246e Agents Used to Treat Parasitic Infections

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Parasitic infections afflict more than half of the world's population and impose a substantial health burden, particularly in underdeveloped nations, where they are most prevalent. The reach of some parasitic diseases, including malaria, has expanded over the past few decades as a result of factors such as deforestation, population shifts, global warming, and other climatic events. Despite major efforts at vaccine development and vector control, chemotherapy remains the single most effective means of controlling parasitic infections. Efforts to combat the spread of some diseases are hindered by the development and spread of drug resistance, the limited introduction of new antiparasitic agents, and the proliferation of counterfeit medications. However, there are good reasons to be optimistic. Ambitious global initiatives aimed at controlling or eliminating threats such as AIDS, tuberculosis, and malaria have demonstrated some early successes. Recognition of the substantial burden imposed by the "neglected" tropical diseases has generated multinational partnerships to develop and deploy effective antiparasitic agents. Vaccines against several tropical diseases are being developed, and clinical trials for vaccines against parasites continue.

This chapter deals exclusively with the agents used to treat infections due to parasites. Specific treatment recommendations for the parasitic diseases of humans are listed in subsequent chapters. Many of the agents discussed herein are approved by the U.S. Food and Drug Administration (FDA) but are considered investigational for the treatment of certain infections. Drugs marked in the text with an asterisk (*) are available through the Centers for Disease Control and Prevention (CDC) Drug Service (telephone: 404-639-3670 or 404-639-2888; *www.cdc.gov/ncpdcid/dsr/*). Drugs marked with a dagger (†) are available only through their manufacturers; contact information for these manufacturers may be available from the CDC.

Table 246e-1 presents a brief overview of each agent (including some drugs that are covered in other chapters), along with major toxicities, spectrum of activity, and safety for use during pregnancy and lactation.

Albendazole Like all benzimidazoles, albendazole acts by selectively binding to free β-tubulin in nematodes, inhibiting the polymerization of tubulin and the microtubule-dependent uptake of glucose. Irreversible damage occurs in gastrointestinal (GI) cells of the nematodes, resulting in starvation, death, and expulsion by the host. This fundamental disruption of cellular metabolism offers treatment for a wide range of parasitic diseases.

Albendazole is poorly absorbed from the GI tract. Administration with a fatty meal increases its absorption by two- to sixfold. Poor absorption may be advantageous for the treatment of intestinal helminths, but successful treatment of tissue helminth infections (e.g., hydatid disease and neurocysticercosis) requires that a sufficient amount of active drug reach the site of infection. The metabolite albendazole sulfoxide is responsible for the drug's therapeutic effect outside the gut lumen. Albendazole sulfoxide crosses the blood-brain barrier, reaching a level significantly higher than that achieved in plasma. The high concentrations of albendazole sulfoxide attained in cerebrospinal fluid (CSF) may explain the efficacy of albendazole in the treatment of neurocysticercosis.

Albendazole is extensively metabolized in the liver, but there are few data regarding the drug's use in patients with hepatic disease. Single-dose albendazole therapy in humans is largely without side effects (overall frequency, ≤1%). More prolonged courses (e.g., as administered for cystic and alveolar echinococcal disease) have been associated with liver function abnormalities and bone marrow toxicity. Thus, when prolonged use is anticipated, the drug should be administered in treatment cycles of 28 days interrupted by 14-day intervals off therapy. Prolonged therapy with full-dose albendazole (800 mg/d) should be approached cautiously in patients also receiving drugs with known effects on the cytochrome P450 system.

Amodiaquine Amodiaquine has been widely used in the treatment of malaria for >40 years. Like chloroquine (the other major 4-aminoquinoline), amodiaquine is now of limited use because of the spread of resistance. Amodiaquine interferes with hemozoin formation

TABLE 246e-1 OVERVIEW OF AGENTS USED FOR THE TREATMENT OF PARASITIC INFECTIONS

Drugs by Class	Parasitic Infection(s)	Adverse Effects	Major Drug-Drug Interactions	Pregnancy Class[a]	Breast Milk
4-Aminoquinolines					
Amodiaquine	Malaria[b]	Agranulocytosis, hepatotoxicity	No information	Not assigned	No information
Chloroquine	Malaria[b]	*Occasional:* pruritus, nausea, vomiting, headache, hair depigmentation, exfoliative dermatitis, reversible corneal opacity. *Rare:* irreversible retinal injury, nail discoloration, blood dyscrasias	Antacids and kaolin: reduced absorption of chloroquine Ampicillin: bioavailability reduced by chloroquine Cimetidine: increased serum levels of chloroquine Cyclosporine: serum levels increased by chloroquine	Not assigned[c]	Yes
8-Aminoquinolines					
Primaquine	Malaria[b]	*Frequent:* hemolysis in patients with G6PD deficiency *Occasional:* methemoglobinemia, GI disturbances. *Rare:* CNS symptoms	Quinacrine: potentiated toxicity of primaquine	Contraindicated	No information
Tafenoquine	Malaria[b]	*Frequent:* hemolysis in patients with G6PD deficiency, mild GI upset. *Occasional:* methemoglobinemia, headaches	No information	Not assigned	No information

(*Continued*)