRUGS USED:**
- Metronidazole- 200 mg TDS for 7 days
- Tinidazole- 0.6 g daily for 7 days.
- Mepacrine- 100 mg TDS for 5 days (most effective, but has side effects).
- Quiniodochlor- 250 mg TDS for 7 days
- **Furazolidine**- a nitrofurantoin compound-100 mg TDS for 5-7 days.
- Used in bacterial enteritis, food poisoning, bacillary dysentery.
- Excreted in urine in ORANGE colour.
- **Side effects** – mild nausea, headache, dizziness.

# TRICHOMONIASIS

- Caused by *Trichomonas vaginalis*- a flagellate protozoan.
- DRUGS USED:
- **1. ORAL ROUTE:**
- **Metronidazole**- 400 mg TDS for 7 days.
- **Tinidazole**- 600 mg daily for 7 days. } **>90% cure**
- Recurrences can be treated by intravaginal treatment.
- Recurrences may be due to reinfection from male partner who is having infection in seminal vesicles.
- **Nimorazole**- 2g single dose with meals.
- **2. INTRAVAGINAL ROUTE:**
- **Diiodohydroxyquin**- 200 mg inserted intravaginally at bed time for 1-2 weeks.
- **Clotrimazole**- 100 mg inserted highup in vagina night for 6-12 days.
- **Hamycin**- 4-8 lac U intravaginally for 15 days.
- **Povidone-iodine**- 400 mg inserted in vagina daily-night-2 weeks.

# LEISHMANIASIS

- Visceral leishmaniasis (Kala-Azar) caused by *Leishmania donovani*.
- Transmitted by the bite of female sandfly phlebotomus.
- In the fly, the parasite exists in the flagellate extracellular form (promastigote).
- **DRUGS USED:**
  1. **ANTIMONIALS** - Sodium stibogluconate, Meglumine antimonate
  2. **DIAMIDINES** - Pentamidine
  3. **OTHERS** - Amphotericin-B, Ketoconazole, Allopurinol.
- **AMPHOTERICIN-B:**
  - As like fungi, Leishmania also has higher amounts of ergosterol.
  - Highly effective in Kala-azar, used in resistance cases of Sod.stibogluconate.
  - High **TOXICITY** and repeated slow I.V infusion rate limits its use.
  - Liposomal AMB delivers drug inside liver and spleen cells.
  - **DOSE:** 1<sup>st</sup> 0.1 mg/kg-increase to 1mg/kg slow i.v infusion-total 20mg/kg. given in alternative days.

# ANTIMONIALS

- **SODIUM STIBOGLUCONATE:**

- Drug of choice for kala azar.
- Water soluble, pentavalent, contains 1/3<sup>rd</sup> antimony by weight.
- MOA is unclear. –SH dependant enzymes are inhibited and bioenergetics of parasites may be interfered.
- Blocks glycolytic and fattyacid oxidation pathways.
- Rapidly absorbed from site of I.M inj, excreted unchanged in urine.
- WHO recommended a dose of 20 mg/kg daily by I.M or I.V inj for 20-30 days or more.
- Cofirmed cure- when NO parasites are detected in splenic or bone marrow.
- Relapses should be retreated immediately by using the same doses.
- In case of failure, combine with allopurinol or AMB.
- **ADVERSE EFFECTS:**
- Nausea, vomiting, metallic taste, cough, abdominal pain, stiffness in muscle, mental. ECG changes are rare. Shock is also reported.
- Less toxic than diamidines.

# DIAMIDINES

- **PENTAMIDINE:**
- MOA not known. It may interfere with aminoacid transport, disrupts mitochondria and inhibits transformation of amastigotes to promastigotes.
- Drug can be seen in urine for 6-8 weeks. Concentrated in liver and a bit enters into brain tissue.
- **ADVERSE EFFECTS:**
- Breathlessness, nausea, vomiting, facial flushing, arrhythmia, hypotension. Local irritation.
- Hepatotoxicity, hypocalcemia, acute renal failure.
- Patients may develop Insulin dependant DM (pancreatic  $\beta$  cells).
- **USES:** Visceral and mucocutaneous leishmaniasis.
- Used in antimonial failure cases.
- Pneumocystis carinii pneumonia in AIDS patients- 1<sup>st</sup> line drug with cotrimoxazole. IM/IV/Inhalation. 300 mg aerosol once for every 4 weeks
- Trypanosomiasis- used before CNS involvement.



# TRYPANOSOMIASIS

- Caused by parasite *Trypanosoma*.
- Two types:
  - 1. **AFRICAN trypanosomiasis- SLEEPING SICKNESS** caused by *T. gambiense* transmitted by tse-tse fly.
  - 2. **SOUTH AMERICAN trypanosomiasis- CHAGAS DISEASE** caused by *T. cruzi* transmitted by blood sucking Reduviid bugs.
- **DRUGS USED:**
  - 1. **Organic UREALs** - Suramin sodium  
Pentamidine isethionate
  - 2. **Organic ARSENICALS** - Melarsoprol,  
Melarsonyl potassium.
- **Suramin sodium** - Organic urea compound. Parasites loses their infectivity. MOA not known. Persists in plasma for 3 months. Painful IM inj. Given Ivly. Doesn't cross BBB. So not useful in encephalitic stage.
- **ADVERSE EFFECTS:** shock, chills, fever, photophobia, nephrotoxicity.
- **DOSE:** 10% sol in dist.water IV 5-7 days – 5-6 injections.
- **Pentaminidine isethionate-** substitute for suramin-3-4 mg/kg 10 doses I.V on alternative days.

# ORGANIC ARSENICALS

- **MELARSOPROL (MEL-B): (Essential medicine)**
- Formerly used in the treatment of Late African Trypanosomiasis (trypanocidal).
- **Mechanism of action:** mainly acts by disrupting the energy generation in parasite. Drug binds with Sulfhydryl groups in parasite (which are necessary for maintenance of structure of proteins and kinase enzymes action).
- As a result, the protein structure disrupts and kinase function diminishes leading to inhibition of ATP synthesis. As a result, the organism dies.
- **KINETICS:** Fairly well absorbed orally (but not given). Mostly I.V.
- Crosses BBB, rapidly excreted in urine.
- NOT indicated in breast-feeding women.
- As it contains **ARSENIC**, supervised medication is necessary.
- **SIDE EFFECTS:** Convulsions, fever, loss of consciousness, rashes, bloody stools, nausea and vomiting. Also causes encephalopathy and sometimes death.
- Peripheral neuropathy. Pain and inflammation at site of injection. Hepatic dysfunction, arrhythmias, arthralgia may also be observed.
- Also used in the treatment of sleeping sickness.
- DOSE: 3.6mg/kg per day for 3 days. Max dose of 180 mg/day.