

Antiprotozoal Drugs

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Illustrated Reviews: Pharmacology

- Protozoal infections are common among people in **underdeveloped tropical and subtropical countries**, where
 - sanitary conditions,
 - hygienic practices, and
 - control of the vectors of transmission are inadequate.
- However, with increased **world travel**, protozoal diseases are no longer confined to specific geographic locales.
- Because they are unicellular eukaryotes, the protozoal cells have metabolic processes **closer to those of the human host than to prokaryotic bacterial pathogens**.

- Therefore, protozoal diseases are **less easily treated than bacterial infections**, and many of the antiprotozoal drugs cause serious **toxic effects** in the host, particularly on cells showing high metabolic activity.
- Most antiprotozoal agents have not proven to be safe for pregnant patients.

II. CHEMOTHERAPY FOR AMEBIASIS

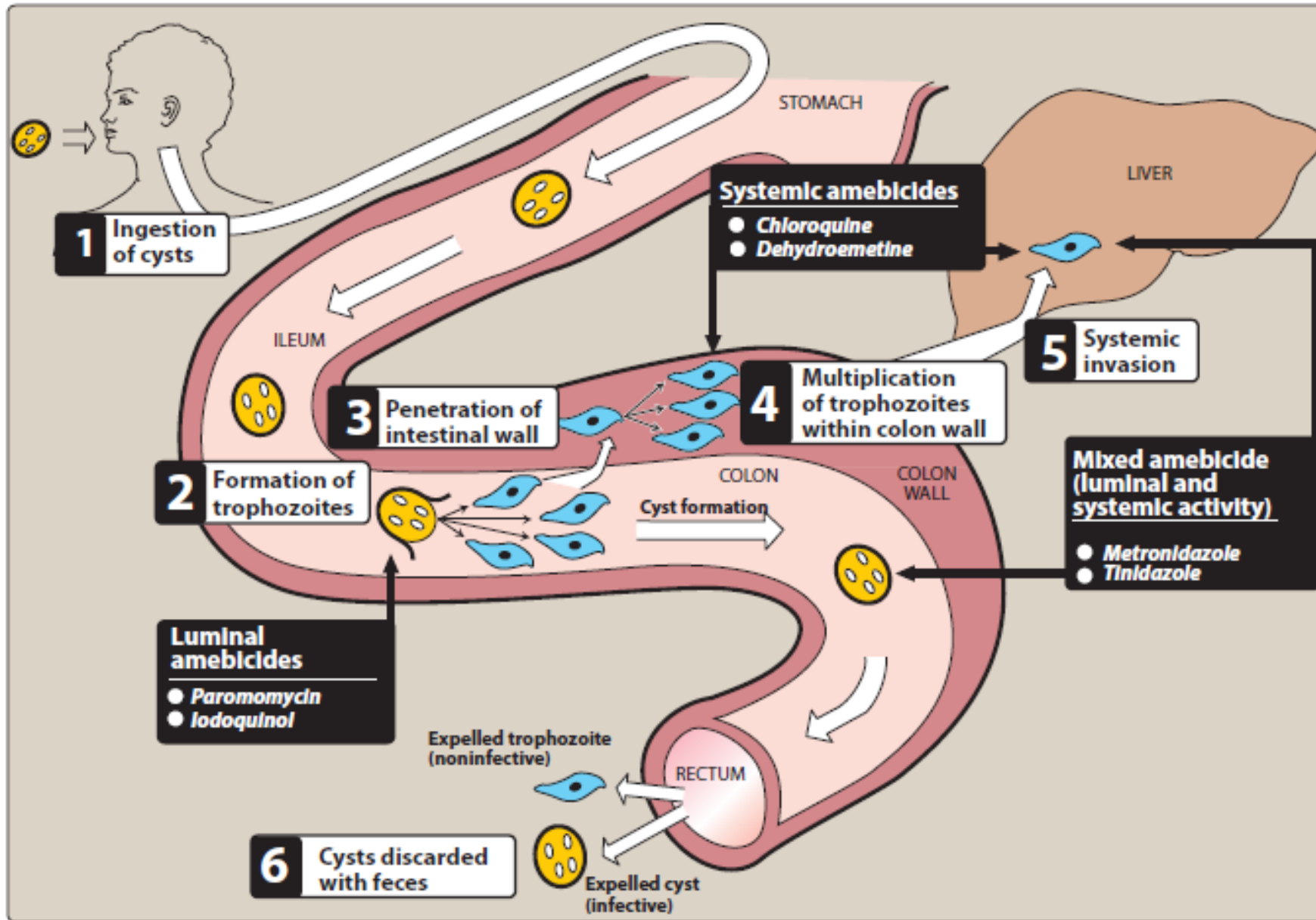
- Amebiasis (also called amebic dysentery) is an infection of the intestinal tract caused by *Entamoeba histolytica*.

The disease can be *acute* or *chronic*, with varying degrees of illness, from no symptoms to mild diarrhea to fulminating dysentery.

The diagnosis is established by isolating *E. histolytica* from feces.

Therapy is indicated for acutely ill patients and asymptomatic carriers, since dormant *E. histolytica* may cause future infections in the carrier and be a potential source of infection for others.

- Therapeutic agents for amebiasis are classified as
 - luminal,
 - systemic, or
 - mixed amebicides according to the site of action.
- For example, luminal amebicides act on the parasite in the lumen of the bowel, whereas systemic amebicides are effective against amebas in the intestinal wall and liver.
- Mixed amebicides are effective against both the luminal and systemic forms of the disease, although luminal concentrations are too low for single-drug treatment.



A. Mixed amebicides

- **Metronidazole:**
- **Tinidazole:**

1. Metronidazole:

- a nitroimidazole, is the mixed amebicide of choice for treating amebic infections.
- [Note: *Metronidazole* is also used in the treatment of infections caused by
 - *Giardia lamblia*,
 - *Trichomonas vaginalis*,
 - anaerobic cocci, and
 - anaerobic gram-negative bacilli (for example, *Bacteroides* species) and is
 - the drug of choice for the treatment of pseudomembranous colitis caused by the anaerobic, gram-positive bacillus *Clostridium difficile*.]

a. Mechanism of action:

- The nitro group of *metronidazole* is able to serve as an electron acceptor, forming **reduced cytotoxic compounds** that bind to proteins and DNA, resulting in death of the *E. histolytica* trophozoites.

b. Pharmacokinetics:

- *Metronidazole* is **completely and rapidly absorbed** after oral administration.
- [Note: For the treatment of amebiasis, it is usually administered with a **luminal amebicide**, such as *iodoquinol* or *paromomycin*.
- This combination provides cure rates of greater than 90%.]
- *Metronidazole* **distributes well throughout body** tissues and fluids. Therapeutic levels can be found in vaginal and seminal fluids, saliva, breast milk, and cerebrospinal fluid (CSF).

- Metabolism of the drug depends on **hepatic oxidation** of the *metronidazole* side chain by mixed- function oxidase, followed by **glucuronidation**.
- Therefore, concomitant treatment with **inducers** of the cytochrome P450, such as *phenobarbital*, **enhances the rate of metabolism**, and **inhibitors**, such as *cimetidine*, **prolong** the plasma half-life of *metronidazole*.
- The drug **accumulates** in patients with severe **hepatic disease**.
- The parent drug and its metabolites are excreted in the urine.

c. Adverse effects:

- The most common adverse effects are nausea, vomiting, epigastric distress, and abdominal cramps
- An unpleasant, **metallic taste** is commonly experienced.
- Other effects include oral moniliasis (yeast infection of the mouth) and, rarely, **neurotoxicity** (dizziness, vertigo, and numbness or paresthesia), which may necessitate discontinuation of the drug.

If taken with alcohol, a *disulfiram-like reaction* may occur.



Nausea



GI disturbance



Metallic taste

Figure 43.3
Adverse effects of
metronidazole.

2. Tinidazole:



- *Tinidazole* [tye-NI-da-zole] is a second-generation nitroimidazole that is similar to *metronidazole* in spectrum of activity, absorption, adverse effects, and drug interactions.
- It is used for treatment of amebiasis, amebic liver abscess, giardiasis, and trichomoniasis.
- *Tinidazole* is as effective as *metronidazole*, with a **shorter course of treatment**, but it is more expensive.
- Alcohol consumption should be avoided during therapy.

B. Luminal amebicides

- After treatment of invasive intestinal or extraintestinal amebic disease is complete, a luminal agent, such as
 - *iodoquinol*,
 - *diloxanide furoate*, or
 - *paromomycin*, should be administered for treatment of the asymptomatic colonization state.

1. Iodoquinol:

- a halogenated 8-hydroxyquinolone, is **amebicidal** against *E. histolytica* and is effective against the **luminal trophozoite** and **cyst** forms.
- Adverse effects of *iodoquinol* include rash, diarrhea, and dose-related peripheral **neuropathy**, including a rare **optic neuritis**.
- Long-term use of this drug should be avoided.

2. Paromomycin:

- *Paromomycin* [par-oh-moe-MYE-sin], an aminoglycoside antibiotic, is only effective against the intestinal (**luminal**) forms of *E. histolytica*, because it is **not significantly absorbed from the gastrointestinal tract**.
- *Paromomycin* is directly **amebicidal** and also exerts its antiamebic actions by reducing the **population of intestinal flora**.
- It is also an alternative agent for cryptosporidiosis and giardiasis. Gastrointestinal distress and diarrhea are the principal adverse effects.

C. Systemic amebicides

- **1. Chloroquine:**
- is used in combination with *metronidazole* (or as a substitute for one of the nitroimidazoles in the case of intolerance) to treat amebic liver abscesses.
- It eliminates trophozoites in liver abscesses, but it is not useful in treating luminal amebiasis.
- Therapy should be followed with a luminal amebicide. *Chloroquine* is also effective in the treatment of malaria.

- **2. Dehydroemetine:**
- is an alternative agent for the treatment of amebiasis.
- The drug **inhibits protein synthesis** by blocking chain elongation.
- **Intramuscular** injection is the preferred route, since it is an irritant when taken orally.
- The use of this ipecac alkaloid is limited by its toxicity, and it has largely been replaced by *metronidazole*.
- Adverse effects include pain at the site of injection, nausea, **cardiotoxicity** (arrhythmias and congestive heart failure), **neuromuscular weakness**, dizziness, and rash.

CLINICAL SYNDROME	DRUG
Asymptomatic cyst carriers	<i>Iodoquinol</i> or <i>paromomycin</i>
Diarrhea/dysentery ExtraIntestinal	<i>Metronidazole</i> plus <i>Iodoquinol</i> or <i>paromomycin</i>
Amebic liver abscess	<i>Metronidazole</i> (or <i>tinidazole</i>) plus <i>Iodoquinol</i> or <i>paromomycin</i>

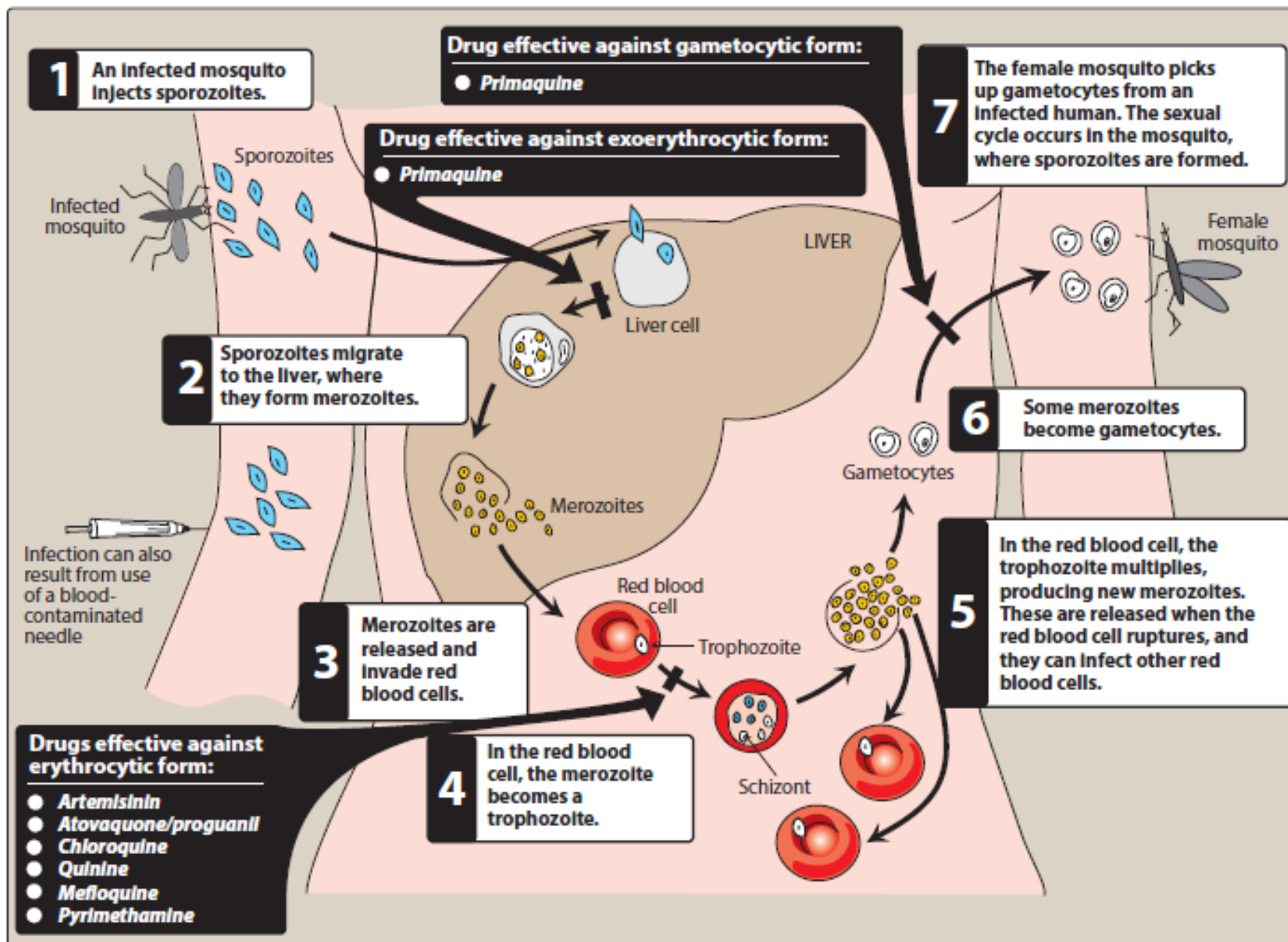
Figure 43.4

Some commonly used therapeutic options for the treatment of amebiasis.

III. CHEMOTHERAPY FOR MALARIA

- Malaria is an acute infectious disease caused by four species of the protozoal genus Plasmodium.
- It is transmitted to humans through the **bite of a female Anopheles mosquito.**
- **Plasmodium falciparum is the most dangerous species,** causing an acute, rapidly fulminating disease that is characterized by
 - **persistent high fever,**
 - **orthostatic hypotension, and**
 - **massive erythrocytosis** (an abnormal elevation in the number of red blood cells accompanied by swollen, reddish limbs).

- P. falciparum infection can lead to **capillary obstruction** and death without prompt treatment.
- Plasmodium vivax causes a milder form of the disease.
- Plasmodium malariae is common to many tropical regions, but Plasmodium ovale is rarely encountered.



A. Primaquine

- *Primaquine* [PRIM-a-kwin], an 8-aminoquinoline, is an oral antimalarial drug that eradicates primary exoerythrocytic (tissue) forms of plasmodia and the secondary exoerythrocytic forms of recurring malaras (*P. vivax* and *P. ovale*).
- [Note: *Primaquine* is the only agent that prevents relapses of the *P. vivax* and *P. ovale* malaras, which may remain in the liver in the exoerythrocytic form after the erythrocytic form of the disease is eliminated.]
- The sexual (gametocytic) forms of all four plasmodia are destroyed in the plasma or are prevented from maturing later in the mosquito, thereby interrupting transmission of the disease.
- [Note: *Primaquine* is not effective against the erythrocytic stage of malaria and, therefore, is used in conjunction with agents to treat the erythrocytic form (for example, *chloroquine* and *mefloquine*).]

- **1. Mechanism of action:**

- While not completely understood, metabolites of *primaquine* are believed to act as oxidants that are responsible for the **schizonticidal action** as well as for the **hemolysis** and methemoglobinemia encountered as toxicities.

- **2. Pharmacokinetics:**

- *Primaquine* is well absorbed after oral administration and is not concentrated in tissues.
- It is rapidly oxidized to many compounds, primarily the deaminated drug. Which compound possesses the schizonticidal activity has not been established.
- The drug is minimally excreted in the urine.

- **3. Adverse effects:**

- *Primaquine* is associated with drug-induced hemolytic anemia in patients with glucose-6-phosphate dehydrogenase deficiency
- Large doses of the drug may cause abdominal discomfort (especially when administered in combination with *chloroquine*) and occasional **methemoglobinemia**.
- *Primaquine* should not be used during pregnancy. All *Plasmodium* species may develop resistance to *primaquine*.

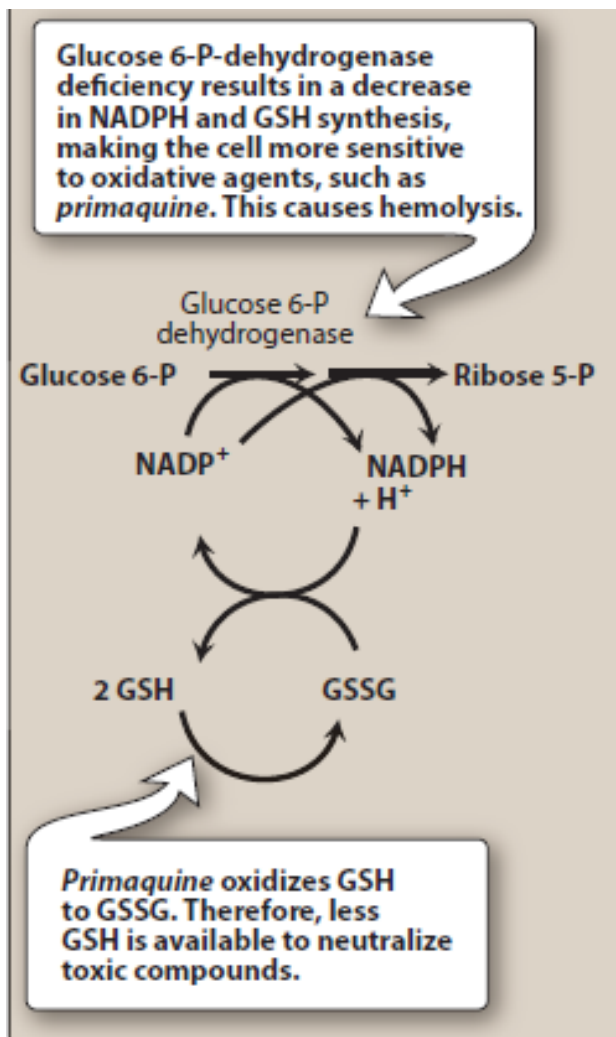


Figure 43.6

Mechanism of *primaquine-induced* hemolytic anemia. GSH = reduced glutathione; GSSG = oxidized glutathione; NADP⁺ = nicotinamide adenine dinucleotide phosphate; NADPH = reduced nicotinamide adenine dinucleotide phosphate.

B. Chloroquine

- *Chloroquine* is a synthetic 4-aminoquinoline that has been the mainstay of antimalarial therapy, and it is the drug of choice in the treatment of erythrocytic *P. falciparum* malaria, except in resistant strains.
- *Chloroquine* is less effective against *P. vivax* malaria. It is highly specific for the asexual form of plasmodia.
- *Chloroquine* is used in the prophylaxis of malaria for travel to areas with known *chloroquine*-sensitive malaria.
- [Note: *Hydroxychloroquine* is an alternative to *chloroquine* for the prophylaxis and treatment of *chloroquine*-sensitive malaria.] It is also effective in the treatment of extraintestinal amebiasis.

1. Mechanism of action

- : Although the mechanism of action is not fully understood, the processes essential for the antimalarial action of *chloroquine* are outlined in Figure 43.7.

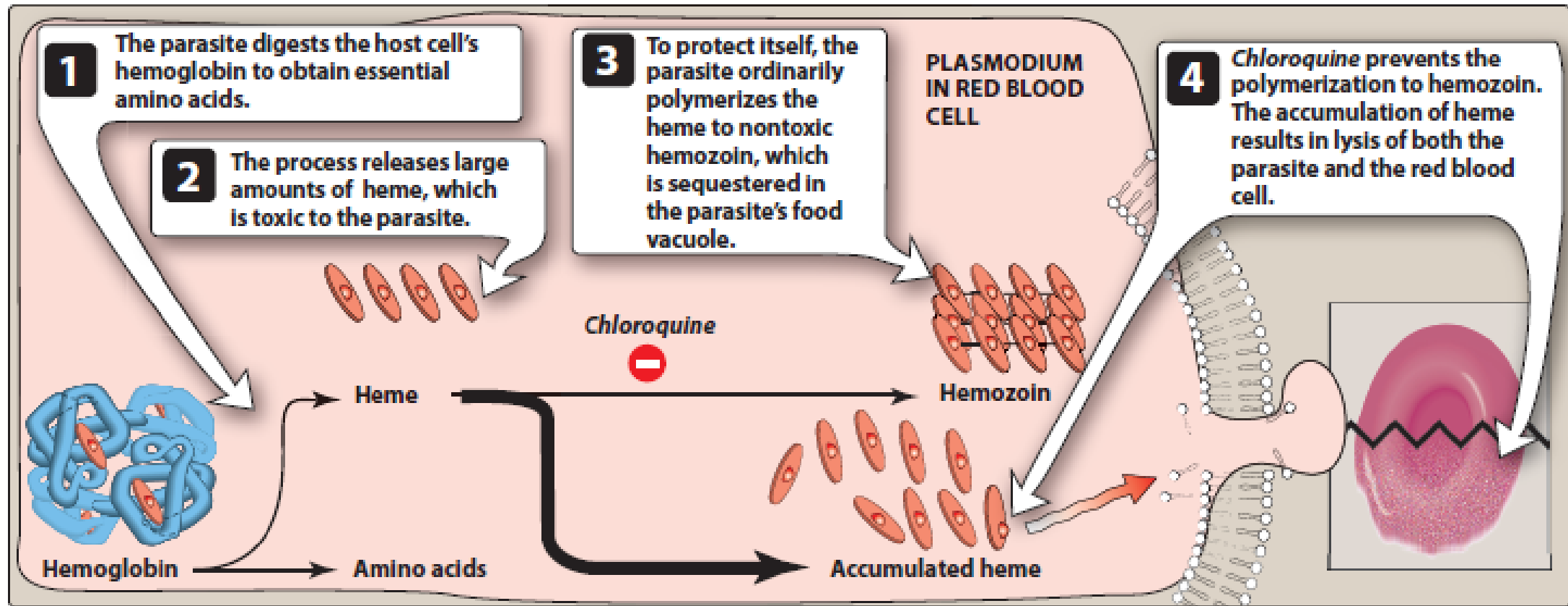


Figure 43.7

Action of *chloroquine* on the formation of hemzoin by Plasmodium species.

2. Pharmacokinetics:

- *Chloroquine* is rapidly and completely absorbed following **oral** administration.
- The drug has a very **large volume of distribution** and concentrates in erythrocytes, liver, spleen, kidney, lung, and melanin-containing tissues, and leukocytes.
- It persists in erythrocytes.
- The drug also penetrates the central nervous system (CNS) and traverses the placenta.
- *Chloroquine* is dealkylated by the hepatic mixed-function oxidase system, and some metabolic products retain antimalarial activity.
- Both parent drug and metabolites are excreted predominantly in urine.

3. Adverse effects:

- Side effects are minimal at low prophylactic doses.
- At higher doses, gastrointestinal upset, pruritus, headaches, and blurred vision may occur
- [Note: An ophthalmologic examination should be routinely performed.]
- Discoloration of the nail beds and mucous membranes may be seen on chronic administration.

- *Chloroquine* should be used cautiously in patients with
 - hepatic dysfunction,
 - severe gastrointestinal problems,
 - or neurologic disorders.
- Patients with **psoriasis** or **porphyria** should not be treated with *chloroquine*, because an acute attack may be provoked.
- *Chloroquine* can prolong the **QT interval**, and use of other drugs that also cause QT prolongation should be avoided if possible.

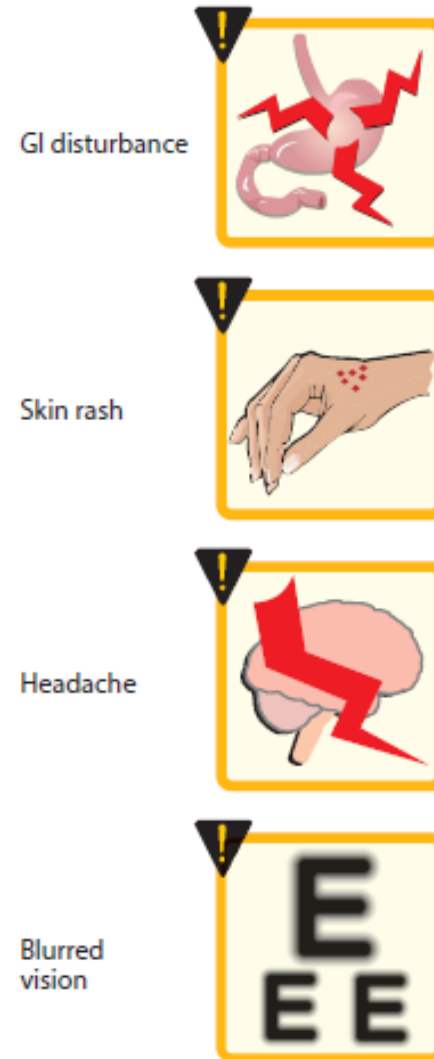


Figure 43.8
Some adverse effects
commonly associated with
chloroquine.

C. Atovaquone–proguanil

- The combination of *atovaquone–proguanil* is effective for *chloroquine-resistant strains* of *P. falciparum*, and it is used in the prevention and treatment of malaria.
- *Atovaquone* inhibits mitochondrial processes such as *electron transport, as well as ATP and pyrimidine biosynthesis*.
- Cycloguanil, the active metabolite of *proguanil*, inhibits plasmodial dihydrofolate reductase, thereby preventing *DNA synthesis*.
- *Proguanil* is metabolized via CYP2C19, an isoenzyme that is known to exhibit a genetic polymorphism resulting in poor metabolism of the drug in some patients.
- The combination should be *taken with food or milk to enhance absorption*. Common adverse effects include nausea, vomiting, abdominal pain, headache, diarrhea, anorexia, and dizziness.

D. Mefloquine

- is an effective single agent for prophylaxis and treatment of infections caused by **multidrug-resistant forms of *P. falciparum***.
- Its exact mechanism of action remains undetermined.
- Resistant strains have been identified, particularly in Southeast Asia.
- *Mefloquine* is well absorbed after oral administration and is widely distributed to tissues

- It has a **long half-life (20 days)** because of **enterohepatic circulation** and its **concentration in various tissues**.
- The drug undergoes extensive metabolism and is primarily excreted via the bile into the feces.
- Adverse reactions at high doses range from nausea, vomiting, and dizziness to disorientation, **hallucinations, and depression**.
- Because of the potential for **neuropsychiatric reactions**, *mefloquine* is usually reserved for treatment of malaria when other agents cannot be used.
- **ECG abnormalities and cardiac arrest are possible** if *mefloquine* is taken concurrently with *quinine* or *quinidine*.

E. Quinine

- *Quinine*, originally isolated from the bark of the cinchona tree, interferes with **heme polymerization**, resulting in death of the erythrocytic form of the plasmodial parasite.
- It is reserved for severe infestations and for *chloroquine*-resistant malarial strains.
- *Quinine* is usually administered in combination with *doxycycline*, *tetracycline*, or *clindamycin*.

- Taken orally, *quinine* is well distributed throughout the body.
- The major adverse effect of *quinine* is cinchonism, a syndrome causing nausea, vomiting, tinnitus, and vertigo.
- These effects are reversible and are not reasons for suspending therapy.
- However, *quinine* treatment should be suspended if hemolytic anemia occurs.
- Drug interactions include **potentiation of neuromuscular- blocking agents** and **elevation of *digoxin* levels** if taken concurrently.
- *Quinine* absorption is reduced by aluminum-containing antacids.

F. Artemisinin



- *Artemisinin* [ar-te-MIS-in-in] is derived from the sweet wormwood plant, which has been used in traditional Chinese medicine for many centuries.
- *Artemisinin* and its derivatives are recommended first-line agents for the treatment of **multidrug-resistant *P. falciparum* malaria**.
- **To prevent the development of resistance, these agents should not be used alone.**

- For instance, *artemether* is coformulated with *lumefantrine* [AR-te-meth-er/loo-me-FAN-treen] and used for the treatment of uncomplicated malaria. [Note: *Lumefantrine* is an antimalarial drug similar in action to *quinine* or *mefloquine*.]
- *Artesunate* [ar-TEZ-oonate] may be combined with *sulfadoxine–pyrimethamine*, *mefloquine*, *clindamycin*, or others.

- The antimalarial action involves the production of free radicals resulting from cleavage of the drug's endoperoxide bridge by heme iron in the parasite food vacuole.
- These agents may also covalently bind to and damage specific malarial proteins.

- Oral, rectal, and intravenous (IV) preparations are available, but the short half-lives preclude the use of these drugs for prophylaxis.
- Adverse effects include nausea, vomiting, and diarrhea.
- High doses may cause prolongation of the QT interval.
- Hypersensitivity reactions and rash have occurred.

G. Pyrimethamine

- inhibits plasmodial dihydrofolate reductase required for the synthesis of tetrahydrofolate (a cofactor needed for synthesis of nucleic acids).
- It acts as a blood schizonticide and a strong sporonticide when the mosquito ingests it with the blood of the human host.
- *Pyrimethamine* is not used alone for *P. falciparum*; it is available as a fixed-dose combination with *sulfadoxine*.

- Resistance to this combination has developed, so it is usually administered with other agents, such as *artemisinin derivatives*.
- *Pyrimethamine* in combination with *sulfadiazine* is also used against *Toxoplasma gondii*.
- If megaloblastic anemia occurs with *pyrimethamine* treatment, it may be reversed with *leucovorin*.

All Plasmodium species except chloroquine-resistant <i>P. falciparum</i>
<i>Chloroquine</i>
Chloroquine-resistant <i>P. falciparum</i>
<i>Atovaquone-proguanil, Artemether/lumefantrine</i> <i>Alternate: Mefloquine, Quinine plus: Doxycycline or clindamycin</i>
Prevention of relapses: <i>P. vivax</i> and <i>P. ovale</i> only
<i>Primaquine</i>
Prevention of malaria
Chloroquine-sensitive geographic areas
<i>Chloroquine</i>
Chloroquine-resistant geographic areas
<i>Atovaquone-proguanil, Doxycycline, Mefloquine</i>
In pregnancy
<i>Chloroquine or mefloquine</i>

Figure 43.9
Treatment and prevention of malaria.

IV. CHEMOTHERAPY FOR TRYPANOSOMIASIS

- **African trypanosomiasis** (sleeping sickness) and **American trypanosomiasis** (also known as Chagas disease) are two chronic and, eventually, **fatal diseases** caused by species of Trypanosoma
- In African sleeping sickness, **T. brucei gambiense** and **T. brucei rhodesiense** initially live and grow in the blood.
- The parasite later **invades the CNS**, causing inflammation of the brain and spinal cord that produces the characteristic lethargy and, eventually, continuous sleep.
- **Chagas disease** is caused by **T. cruzi** and is endemic in Central and South America.

TRYPANOSOMIASIS

AMERICAN: Caused by Trypanosoma cruzi

- Causes cardiomyopathy
- Common in infants
- Transmitted by insect feces contaminating the eye or a break in the skin
- Treated with *nifurtimox*

AFRICAN: Caused by Trypanosoma brucei

- Transmitted by the bite of the tsetse fly
- Causes "sleeping sickness"

Trypanosoma brucei gambiense

- Slow to enter the CNS
- *Suramin* and *pentamidine* are used only in the early stages of disease

Trypanosoma brucei rhodesiense

- Early invasion of the CNS
- Usually fatal if not treated
- *Melarsoprol* used when there is CNS involvement

A. Pentamidine

- *Pentamidine* [pen-TAM-i-deen] is active against a variety of protozoal infections, including **African trypanosomiasis due to *T. brucei gambiense***, for which it is used to treat the first stage (hemolymphatic stage without CNS involvement).
- *Pentamidine* is also an alternative for prophylaxis or treatment of infections caused by ***Pneumocystis jirovecii***. [Note: *P. jirovecii* is an atypical fungus that causes pneumonia in immunocompromised patients, such as those with HIV infection.
- *Pentamidine* is also an alternative drug for the treatment of **leishmaniasis**.

- The drug distributes widely and is concentrated in the liver, kidney, adrenals, spleen, and lungs.
- Because it **does not enter the CSF**, it is ineffective against the second stage (**CNS involvement**) of trypanosomiasis.

B. Suramin

- is used primarily in the first stage (without CNS involvement) of **African trypanosomiasis** due to *T. brucei rhodesiense*.
- It is very reactive and inhibits many enzymes, especially those involved in energy metabolism, which appears to be the mechanism correlated with trypanocidal activity.
- *Suramin* must be injected intravenously.
- It binds to plasma proteins and **does not penetrate the blood–brain barrier** well.
- It has a long elimination half-life (**more than 40 days**) and is mainly excreted unchanged in the urine.

C. Melarsoprol

- is used for the treatment of African trypanosomal infections in the second stage (CNS involvement).
- It is the only drug available for second stage trypanosomiasis due to *T. brucei rhodesiense*.
- Some resistance has been noted, and it may be due to decreased transporter uptake of the drug.
- *Melarsoprol* is administered by slow IV injection and can be very irritating to the surrounding tissue.
- Adequate trypanocidal concentrations appear in the CSF, making *melarsoprol* the agent of choice in the treatment of *T. brucei rhodesiense*, which rapidly invades the CNS.

- The drug has a very short half-life and is rapidly excreted in urine.
- The use of *melarsoprol* is limited by CNS toxicity.
- Reactive encephalopathy may occur, which can be fatal in 10% of cases.
- Hemolytic anemia has been seen in patients with glucose-6-phosphate dehydrogenase deficiency.

D. Eflornithine

- The IV formulation of *eflornithine* is a **first-line treatment for second- stage African trypanosomiasis** caused by *T. brucei gambiense*.
- [Note: **Topical *eflornithine*** is used as a treatment for unwanted facial hair in women.]
- The short half-life of *eflornithine* necessitates frequent IV administration, making the treatment regimen difficult to follow.
- *Eflornithine* is less toxic than *melarsoprol*, although the drug is associated with anemia, seizures, and temporary hearing loss.

E. Nifurtimox

- is used in the treatment of *T. cruzi* infections (**Chagas disease**), although treatment of the chronic stage of such infections has led to variable results.
- It may also be useful for the treatment of **second-stage *T. brucei gambiense*** in combination with *eflornithine*.
- *Nifurtimox* is administered orally.
- Major toxicities include **hypersensitivity** reactions (anaphylaxis, dermatitis) and **gastrointestinal** problems that may be severe enough to cause weight loss.

F. Benznidazole

- It tends to be better tolerated than *nifurtimox* and is an alternative for the treatment of Chagas disease.
- Adverse effects include dermatitis, peripheral neuropathy,
- insomnia, and anorexia.

LEISHMANIASIS

- There are three types of leishmaniasis:
 - cutaneous,
 - mucocutaneous, and
 - visceral.
- [Note: In the visceral type (liver and spleen), the parasite is in the bloodstream and can cause very serious problems.]
- Leishmaniasis is transmitted from animals to humans (and between humans) by the bite of infected **sandflies**.

- For visceral leishmaniasis, parenteral treatments may include *amphotericin B* and *sodium stibogluconate*, with *pentamidine* and *paromomycin* as alternative agents.
- *Miltefosine* is an orally active agent for visceral leishmaniasis.
- The choice of agent depends on the species of *Leishmania*, host factors, and resistance patterns noted in area of the world where the infection is acquired.

A. Sodium stibogluconate

- The exact mechanism of action has not been determined.
- Because it is not absorbed after oral administration, *sodium stibogluconate* must be administered **parenterally**, and it is distributed in the extravascular compartment.
- Metabolism is minimal, and the drug is excreted in urine.
- Adverse effects include injection site pain, pancreatitis, elevated liver enzymes, arthralgias, myalgias, gastrointestinal upset, and cardiac arrhythmias.
- **Renal and hepatic function** should be monitored periodically.

B. Miltefosine

- is the first orally active drug for **visceral** leishmaniasis.
- It may also have some activity against **cutaneous** and **muco-cutaneous** forms of the disease.
- Nausea and vomiting are common adverse reactions.
- The drug is **teratogenic** and should be avoided in pregnancy.

TOXOPLASMOSIS

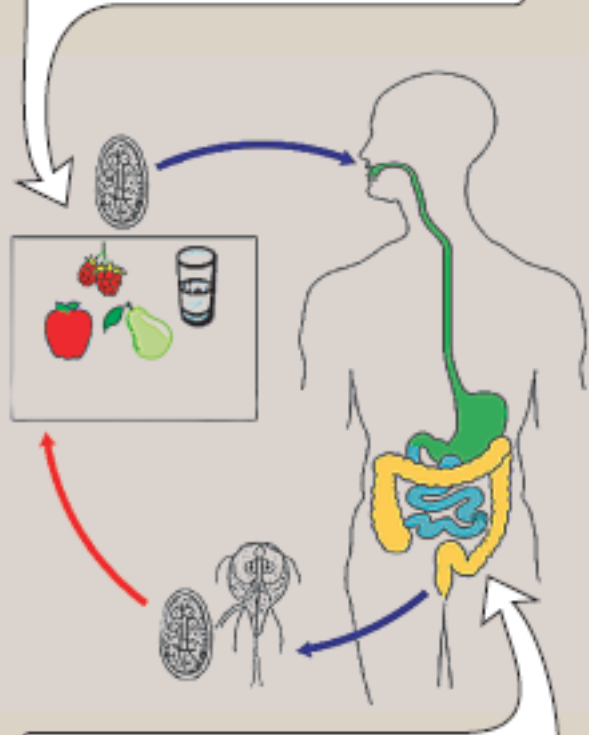
- One of the most common infections in humans is caused by the protozoan *T. gondii*, which is transmitted to humans when they consume raw or **inadequately cooked infected meat**.
- An infected pregnant woman can transmit the organism to her fetus.
- Cats are the only animals that shed oocysts, which can infect other animals as well as humans.

- The treatment of choice for this condition is a combination of *sulfadiazine and pyrimethamine*.
- *Leucovorin* is commonly administered to protect against folate deficiency.
- *Pyrimethamine* with *clindamycin*, or the combination of *trimethoprim* and *sulfamethoxazole*, are alternative treatments.

GIARDIASIS

- Giardia lamblia is the most commonly diagnosed intestinal parasite in the United States.
- **Ingestion**, usually from contaminated drinking water, leads to infection.
- **The trophozoites exist in the small intestine** and divide by binary fission.
- Occasionally, cysts are formed that pass out in stools.
- Although some infections are asymptomatic, **severe diarrhea** can occur, which can be very serious in immunocompromised patients.

Both cysts and trophozoites can be found in feces. Infection occurs by the ingestion of cysts in contaminated water or food, or by the fecal-oral route (via hands or fomites).



In the small intestine, excystation releases trophozoites. Trophozoites multiply in the lumen of the proximal small bowel, where they can be free or attached to the mucosa by a sucking disk. Encystation occurs as the parasites move toward the colon.

- The treatment of choice is oral *metronidazole* for 5 days.
- An alternative is *tinidazole*, which is as effective as *metronidazole* in the treatment of giardiasis.
- This agent is administered orally as a single dose.
- *Nitazoxanide* is also approved for the treatment of giardiasis.
- For giardiasis, *nitazoxanide* is administered as a 3-day course of oral therapy.
- The anthelmintic drug *albendazole* may also be efficacious for giardiasis, and
- *paromomycin* is sometimes used for treatment of giardiasis in pregnant patients.

- After the acute infection, which of the following medications is given to treat the asymptomatic colonization state of *E. histolytica*?
- A. Chloroquine.
- B. Iodoquinol.
- C. Metronidazole.
- D. Primaquine.

- 43.3 Which of the following agents is available as an oral therapy for the treatment of visceral leishmaniasis?
- A. Artemether/lumefantrine.
- B. Miltefosine.
- C. Nitazoxanide.
- D. Tinidazole.

- 43.4 An 18-year-old male is diagnosed with Chagas disease.
- Which medication would be the best for this patient?
- A. Nifurtimox.
- B. Suramin.
- C. Sodium stibogluconate.
- D. Metronidazole.