

# ANTI-PROTOZOAL DRUGS

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- Protozoa are a diverse group of mostly motile unicellular eukaryotic organisms

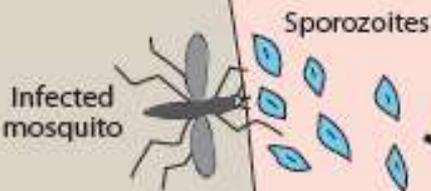
## 1. Treatment of Malaria:

- Malaria is an acute infectious disease caused by four species of the protozoal genus Plasmodium.

*P falciparum*, *P vivax*, *P malariae*, and *P ovale*

- *P falciparum* is the most dangerous species, causing an acute, rapidly fulminating disease that is characterized by persistent high fever, orthostatic hypotension, and massive erythrocytosis. This infection can lead to capillary obstruction and death if not treated.
- *P malariae* is common to many tropical regions,

**1** An infected mosquito injects sporozoites.



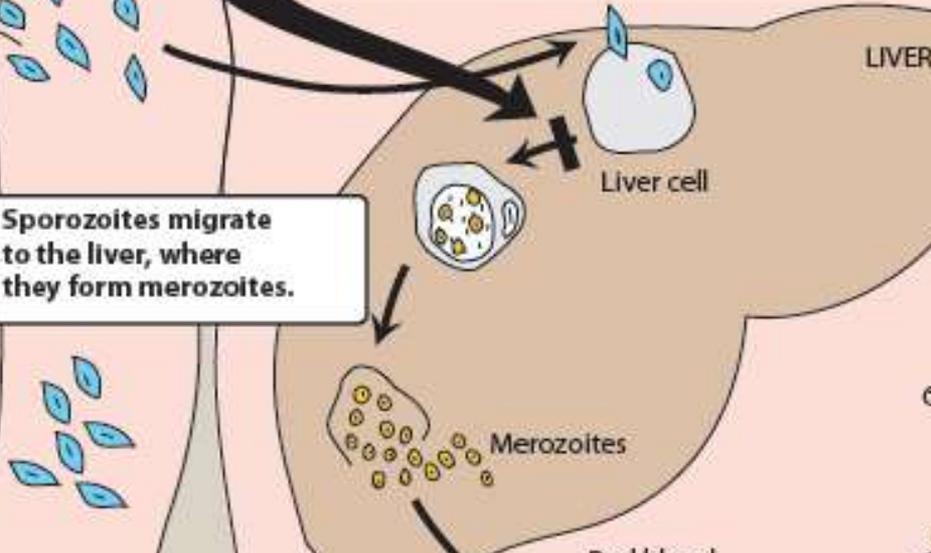
**Drug effective against gametocytic form:**

- Primaquine

**Drug effective against exoerythrocytic form:**

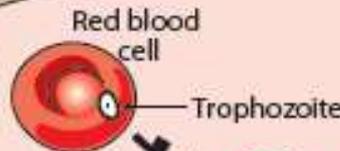
- Primaquine

**2** Sporozoites migrate to the liver, where they form merozoites.



Infection can also result from use of a blood-contaminated needle

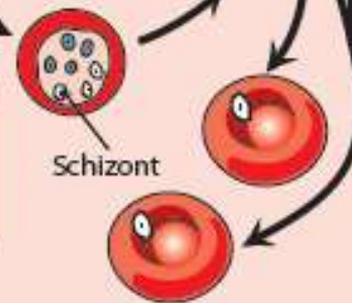
**3** Merozoites are released and invade red blood cells.



**Drugs effective against erythrocytic form:**

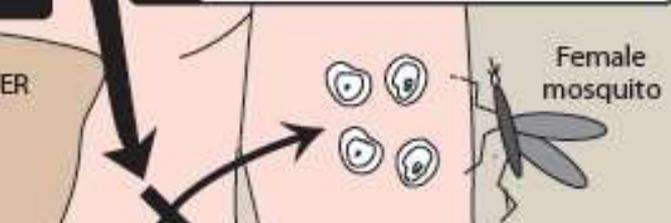
- Artemisinin
- Chloroquine
- Quinine
- Mefloquine
- Pyrimethamine

**4** In the red blood cell, the merozoite becomes a trophozoite.



**7** The female mosquito picks up gametocytes from an infected human. The sexual cycle occurs in the mosquito, where sporozoites are formed.

**6** Some merozoites become gametocytes.



**5** In the red blood cell, the trophozoite multiplies, producing new merozoites. These are released when the red blood cell ruptures, and they can infect other red blood cells.

**5**

# CLASSIFICATION OF ANTI-MALARIALS

Several classes of antimalarial drugs are available:

- 1. Tissue schizonticides (Exoerythrocytic):** Drugs that eliminate developing or dormant liver forms (**Primaquine**)
- 2. Blood schizonticides (erythrocytic):** those that act on erythrocytic parasites (**Artemisinin, chloroquine, quinine, mefloquine, pyrimethamine**)
- 3. Gametocides:** those that kill sexual stages and prevent transmission to mosquitoes. (**primaquine**)
- 4. Radical cure:** eliminate both hepatic and erythrocytic stages. **Primaquine**
- 5. Causal prophylactic drugs:** those capable of preventing erythrocytic infection. **Chloroquine and Pyrimethamine**

# 1. TISSUE SCHIZONTICIDES:

- *Primaquine* eradicates exoerythrocytic forms of recurring malarial and has gametocidal action.
- *Primaquine* is the only agent that can lead to radical cures of malarial,

## **Mechanism of action:**

- It interferes with plasmodial mitochondria

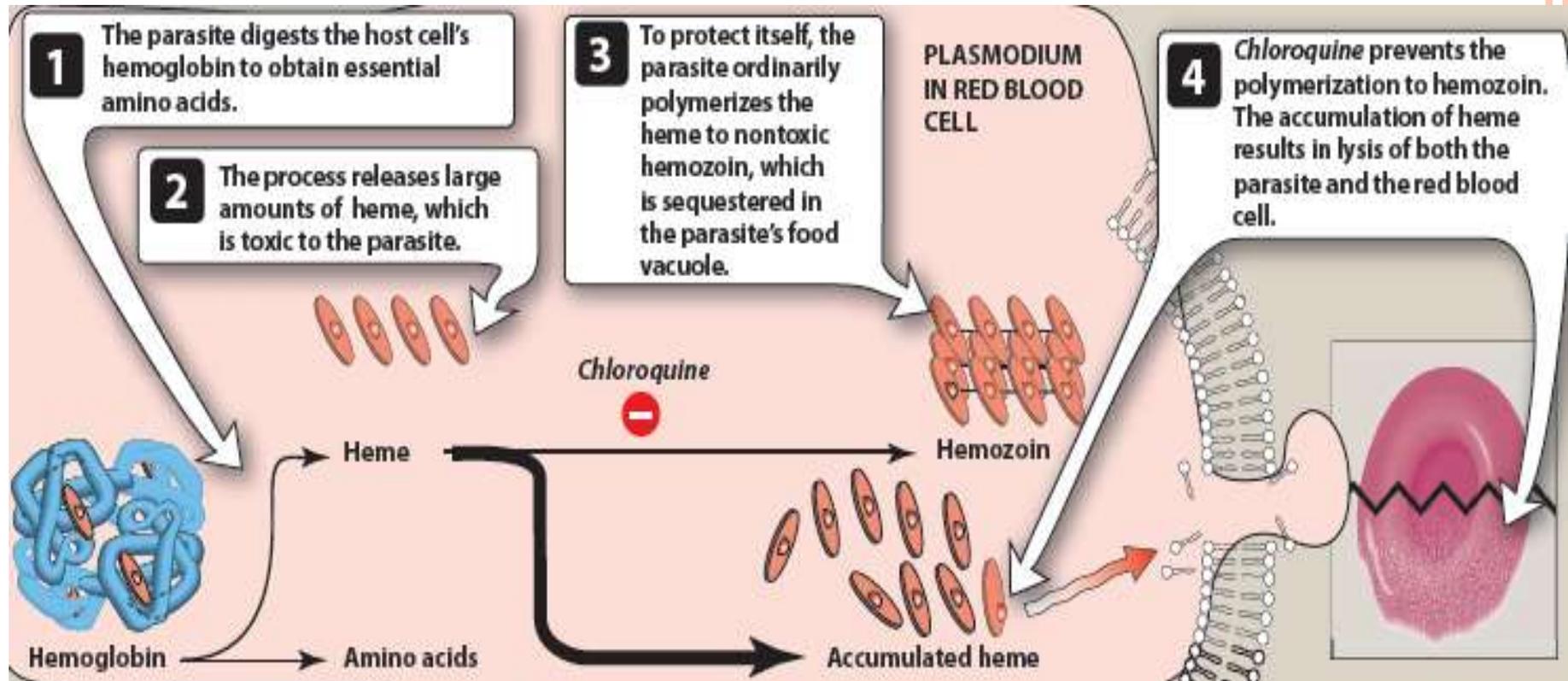
## **Adverse effects**

1. GI upset.
2. Jaundice.
3. Haemolytic anaemia (in patients with glucose-6-phosphate dehydrogenase deficiency).

## 2. BLOOD SCHIZONTICIDES:

### 1. Chloroquine :

- is the drug of choice in the treatment of erythrocytic malaria
- It prevents polymerization of heme to hemozoin leading to lysis of parasite and red blood cells



## **Therapeutic uses:**

1. Treatment & prophylaxis of malaria.
2. Hepatic amoebiasis
3. Others as in rheumatoid arthritis for its anti-inflammatory actions.

## **Adverse effects:**

1. GI upset.
2. Rashes & pruritis.
3. Pigmentation of skin & mucous membrane.
4. Deposition in cornea, iris & retina (retinopathy) causing various ocular manifestations.

## **Precautions:**

1. Should not be taken by patients with psoriasis because of risk of exacerbation of the disease.
2. Regular ocular examination is needed during prolonged therapy to detect early ocular complications.

## 2. Quinine:

➤ It interferes with heme polymerization leading to death of parasites

➤ *Cinchonism or quinism*

### Adverse effects

➤ GI upset (nausea & vomiting).

➤ Blood disorders (haemolysis and thrombocytopenia)

➤ Allergic rashes

➤ Cinchonism.

➤ Hypotension, convulsion, respiratory depression and ventricular tachycardia (following rapid IV).

## 3. Mefloquine

➤ Used for multi-resistant forms of *P. falciparum*, single, produce cure

➤ Damage parasite membrane as quinine

## 4. Artemisinin

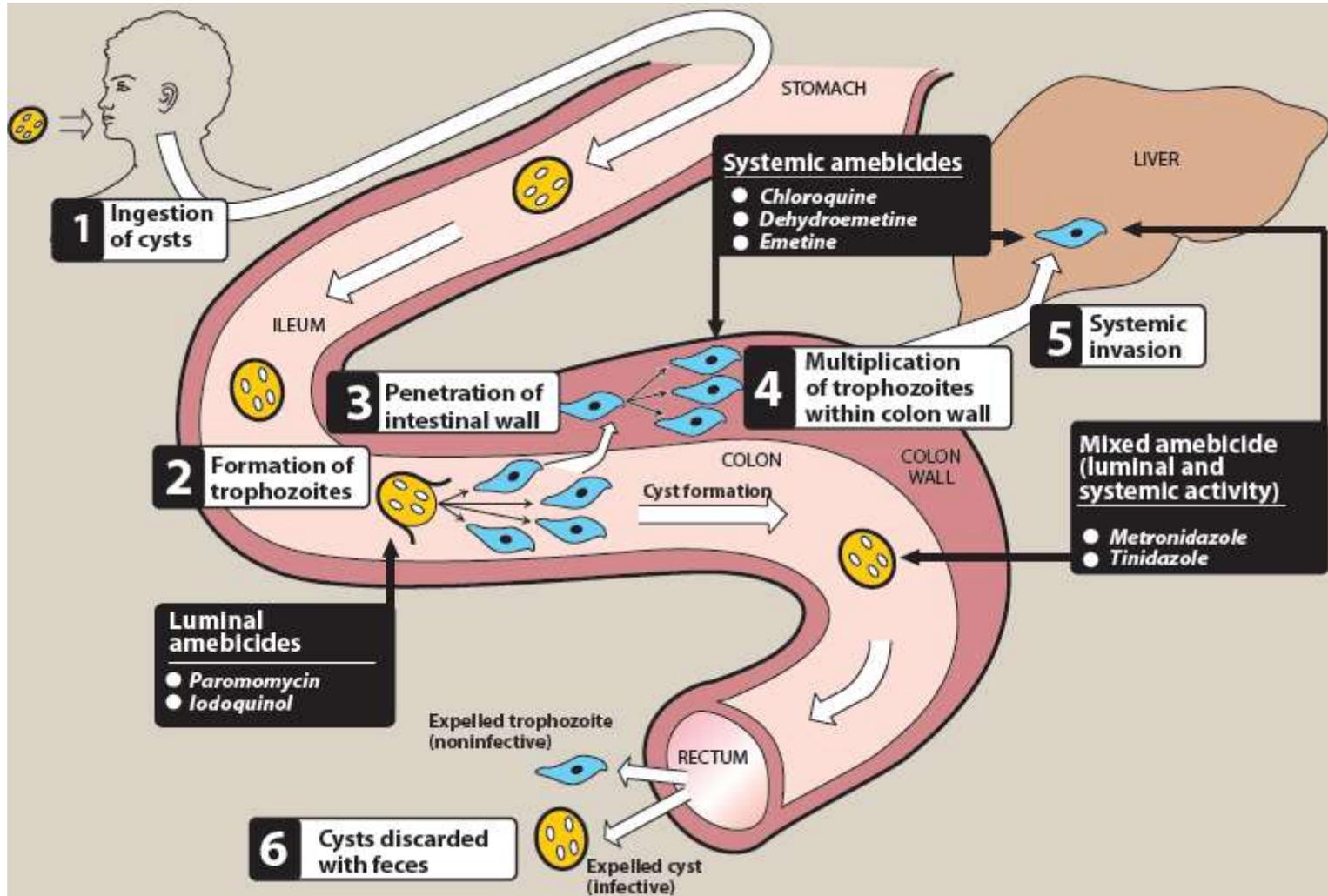
- For multi-resistant *Falciparum* malaria
- It acts by Production of free radicals
- It produces Neurotoxicity

## 5. Pyrimethamine

- It is a dihydrofolate reductase inhibitor useful in the prophylaxis of malaria and treatment of chloroquine-resistant malaria.
- Prolonged use may lead to bone marrow depression & therefore, blood counts are needed.
- Folate deficiency: **Folinic acid** is commonly administered to protect against folate deficiency

# DRUG THERAPY OF AMOEBIASIS

- Amebiasis (amebic dysentery) is an infection intestinal tract caused by *Entamoeba histolytica*.
- mild diarrhea to fulminating dysentery.



## ***A.Mixed Ambicides (Luminal and systmic) :***

### **1. Metronidazole (Flagyl)**

- This is an anti-microbial agent that has an amoebicidal activity against the vegetative form of the *Entamoeba histolytica*.

### **Mechanism of action**

Metronidazole acts by interference with DNA.

### **Therapeutic uses**

- Acute amoebic dysentery.
- Hepatic amoebiasis & pulmonary amoebiasis.
- Anaerobic bacterial infections.
- Postoperative prophylaxis.
- Trichomoniasis: is primarily an infection of the urogenital tract
- Giardiasis.
- Ulcertive gingivitis.
- Non-specific vaginitis.

## Adverse effects

1. Metallic taste in the mouth.
  2. GI disturbances.
  3. Headache
  4. Allergy
- Metronidazole is **contraindicated** in the first trimester of pregnancy.

## 2. Tinidazole:

- is a second-generation imidazole family that is similar to metronidazole in spectrum of activity.
- Treatment of amebiasis, amebic liver abscess, giardiasis, and trichomoniasis
- Tinidazole is as effective as metronidazole, with a *shorter course of treatment*.

## ***B. Luminal amebicides:***

- A luminal agent should be administered for treatment of the *asymptomatic colonization state*(carrier to disease).

### **1. Iodoquinol:**

- is amebicidal against *E. histolytica* and is effective against the luminal trophozoite and cyst forms.
- Side effects include rash and diarrhea

### **2. Paromomycin:**

- Effective against the intestinal (luminal) forms of *E. histolytica*.
- It exerts its antiamebic actions by *reducing the population of intestinal flora*. Its direct amebicidal action is probably due to the effects it has on cell membranes, causing leakage.
- Adverse effects: diarrhea

## C. Systemic amebicides:

- liver abscesses and intestinal wall infections

**1. Chloroquine: is used in combination with metronidazole** to treat and prevent amebic liver abscesses

### **2. Emetine Hcl & dehydroemetine**

- They are used in amoebiasis when there is intolerance to metronidazole or when there is no response to it.
- They have low safety index & may cause cardiotoxicity.
- Dehydroemetine is less cumulative & less cardiotoxic.

### **Adverse effects**

These agents are given as IM injection in hospital under close supervision because of risk of toxicity.

- GI upset (nausea & vomiting).
- Allergy (rashes & urticaria).
- Cardiovascular effects like chest pain, tachycardia, hypotension & ECG abnormalities.

# CHEMOTHERAPY FOR GIARDIASIS

- Giardia lamblia
- Although some infections are asymptomatic, severe diarrhea can occur, which can be very serious in immune-suppressed patients.

## **Treatment :**

1. Metronidazole for 5 days.

Or

2. Tinidazole, which is equally effective as metronidazole in the treatment of giardiasis but with a much shorter course of therapy (2 grams given once).

# CHEMOTHERAPY FOR LEISHMANIASIS

- There are three types of leishmaniasis: cutaneous, mucocutaneous, and visceral.
- Pentavalent antimonials, such as sodium stibogluconate, are the conventional therapy used in the treatment of leishmaniasis.

## 1. Sodium stibogluconate

- Given daily by IV or IM injections or topically in cutaneous lesions.

# CHEMOTHERAPY FOR TOXOPLASMOSIS

- *Toxoplasma gondii*, which is transmitted to humans when they consume raw or inadequately cooked infected meat.
- An infected pregnant woman can transmit the organism to her fetus.

## Treatment:

- A combination of **sulfadiazine and pyrimethamine**.
- **Folinic acid** is commonly administered to protect against folate deficiency

# Anthelmintics

# 1. TREATMENT OF NEMATODES

- They cause infections of the intestine as well as the blood and tissues (round worm)

## A. Mebendazole:

- Mebendazole acts by inhibiting microtubule synthesis and also by decreasing glucose uptake.

### **Therapeutic uses :**

ascariasis, enterobiasis & ancylostomiasis.

### **Contraindications :**

- Pregnancy: it has been shown to be embryotoxic and teratogenic in experimental animals
- Children under 2 years of age.

## 2. TREATMENT OF CESTODES

- The cestodes, or “true tapeworms,” typically attach to the host’s intestine

### A. Albendazole:

- inhibits microtubule synthesis and glucose uptake
- It is used as alternative to mebendazole against intestinal lumen nematodes; it is given as single oral daily dose.
- Its primary therapeutic application, however, is in the treatment of cestodal infestations, such as cysticercosis (caused by *Taenia solium* larvae or pork tape worm) and hydatid disease
- Treatment of hydatid disease (3 months) has a risk of hepatotoxicity and, rarely, agranulocytosis or pancytopenia

### **3. TREATMENT OF TREMATODES**

- The trematodes (flukes) are leaf-shaped flatworms that are generally characterized by the tissues they infect. For example, they may be categorized as liver, lung, intestinal, or blood flukes

#### **A. Praziquantel:**

- agent of choice for the treatment of all forms of schistosomiasis .
- It increases permeability of the cell membrane to calcium, causing contracture and paralysis of the parasite.