Chapter 6 Parasitic Infections



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Parasitic Infections Encountered in Refugees (Section I)

Parasitic infections are one of the most common infections encountered in refugees, with prevalence estimates for intestinal parasites among North American refugees ranging from 8.4% to 84% [1, 2]. One such study on intestinal parasites burden is shown in Fig. 6.1 [3]. Quantifying the burden of individual parasitic infections can be difficult, and the variance in rates reported in studies results from many factors such as different populations/risks and variance in diagnostic/screening tests employed. For example, diagnostic tests vary in sensitivity and specificity (e.g., direct stool examination versus serology) as well as differing characteristics of refugees (e.g., country of origin, age, education level). In addition, for US-bound refugees, pre-departure presumptive treatment programs including albendazole, ivermectin, and, in some populations, praziquantel are standard and must be considered during the refugee's new arrival and ongoing care after arrival to the United States. Therefore, the risk of each refugee population, and individual, must be considered by the clinician when deciding when to presumptively treat, to screen and treat, or to only perform diagnostic testing in symptomatic people.

The number of parasites that have the potential for human infection can be overwhelming, so this chapter will focus on those that have particular relevance in refugee populations. Broadly, classification of parasites is clinically referred to by phylum

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Parasite*	Total (N = 26,956)	Somalia (N = 11,602)	Ethiopia (N = 3278)	Liberia (N = 2723)	Other African Countries (N = 1063)†	Laos (N = 5959)	Vietnam (N = 1215)	Burma (N = 1116)
				number of refu	gees (percent)			
Any	4897 (18.2)	1775 (15.3)	423 (12.9)	565 (20.7)	242 (22.8)	1412 (23.7)	296 (24.4)	184 (16.5)
Multiple	436 (1.6)	138 (1.2)	41 (1.3)	85 (3.1)	34 (3.2)	75 (1.3)	55 (4.5)	8 (0.7)
Protozoans								
Any	2763 (10.3)	904 (7.8)	198 (6.0)	221 (8.1)	109 (10.3)	1119 (18.8)	57 (4.7)	155 (13.9)
Multiple	52 (0.2)	25 (0.2)	5 (0.2)	2 (0.1)	7 (0.7)	12 (0.2)	0	1 (0.1)
Giardia intestrinalis	2368 (8.8)	629 (5.4)	179 (5.5)	204 (7.5)	80 (7.5)	1089 (18.3)	49 (4.0)	138 (12.4)
Entamoeba‡	447 (1.7)	300 (2.6)	24 (0.7)	19 (0.7)	36 (3.4)	42 (0.7)	8 (0.7)	18 (1.6)
Nematodes								
Any	1975 (7.3)	940 (8.1)	106 (3.2)	237 (8.7)	86 (8.1)	327 (5.5)	250 (20.6)	29 (2.6)
Multiple	172 (0.6)	27 (0.2)	12 (0.4)	37 (1.4)	10 (0.9)	34 (0.6)	45 (3.7)	7 (0.6)
Trichuris trichiura	1243 (4.6)	900 (7.8)	68 (2.1)	136 (5.0)	33 (3.1)	21 (0.4)	70 (5.8)	15 (1.3)
Hookworm	494 (1.8)	21 (0.2)	21 (0.6)	88 (3.2)	35 (3.3)	193 (3.2)	121 (10.0)	15 (1.3)
Ascaris lumbricoides	237 (0.9)	46 (0.4)	17 (0.5)	34 (1.2)	14 (1.3)	16 (0.3)	107 (8.8)	3 (0.3)
Strongyloides stercoralis	205 (0.8)	3 (<0.1)	13 (0.4)	23 (0.8)	15 (1.4)	132 (2.2)	13 (1.1)	6 (0.5)
Trematodes								
Schistosoma species	406 (1.5)	26 (0.2)	147 (4.5)	164 (6.0)	69 (6.5)	0	0	0

A revised form for refugee screening data permitted reporting of additional infections to the Minnesota Department of Health beginning in 1998. The following intestinal parasites detected among newly arrived refugees were excluded from the analysis of the effect of albendazole treatment. Blastocystis hominis (1529 cases), Hymenolepis nana (360), Dientamoeba fragilis (100), Clonorchis sinensis (11), fasciola species (4),

taenia species (17), H. diminuta (2), and diphyllobothrium species (1). † Other countries included Benin, Burundi, Cameroon, Ivory Coast, Democratic Republic of Congo, Eritrea, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, Sudan, Togo, and Uganda. ‡ This category includes pathogenic Entamoeba histolytica and nonpathogenic E. moshkovskii and E. dispar, which cannot be morphologically

differentiated by means of standard light microscopy

Fig. 6.1 Prevalence of intestinal parasites in a large refugee sample in Minnesota. (Figure from Swanson et al. [3])

(Fig. 6.2), starting with endoparasitic protozoans (single-celled organisms), multicellular helminths (worms), and ectoparasites. Helminths are often also referred to by the following groups: nematodes (round worms), trematodes (flat worms, specifically flukes), and cestodes (flat worms, specifically tapeworms). Geographic origin plays a very important role in generating the initial differential formed when seeing a refugee patient (see Table 6.1), especially with certain less common parasites such as the nonschistosome flukes (e.g., Paragonimus) and the cestodes (e.g., Hymenolepis). Common parasites are reviewed below, with recommended treatments.

Protozoa

The protozoa are single-celled organisms that are further characterized by their adult mobility or lack thereof, including amoeba, flagellates, ciliates, and the nonmotile sporozoa. Malaria (Plasmodia) is the most clinically important protozoal infection internationally due to the sheer morbidity and mortality burden, and because of this they will be discussed in a separate chapter (Chap. 8).

The intestinal protozoa cause a range of clinical presentations from no symptoms to mild-moderate symptoms of abdominal discomfort, nausea, diarrhea (bloody or





Global	Africa	Asia	Latin America	Middle East	Eastern Europe
Ascaris lumbricoides Trichuris trichiura Hookworm	Schistosoma sp. (mansoni, haematobium, intercalatum)	Fasciolopsis buski Southeast Asia: Opisthorchis	Taenia solium Schistosoma mansoni Opisthorchis guayaquilensis	Echinococcus	Diphyllobothrium latum Opisthorchis felineus
(Ancylostoma duodenale, Necator americanus) Strongyloides stercoralis Enterobius vermicularis (pinworm) Fasciola hepatica Hymenolepis Most protozoa, especially Giardia intestinalis (lamblia)	Taenia saginata	viverrini Clonorchis sinensis Schistosoma sp. (japonicum mekongi) <u>South Asia</u> : Taenia solium	2 <i>)</i>		

Table 6.1 Predominant geographic distribution of intestinal parasites found in refugee populations

Adapted from CDC Domestic Guidelines [4]. Organisms listed by region are either unique to the location or particularly common or overrepresented

non-bloody), or more serious systemic symptoms including fever. The intestinal protozoans are transmitted by the fecal-oral route. Intestinal protozoa of note are as follows. Table 6.2 outlines treatment regimens for some intestinal protozoan infections.

Entamoeba histolytica Like most protozoa, *E. histolytica* is usually asymptomatic [5]. The most common clinical manifestations include mild gastrointestinal symptoms of abdominal discomfort and loose, non-bloody stools. However, it can cause more severe disease including bloody diarrhea (dysentery) and abscesses [6]. The most common site of metastatic infection is the liver (referred to as amoebic liver abscess (ALA)), although it rarely may also infect the lungs, brain, or other abdominal sites. In refugees, *E. histolytica* causing clinical disease after arrival to the United States is rare. Although *Entamoeba* cysts are commonly reported in stool ova and parasite examination, these cysts are more likely to be the indistinguishable, nonpathogenic species *E. dispar*. When reported in an asymptomatic person, the diagnosis of *E. histolytica* should be confirmed with a stool antigen or PCR testing prior to treating.

Giardia spp. *Giardia* is the most common parasitic cause of infectious diarrhea in both developed and developing countries and is one of the most commonly encountered infections in refugee populations who are screened for intestinal parasites. It preferentially affects those in poorer socioeconomic areas due to sanitation issues and can be found in large proportions of the population. A vast majority of infections are asymptomatic [7]. Common symptoms include bloating, burping, abdominal

Parasite	Treatment
Entamoeba histolytica [‡]	Metronidazole 500–750 mg orally 3 times daily for 7–10 days
[6, 9, 10]	FOLLOWED BY
	Paromomycin 25–30 mg/kg per day in 3 divided doses for
	5–10 days
<i>Giardia</i> spp. ^{*,‡} [11–14]	Tinidazole 2 g orally as a single dose
	OR
	Nitazoxanide 500 mg orally twice a day for 3 days
	OR
	Metronidazole 250 mg orally three times a day for 5–7 days
Blastocystis hominis ^{*,‡}	Metronidazole [†] , 250 mg to 750 mg orally 3 times daily for 10 days
[15]	OR
	Nitazoxanide [†] , 500 mg orally twice daily for 3 days
	OR
	TMP-SMX [†] , (6 mg/kg TMP [max 320 mg] and 30 mg/kg SMX
	[max1600 mg] daily for 7 days
	OR
	Tinidazole 2 g orally as a single dose
Dientameoba fragilis [‡] [9,	Iodoquinol [†] 650 mg orally three times daily for 20 days
10]	OR
	Paromomycin [†] 25–35 mg per kg per day orally, in three divided
	doses, for 7 days
	OR
	Metronidazole [†] 500–750 mg 3 times daily for 10 days

 Table 6.2
 Adult treatment regimens of select intestinal protozoan infections

*First-line therapy listed; alternative therapies can be reviewed at CDC's Parasite Home for Medical Professionals [9]

[†]Not an FDA-approved medication for this infection

[‡]Review alternatives for special hosts (children, pregnant and breastfeeding mothers, immunocompromised)

discomfort, non-bloody foul-smelling diarrhea, weight loss, or failure to thrive in small children. Symptoms, particularly in children, can be subtle. There is lack of data and therefore no consensus regarding benefit versus risk (cost, drug side effects, etc.) of treating asymptomatic persons. In addition, the organism frequently fails to respond to treatment and if repeatedly treated for asymptomatic infection, the risk of adverse effects of the medication may outweigh the benefit. Routine screening of asymptomatic persons is not recommended. Some experts would screen children <5 years of age since it can be difficult to determine if young children are experiencing symptoms. When giardia is identified in an asymptomatic individual, we recommend treating with a first-line medication and not repeating diagnostic treating (doing a "test of cure") unless the individual develops symptoms.

Blastocystis hominis This organism is ubiquitous throughout the world, making *Blastocystis* one of the most commonly encountered organisms in screening fecal samples in new refugee arrivals. One study has identified *Blastocystis* in the gastro-intestinal (GI) tract of over 50% of healthy adults [8]. In most individuals, this protozoan, like *Giardia*, does not cause symptoms. In fact, some argue it should not be considered a pathogen. However, it has been associated with disease in certain individuals, particularly those with underlying immunodeficiency (e.g., HIV) and in

travelers. If a person has gastrointestinal symptoms and no other etiology is found, it is reasonable to consider treatment.

Dientameoba fragilis A common parasite, *D. fragilis* can cause acute or chronic abdominal pain, persistent diarrhea, and flatulence and has been associated with eosinophilia, although many who are infected have no signs or symptoms. When symptomatic, the patient may benefit from treatment.

Protozoan parasites can also infect blood and tissues with minimal to no intestinal involvement. Unlike intestinal protozoan parasites, which cause similar symptoms, the clinical presentations of blood/tissue protozoan infections can vary widely. Blood and tissue protozoa encountered in refugees are described below. Treatment for these infections is complex and should involve subspecialists and often the consultation with the CDC, so it will not be covered here.

Leishmania spp. Leishmania is an intracellular protozoan parasite that is transmitted by the bite of an infected phlebotomine sandfly. Leishmaniasis is caused by a variety of different Leishmania species and has several different clinical presentations, including cutaneous, mucocutaneous, and visceral disease. It is estimated that Leishmania species are present in at least 88 different countries, and as a result this parasitic infection can be found in refugees from Central and South Asia, Africa, the Middle East, the Mediterranean, Mexico, and Central and South America. The cutaneous form can present either as acute or chronic disease, which typically starts as a red papule found on exposed skin that steadily enlarges and ulcerates. The lesions are typically painless unless secondarily infected, and diagnosis can be made with biopsy of leading edge of the ulcer for histopathology and culture. Molecular PCR techniques are also available to confirm specific species, as they are visually indistinguishable. The mucocutaneous form is typically seen in patients from Latin America and presents as ulcerative and potentially highly destructive lesions of the mucus membranes of the nose, mouth, and pharynx. Visceral leishmaniasis presents as a chronic illness with symptoms of fever, weight loss, splenomegaly, lymphadenopathy, and pancytopenia. This form is most common in patients from Central Asia, Sudan, and Brazil. Treatment of leishmaniasis depends on specific species and also presenting form of the disease and varies widely from topical therapies alone for mild cutaneous disease to prolonged systemic therapies with antimonials or antifungals. The species causing infection is important since treatment may vary; specific treatment will not be discussed further here [9]. Since geographic exposure is paramount in determining species and treatment, a specific issue with refugees that should be kept in mind is their geographic route of migration. For example, anecdotally, many Somali refugees have been diagnosed with cutaneous leishmaniasis species of Central American origin-this is due to them migrating through Central America en route to the United States. When considering the diagnosis, a thorough history of areas/countries of exposure is crucial.

Trypanosoma cruzi T. cruzi causes an infection known as Chagas disease or American trypanosomiasis. African trypanosomiasis is caused by different *Trypanosoma* species and is extremely rare in refugees and therefore will not be reviewed further here. *T. cruzi*, although common in some areas of Latin America, is not often encountered in refugees to the United States since in the past, and cur-

rently, the United States has not received large numbers of refugees from highly endemic areas. In Europe, such as Spain, that receives many refugees/immigrants

endemic areas. In Europe, such as Spain, that receives many refugees/immigrants from areas such as Bolivia, it is much more frequently encountered. It is transmitted by the bite of an infected triatomine insect (aka "kissing bug") and is present in rural areas of Latin America. Infected patients are typically asymptomatic but may present with acute disease with symptoms including fever, malaise, lymphadenopathy, hepatosplenomegaly, and rarely myocarditis. During the acute stage, parasites can be detected in the blood via PCR. Patients then develop chronic disease, with most patients never manifesting any symptoms of chronic infection. It is currently estimated that up to 300,000 people in the United States are chronic carriers of T. cruzi, largely due to migration but also rare cases of transmission in parts of the United States where the triatomine vector is present or from blood and organ donation; 10-30% of chronic carries can later develop cardiac and/or GI disease including cardiomyopathy, cardiac arrhythmias, megaesophagus, and/or megacolon. Treatment of Chagas disease includes either benznidazole or nifurtimox, which are only available through consultation with the CDC and may be of questionable to no benefit in patients with late stages of chronic symptomatic cardiac or GI disease [9].

Helminths

Helminths are transmitted to humans by a variety of methods, including fecal-oral contamination, direct skin penetration, and vector-borne transmission. Infections frequently involve the GI tract but also can be found in many other areas of the body, depending on the specific parasite and characteristics of the human host.

Nematodes

Nematodes (roundworms) are among the most common cause of infection and disease in the developing world. Infection can be both acute and chronic. Chronic infection in children can cause significant morbidity through stunting and impaired cognitive development [16]. Treatment of nematode infections is reviewed in Table 6.3.

Soil transmitted helminths (STH) are a group of nematodes which includes *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworms. They are commonly referred to together because of their very high prevalence, similarity in life cycle, and worldwide distribution [17]. All soil transmitted helminths need a soil cycle and transmission in the United States is uncommon. They all have a limited life span and within 5 years of leaving an endemic area a refugee will be free of infection due to death of the adult worm.

Ascaris lumbricoides Ascaris is the most common of the soil-transmitted helminths, with nearly 1 in 6 (roughly 1.2 billion) people infected [18]. Human infection occurs after ingesting the Ascaris eggs. The majority of infected individuals are asymptomatic, but with a large worm burden, patients can suffer intestinal blockage, most common in children. Additionally, Ascaris may migrate into anatomic

Parasite	Treatment
Ascaris lumbricoides ^{*,‡} [9, 18]	Albendazole 400 mg orally as a single dose OR
	Mebendazole 100 mg orally twice daily for 3 days
	or 500 mg orally as a single dose
	OR
	Ivermectin [†] 150–200 mcg/kg orally as a single
<i>Trichuris trichiura</i> ^{*,‡} [21, 22]	Mebendazole 500 mg once daily for 3 days OR
	Albendazole 400 mg per day for 3 days
Hookworm (Ancylostoma duodenale, Necator americanus) [9, 10]	Albendazole [†] 400 mg as a single dose OR
	Mebendazole 100 mg orally twice a day for 3 days or 500 mg orally as a single dose OR
	Pyrantel pamoate 11 mg/kg (up to a maximum of 1 g) orally daily for 3 days
Strongyloides stercoralis ^{*,‡,\$} [9]	<i>Ivermectin</i> [¶] 200 µg/kg orally daily for 1–2 days. Consider repeat course after 2 weeks
Loa loa [9]	
Symptomatic loiasis with microfilariae/ mL <8000	Diethylcarbamazine (DEC)° 8–10 mg/kg/day orally in 3 divided doses for 21 days
Symptomatic loiasis, with MF/mL <8000 and failed 2 rounds DEC OR	Albendazole 200 mg orally twice daily for 21 days
Symptomatic loiasis, with MF/ml ≥8000 to reduce level to <8000 prior to treatment with DEC	
Lymphatic filariasis Wuchereria bancrofti*	Diethylcarbamazine (DEC)° 2 mg/kg orally three
[9]	times daily for 1 or 12 day.
Onchocerca volvulus [9]	To kill microfilariae: Ivermectin [¶] 150 mcg/kg orally in one dose and then every 6 months To hinder reproductive abilities of macrofilariae: Doxycycline 200 mg orally daily for 6 weeks (initiate 1 week after Ivermectin treatment)

 Table 6.3
 Adult treatment regimens of select nematode infections

*First-line therapy listed; alternative therapies can be reviewed at CDC's Parasite Home for Medical Professionals [9]

[†]Not an FDA-approved medication for this infection

^{*}Review alternatives for special hosts (children, pregnant and breastfeeding mothers, immunocompromised)

[¶]Must be used with caution in people from *Loa loa* endemic countries due to the risk of a fatal encephalitic reaction to ivermectin (see Table 6.8). *Consider expert consultation*

^{\$}Hyperinfection/dissemination infection requires prolonged therapy.

[°]DEC is only available in the United States through the CDC and expert consultation and alternative therapy should be considered for individuals in which *Onchocerca* or *Loa loa* infection is possible. areas which leads to disease, coined "wandering *Ascaris*," such as gallbladder outlet obstruction (causing cholecystitis) or appendiceal obstruction (causing appendicitis). Because of its life cycle which involves passing through the lungs, patient may also present with respiratory symptoms such as cough, dyspnea, and wheezing.

Trichuris trichiura Trichuris is a parasite which inhabits the large intestine and is found in many areas where human feces are used as fertilizer. Infection begins with ingestion of *Trichuris* eggs. Over 90% of people who are infected are asymptomatic, but those who are symptomatic may experience watery, bloody, and painful bowel movements. *Trichuris* has been associated with rectal prolapse and can cause anemia. In children with heavy infections, stunting can occur [9].

Ancylostoma duodenale, Ancylostoma ceylanicum, and Necator americanus (*Hookworm*) Hookworm is found in areas where human feces are used as fertilizer or in areas where human wastes are deposited on the soil. Infection occurs via direct penetration of the worm through the skin, often of the lower extremities, and the first symptom is often an itchy rash at the site of penetration. Once established in the small intestine, hookworm can cause abdominal pain, weakness, and fatigue. The hookworm species are most notable for the chronic anemia which may result from chronic infection, causing stunting and impaired cognitive development in children [19, 20]. Hookworm is among the most pathogenic of the soil-transmitted helminths.

Strongyloides stercoralis Strongyloides is a roundworm whose infective larvae are found in the soil and which like hookworm infects humans via skin penetration, often of the lower extremities. Found throughout the world but predominantly in tropical areas, *Strongyloides* often manifests with dermatologic, pulmonary, and intestinal symptoms such as rash, dry cough, and abdominal discomfort.

Unlike most other helminths, Strongyloides is capable of autoinfection, where the parasite can continue to reproduce and reinfect the human host, thus resulting in a persistent and potentially lifelong infection. Also, Strongyloides can develop "hyperinfection," where the reproduction of the parasite is accelerated and leads to rapid increase in worm burden. Hyperinfection is most often caused by immunosuppression, particularly following the administration of corticosteroids or in individuals coinfected with the virus HTLV-1. Hyperinfection can further lead to disseminated disease; this is where the parasite migrates throughout the body, potentially carrying enteric bacteria along, which has a high mortality rate largely related to the resulting Gram-negative sepsis. The capability for autoinfection and risk of potentially fatal hyperinfection and disseminated disease makes evaluation for chronic strongyloidiasis of particular importance for refugee patients who may require immunosuppression in the future. Any refugee from a Strongyloides endemic area should be carefully evaluated for chronic infection prior to initiating immunosuppressive therapy and treated if infection present. If unable to complete evaluation due to urgent need for immunosuppression, refugee patients should be given empiric ivermectin treatment if no other contraindication to therapy.

Loa loa Loa loa is a nematode transmitted by the bite of deerflies of the genus *Chrysops*. Loiasis most often results in "eye worm" where the nematode can be seen moving across the eye. It can also manifest as red, itchy swelling of the skin,

termed Calabar swellings. It is found throughout west central sub-Saharan Africa, in areas of high-canopied rain forest. One key factor making *Loa loa* infection of prime importance is that for patients given ivermectin to treat *Strongyloides* who are coinfected with *Loa loa*, there have been reports of encephalitis precipitated by treatment. Using ivermectin (e.g., for *Strongyloides*) in populations at risk for *Loa loa* infection must be done carefully—this is discussed further in section II [9].

Lymphatic filariasis Filariasis is caused by multiple different species of roundworms, all transmitted by the bite of an infected insect vector. The microfilaria are found in the bloodstream, often with specific nocturnal or diurnal periodicity, while the adult worms reside in the lymphatics [9]. The most common species include Wuchereria bancrofti (Asia, Africa, Latin America, Pacific Islands) and Brugia malavi (Southeast Asia). While Wuchereria, Brugia, and other less common types of filaria are all similar in terms of transmission, presentation, and diagnosis, Onchocerca has notable differences and is therefore discussed separately below. Filarial parasites are transmitted by either day or night biting mosquitos. Acute manifestations can include filarial fever (acute onset of fever, chills, and lymphadenitis) or tropical pulmonary eosinophilia (paroxysmal cough and wheezing with diffuse pulmonary infiltrates on chest x-ray). Chronic manifestations develop due to damage to the lymphatics and include elephantiasis (uni- or bilateral leg swelling), hydrocele, and scrotum/vulva swelling. Diagnosis can be made by blood smears (with timing of blood collection specific for the species in question) and/or serology. Adult worms can also be seen by ultrasound of the lymphatic system, most classically in the scrotal lymphatics ("filarial dance sign").

Onchocerca (River blindness) Onchocerciasis is also a filarial infection transmitted by *Simulium* black flies. *Onchocerca volvulus* is endemic to Africa, Latin America, and parts of the Middle East. *Onchocerca* microfilariae are not found in blood and are instead found in skin and subcutaneous tissues [9]. Therefore, instead of blood smears diagnosis can be made by skin snips, where the microfilariae can be seen emerging from the skin after incubation in saline. Onchocerciasis is also notable for historically being the world's second leading cause of blindness, due to the presence of microfilaria in the cornea and anterior chamber. Adult worms can be found in subcutaneous nodules, which are often prominent over bony areas, and can be seen by ultrasound of subcutaneous nodules. A common symptom is skin itching, and acute and chronic papular lesions can also be seen on the skin. Chronic lesions can lead to skin atrophy and hyperpigmentation, leading to the characteristic "leopard skin" appearance.

Trematodes

Trematodes, also known as flat worms or "flukes," are parasites which infect many different types of vertebrate hosts, including humans. Their life cycle typically involves a freshwater snail as an intermediate host before infection of the definitive vertebrate host. Treatment of trematode infections is reviewed in Table 6.4.

Parasite	Treatment
S. mansoni, S. haematobium, S. intercalatum [9]	Praziquantel 40 mg/kg per day orally in two divided doses for one day, 6–8 hours apart
S. japonicum, S. mekongi [9]	Praziquantel 60 mg/kg per day orally in three divided doses for one day, 6–8 hours apart
<i>Opisthorchis viverrini</i> [*] [9]	Praziquantel 25 mg/kg orally 3 times per day for 2 consecutive days
Clonorchis sinensis [*] [9]	Praziquantel 25 mg/kg orally 3 times per day for 2 consecutive days
Fasciola hepatica [9]	Triclabendazole° 10 mg/kg for 1 to 2 days (depending on parasite burden)
Paragonimus westermani* [9]	Praziquantel 25 mg/kg given orally 3 times per day for 2 consecutive days
Fasciolopsis buski [9]	Praziquantel [†] 25 mg/kg/day orally three times a day for 1 day

 Table 6.4
 Adult treatment regimens of select trematode infections

*First-line therapy listed; alternative therapies can be reviewed at CDC's Parasite Home for Medical Professionals [9]

[†]Not an FDA-approved medication for this infection

[‡]Review alternatives for special hosts (children, pregnant and breastfeeding mothers, immunocompromised)

Schistosoma spp. Widespread throughout the tropical world, Schistosoma species are important and at times overlooked parasites, which can cause significant morbidity when chronic. Schistosomes have a complex life cycle which must involve certain freshwater snails, and humans are infected via the skin, usually by wading in freshwater where the snail intermediate host is present. Initially patients may have a dermatologic reaction at the site of skin penetration, including rash with vesicles and pruritus. Approximately 5–7 weeks after infection, patients may develop "Katayama fever," the syndrome of fever, headache, myalgias, abdominal pain (often right upper quadrant), bloody diarrhea, and eosinophilia [21]. Serious neurologic complications can also occur at this time, including seizures and transverse myelitis. Untreated infections, which may last many years, lead to a chronic granulomatous disease due to the deposition of eggs into local tissues. Chronic infection with the species *S. mansoni, S. japonicum*, and *S. mekongi* can cause liver disease and large intestinal symptoms whereas chronic infection with *S. haemato-bium* can lead to disease of the GU tract and bladder cancer [9].

Opisthorchis spp., *Clonorchis sinensis* Found in Asia, Southeast Asia, Eastern Europe, and countries of the former Soviet Union, these trematodes are known as "liver flukes" and are contracted by eating undercooked freshwater fish. They inhabit the biliary tree of humans and, when they cause disease, can result in symptoms of abdominal discomfort, diarrhea, and constipation secondary to bile duct inflammation and biliary obstruction. Some species may be mistaken for gallstones and only be discovered upon surgery. Chronic infection results in inflammation and scarring of the biliary tree, which can lead to gallbladder and bile duct cancers. The most commonly encountered liver flukes in refugees are *Opisthorchis* and *Clonorchis* and are seen mainly in Southeast Asian refugees (e.g., Laotian) [9].

Fasciola hepatica Fasciola is another liver fluke found in a broader geographical range including South America and is acquired by eating raw freshwater plants, such as watercress (as well as undercooked sheep or goat livers) [23]. Symptoms are similar to the other liver flukes, although this parasite actively burrows through the liver parenchyma to arrive at the biliary tree.

Paragonimus westermani This trematode is also referred to as the "lung fluke" due to its propensity to infect the pulmonary tree. Paragonimiasis is most common in south and Southeast Asia, although it can also be found in other regions including South America. Humans are infected by eating raw or undercooked crab or crayfish. Symptoms of infection first involve the abdominal tract, with nausea, vomiting, and diarrhea. The GI symptoms may then be followed by pulmonary symptoms as the fluke migrates to the lungs, including chest pain, fever, and cough. Hemoptysis may develop, and therefore it is frequently initially thought to be tuberculosis [24]. Infection can also cause a pleural effusion with a predominance of eosinophils on fluid analysis. Paragonimiasis is seen primarily in Southeast Asian refugees, currently most common in Burmese refugees.

Fasciolopsis buski F. buski is the largest of the intestinal flukes, growing to up to 7 cm in length and infects the small intestine. It is found in south and Southeast Asia, and pigs are an important reservoir. Infection occurs when people ingest freshwater vegetation, such as bamboo shoots and water chestnuts, infested with the infected snails. Most patients are asymptomatic; however, ulcers can develop at the attachment site of the parasite causing epigastric pain similar to peptic ulcer disease. Heavy infections in the intestine can cause ileus or intermittent obstruction.

Cestodes

Cestodes are flat worms also known as tapeworms. Cestodes may eventually pass in entirety in the stool upon death of the worm. Alternatively, cestodes can also pass smaller segments intermittently in the stool known as proglottids, which are typical gravid (egg-laden) segments. Treatment of cestode infections is reviewed in Table 6.5.

Hymenolepis nana Found throughout the world, particularly where there is poor access to safe water and sanitation, this parasite is commonly called the "dwarf tapeworm." Humans are infected by fecal-contaminated food or water, and most patients are asymptomatic because of the small size of this tapeworm. Symptoms if present usually include abdominal discomfort and weakness. Children with heavy infection may have perineal pruritus and therefore be misdiagnosed with pinworm infection. This infection is particularly common in Ethiopian and Somali refugees and may persist for prolonged periods after arrival and following travel back to endemic areas.

Taenia saginata (*Beef Tapeworm*) Found throughout the world, *Taenia saginata* is the largest tapeworm to cause human disease, reaching lengths of up to 10 meters. Humans are infected by eating raw or undercooked beef and when symptomatic will often have abdominal discomfort, weight loss, and anorexia.

Parasite	Treatment
Hymenolepis nana [*] [9]	Praziquantel 25 mg/kg orally as a single dose
Taenia (T. saginata and T. solium ^{\$})* [9]	Praziquantel 5–10 mg/kg orally as a single dose
Diphyllobothrium latum [*] [9]	Praziquantel [†] 5–10 mg/kg orally as a single dose
Echinococcus [*] [¶] [9]	Albendazole 10–15 mg/kg orally divided twice daily for 1–6 months PLUS Percutaneous aspiration, injection of chemicals, and reaspiration (PAIR) therapy or surgery

 Table 6.5
 Adult treatment regimens of select cestode infections

*First-line therapy listed; alternative therapies can be reviewed at CDC's Parasite Home for Medical Professionals [9, 10]

[†]Not an FDA-approved medication for this infection

[‡]Review alternatives for special hosts (children, pregnant and breastfeeding mothers, immunocompromised)

^sRecommended treatment for gastrointestinal infection. Use with caution if there is suspicion of neurocysticercosis. Praziquantel is cysticidal and may cause inflammation, seizures, and other CNS sequelae. See the CDC's Parasite Home for Medical Professionals [9] for review of neurocysticercosis treatment

[¶]Size and location of cyst can influence recommended approach. Consider expert consultation

Taenia solium (*Pork Tapeworm*) The pork tapeworm, like the beef tapeworm, is found throughout the world and causes a similar clinical presentation when it affects the gastrointestinal system. However, unlike the beef tapeworm, *Taenia solium* eggs can be directly infectious to humans (i.e., there is the possibility of human to human infection). When another human is directly infected by ingesting *Taenia* eggs, the parasite can migrate to any number of different tissues and develop into its larval cyst form. The most worrying location is the central nervous system, which results clinically in neurocysticercosis and is a significant cause of adult onset seizures in many parts of the developing world [25]. In an immigrant, particularly from Central or South America, who presents with new onset seizures, neurocysticercosis must be on the differential.

Diphyllobothrium latum (*Fish Tapeworm*) Obtained by eating raw or undercooked fish, diphyllobothriasis is found primarily throughout the northern hemispheres and is more common within the United States than in refugee populations entering the United States. Symptoms, when present, may be vomiting, diarrhea, and weight loss. Chronic infection can also cause vitamin B12 deficiency and consequent macroscopic anemia.

Echinococcus The most common form of this tapeworm infection is caused by the parasite *Echinococcus granulosus*, which is found worldwide. Definitive hosts are dogs, with intermediate hosts including sheep, cattle, pigs, camels, and goats. Humans are infected by ingesting eggs in canine feces. This parasite grows very slowly and humans may be asymptomatic for years. Infected humans develop cysts most commonly in the liver but also in the lung, brain, bone, and other organs. The cysts can spontaneously rupture which can cause an anaphylactic reaction. Diagnosis

can be made by classic radiographic images and/or serology. Definitive diagnosis is aspiration of cyst material showing protoscoleces or hydatid membranes. WHO stages disease based on ultrasound examination and activity/viability of the cysts. Treatment options depend on size, location, and stage of cysts and can include systemic therapy with albendazole and/or praziquantel, surgical removal, or percutaneous aspiration-injection of protoscolicidal solutions-reaspiration (PAIR) therapy [9] (Table 6.5).

Ectoparasites

Ectoparasites inhabit the outside of the human body and can be a common cause of pruritic skin lesions in refugees. Common ectoparasites seen in refugees include scabies, pediculosis (lice), and tungiasis.

Scabies Scabies is caused by the mite *Sarcoptes scabiei*. It is commonly encountered in refugee settings overseas but treatment and control programs currently decrease how often it is encountered in refugees migrating to the United States. Infection spreads person to person via close contact. Mites burrow into the stratum corneum layer of the skin which causes an intensely pruritic rash due to a hypersensitivity reaction to mite feces. Classic locations on the body include interdigital web spaces of the hands, flexor surfaces of wrists and elbows, axillae, male genitalia, under the breasts, and at the belt line. However, in young children, a more diffuse rash can be seen. Patients with immunosuppression can develop crusted or "Norwegian" scabies, which is an aggressive form of infection with hyperkeratotic plaques and crusts that can lack the characteristic pruritus and distribution. Definitive diagnosis can be made by microscopic identification of the mite or eggs obtained by scraping the lesions. Treatment can be topical permethrin or systemic ivermectin, with another key component being decontamination of fomites including clothes, bedsheets, etc [9].

Pediculosis (*Lice*) There are three different lice species that cause human infestation, including *Phthirus pubis* (pubic louse), *Pediculus humanus humanus* (body louse), and *Pediculus humanus capitis* (head louse). Transmission is via close contact with other infected people or fomites. Pruritus at the infestation site is common, and both the adult lice and the eggs (nits) can be seen by the naked eye. Body lice live in seams of clothing and are therefore rarely seen on skin. Body lice are also the only louse type known to transmit bacterial infection (*Rickettsia prowazekii* causing epidemic typhus, *Bartonella quintana* causing trench fever, and *Borrelia recurrentis* causing relapsing fever). Treatment for pubic and head lice is with topical insecticides, manual removal of nits, and aggressive decontamination of fomites; treatment of body lice only involves treatment of clothing [9].

Tungiasis Tungiasis is caused by the female sand flea *Tunga penetrans* which burrows into the skin, most commonly of the feet. The fleas feed on the blood of the host and grow in size, causing localized irritation and pruritus, and may also become superinfected with bacteria. Animals serve as reservoirs for human disease, and transmission to humans occurs when skin comes into contact with soil containing

the adult sand fleas. Tungiasis is found in all tropical and subtropical parts of the world, particularly in areas with high rates of poverty. Chronic infection can lead to pain, disfigurement, and disability. Treatment includes surgical removal of embedded sand fleas and/or topical therapies to protect against infection [9].

Presumptive Therapy and Screening Recommendations (Section II)

The term "presumptive therapy" encompasses treatment for parasites which refugees coming from certain areas of the world can be "presumed" to have based on prevalence data from the area and targets soil-transmitted helminths, *Strongyloides*, and *Schistosoma*. This began in 1999 for pre-departure treatment of refugees bound for the United States when albendazole was introduced, and this has significantly decreased prevalence and changed the distribution of parasites seen in newly arrived refugees to the United States (Fig. 6.3) [3]. Prior to the broad use of pre-departure albendazole therapy, the most common parasites found during arrival screening included hookworm and *Giardia*. After implementation of empiric albendazole therapy in 1999 the most commonly encountered nematode was *Trichuris* [3].

Subsequent data indicated that *Schistosoma* species and *Strongyloides*, which is not adequately treated with a single dose of albendazole, were also highly prevalent infections in refugees [3]. These two parasites are of particular concern, since they are very common and can cause chronic infection resulting in serious morbidity and even mortality. To combat this concern, in 2007 both ivermectin for *Strongyloides* and praziquantel for *Schistosoma* were also recommended for pre-departure therapy for high-risk refugees coming to the United States. An up-to-date list of pre-departure therapy received by each major resettlement group may be found at the CDC's website for Immigrant and Refugee Health (http://www.cdc.gov/immigrantrefugeehealth/guidelines/overseas/interventions.html).



Fig. 6.3 Change in intestinal parasitosis with empiric pre-departure therapy. (Figure from Swanson et al. [3])

Now, optimally, refugees arriving to the United States from Africa, Asia, and Southeast Asia should receive some form of presumptive therapy for parasitic infections. This is typically performed by the International Organization for Migration (IOM) in their home countries or refugee camps within days prior to departure for the United States. Recommended pre-departure presumptive treatment is outlined in Table 6.6. Refugees from Asia, Middle East, North Africa, Latin America, and

	Regimens by path	ogen	
Refugee	Soil-transmitted		
population	helminths	Strongyloidiasis	Schistosomiasis
Adults			
Asia, Middle East, North Africa, Latin American, and Caribbean	Albendazole 400 mg orally once	Ivermectin 200 µg/kg/day orally once daily for 2 days	Treatment not recommended
Africa, non- <i>Loa</i> <i>loa</i> endemic area	Albendazole 400 mg orally once	Ivermectin 200 µg/kg/day once daily for 2 days	Praziquantel, 40 mg/ kg once (may be divided and given in two doses for better tolerance)
Africa, <i>Loa loa</i> endemic area	Albendazole 400 mg orally once	If <i>Loa loa</i> cannot be excluded, treatment may be deferred until after arrival in the United States OR Albendazole 400 mg twice daily for 7 days	Praziquantel, 40 mg/ kg once (may be divided and given in two doses for better tolerance)
Pregnant women			
Asia, Middle East Latin America, Caribbean	Not recommended	Not recommended	Not applicable
Africa	Not recommended	Not recommended	Praziquantel 40 mg/kg once (may be divided and given in two doses for better tolerance)
Children			
Asia, Middle East Latin American, Caribbean	<12 month: Not recommended 12–23 months of age: Albendazole 200 mg orally once	Weight ≤15 kg: Not Recommended Weight >15 kg: Ivermectin, 200 µg/kg/day orally once daily for 2 days	Not applicable
Africa	<12 month: Not recommended 12–23 months of age: Albendazole 200 mg orally once	From <i>Loa loa</i> endemic country: Not recommended Weight ≤15 kg: Not Recommended Weight >15 kg: Ivermectin, 200 µg/kg/day orally once daily for 2 days	Children under ≤4 years of age should not receive presumptive treatment with praziquantel

 Table 6.6
 Recommended medication regimen for presumptive treatment of parasitic infections

Adapted from the Centers for Disease Control and Prevention [26, 27]

Caribbean are to be treated with albendazole and ivermectin, with the exception of those with contraindications (Table 6.7). It is also recommended that all refugees from Africa without contraindications be treated with praziquantel in addition to albendazole and ivermectin.

Certain exceptions, contraindications, and adverse events are important to point out. An exception to the presumptive treatment with ivermectin include those who originate, or have lived, in countries endemic for *Loa loa*. In areas of *Loa loa* endemicity (as listed in Table 6.8), encephalitis can occur after ivermectin therapy in patients who have a concomitant *Loa loa* infection with a high microfilarial parasite

Medication	Population
Albendazole contraindications	Children <12 months of age
	Pregnancy
	Refugees with known neurocysticercosis
	Evidence of cysticercosis (e.g., subcutaneous nodules)
	A history of unexplained seizures
Praziquantel contraindications	Children <4 years of age
	Refugees with known neurocysticercosis
	Evidence of cysticercosis (e.g., subcutaneous nodules)
	A history of unexplained seizures
Ivermectin contraindications	Children <15 kg or measuring <90 cm
	Pregnant women in any trimester
	Breastfeeding women within the first week of delivery
	Refugee is departing from or has lived in a Loa loa endemic
	area

 Table 6.7 Contraindications to presumptive therapy

Adapted from the Centers for Disease Control and Prevention [26]

African countries NOT endemic for Loa loa		African countries endemic for Loa loa		
(may use ivermectin for presumptive		(use albendazole for 7 days for presumptive		
Strongyloides therap	py)	Strongyloides therapy)		
Algeria	Mauritania	Angola		
Botswana	Mauritius	Cameroon		
Burkina Faso	Morocco	Central Africa Republic		
Burundi	Mozambique	Chad		
Côte d'Ivoire	Namibia	Democratic Republic of the Congo		
Egypt	Niger	Equatorial Guinea		
Ethiopia	Rwanda	Gabon		
Eritrea	Senegal	Nigeria		
Gambia	Somalia	Republic of the Congo		
Ghana	South Africa	South Sudan		
Guinea	Sudan			
Guinea-Bissau	Swaziland			
Kenya	Tanzania			
Liberia	Togo			
Libya	Uganda			
Madagascar	Zambia			
Malawi	Zimbabwe			
Mali				

Table 6.8 Loa loa endemic countries in Africa

Adapted from the Centers for Disease Control and Prevention [27, 28]

load. Therefore, any refugee from a *Loa loa* endemic country will not receive ivermectin presumptively before departure and should *not* be treated presumptively without ruling out high microfilarial *Loa loa* load. In addition, albendazole or praziquantel can precipitate seizures in individuals with neurocysticercosis, and therefore those individuals in whom there is concern for neurocysticercosis, including unexplained seizures or subcutaneous nodules suggestive of cysticercosis, should not have presumptive treatment with albendazole or praziquantel [26]. Both albendazole and ivermectin are category C drugs in the United States and are not recommended for the presumptive treatment for US-bound refugees during any trimester of pregnancy [26]. Albendazole and ivermectin (1 week after birth) can be administered during breastfeeding [26].

Post-arrival screening is recommended in refugees based on their geographic origin and their preventative treatment history. These recommendations are not uniformly implemented due to complicated logistics and lack of funding. Please see Table 6.9 for post-arrival screening recommendations.

Eosinophilia (Section III)

A complete blood count with differential (CBC with diff) is recommended during the new arrival screening, and accordingly, eosinophilia is frequently encountered. Eosinophilia refers to an absolute eosinophil count of greater than 400–500 per cubic millimeter in a peripheral blood sample (the absolute count should be used

No pre-departure treatment	Pre-departure treatment with albendazole	Pre-departure treatment with albendazole and praziquantel	Complete pre-departure treatment including ivermectin
Eosinophil count (all	Eosinophil count (all	Eosinophil count	Eosinophil
refugees)	refugees)	Presumptive	count-if
Stool O&Px2 or presumptive	Presumptive treatment or	treatment or	elevated
albendazole (all refugees)	Schistosoma serology	Strongyloides	recheck in
Presumptive treatment or	(refugees from sub-	serology (all	3–6 months
Schistosoma serology	Saharan Africa)	refugees from	
(refugees from sub-Saharan	Presumptive treatment or	non-Loa loa	
Africa)	Strongyloides serology	endemic areas of	
Presumptive treatment or	(all refugees from	sub-Saharan	
Strongyloides serology (all	non-Loa loa endemic	Africa)	
refugees from non-Loa loa	areas of sub-Saharan	Strongyloides	
endemic areas of sub-Saharan	Africa)	serology and treat	
Africa)	Strongyloides serology	only if no	
Strongyloides serology and	and treat only if no	contraindications	
treat only if no	contraindications	(refugees from Loa	
contraindications (refugees	(refugees from Loa loa	loa endemic areas	
from Loa loa endemic areas	endemic areas of	of sub-Saharan	
of sub-Saharan Africa)	sub-Saharan Africa)	Africa)	

Table 6.9 Overview of post-arrival screening recommendations

Adapted from CDC Guidelines on Domestic Intestinal Parasites [26]

and not the percentage). Because of the high pretest probability of parasitic infection, we prefer to use 400 as the cutoff for refugees. An elevated eosinophil count may result from either infectious or noninfectious etiologies (Tables 6.10 and 6.11). Eosinophilia can be the only indication that the affected individual has an asymptomatic parasitic infection. However, eosinophilia persists for months after successful treatment of a parasitic infection. In addition, eosinophilia has a poor negative and poor positive predictive value as a marker of parasitosis and neither rules in nor rules out parasitic infection [29].

Parasites causing		Parasites commonly	
eosinophilia	Other parasitic	found in the stool NOT	
commonly found on	infections associated	typically associated with	Nonparasitic causes
stool exam	with eosinophilia	eosinophilia	of eosinophilia
Ascaris lumbricoides	Echinococcus spp.	Entamoeba spp.	Asthma
Hookworm species	Filariasis	Cryptosporidium spp.*	Atopy
(Necator americanus,	(Wuchereria	Giardia intestinalis	Drug allergy
Ancylostoma duo	bancrofti, Brugia	(a.k.a. G. lamblia and G.	Eosinophilic
denale)	spp, Onchocerca	duodenalis)	leukemia
Trichuris trichiura	volvulus, Loa loa)		Hodgkin's lymphoma
Strongyloides	Angiostrongylus*		Hypereosinophilic
stercoralis	Anisakis*		syndrome
Taenia species	Capillaria spp.*		Pemphigoid
(solium and saginata)			Pemphigus
Schistosoma species			Polyarteritis nodosa
(S. mansoni, S.			Rheumatologic
haematobium, S.			disease (e.g.,
japonicum)			Churg-Strauss)
Liver flukes			
(Paragonimus,			
Opisthorchis,			
Fasciola)			

 Table 6.10
 Causes of eosinophilia, from CDC Domestic Intestinal Parasite Guidelines [26]

*Not covered in this chapter but detailed description of presentation, diagnosis, and treatment can be found at the CDC parasitic website for health professionals [9]

Table 6.11	Causes of eosinophilia in refugees, by region, from CDC Domestic Intestinal Parasite
Guidelines	[4]

Region	Parasites causing eosinophilia
Global	Ascaris lumbricoides, Trichuris trichiura, Hookworm species (Ancylostoma, Necator) Strongyloides stercoralis, Fasciola hepatica
Africa	Schistosoma mansoni, haematobium, intercalatum, Taenia saginata (esp. Ethiopia and Eritrea)
Asia	Overall: Fasciolopsis buski Southeast Asia: Opisthorchis viverrini, Clonorchis sinensis, Schistosoma japonicum, mekongi South Asia: Taenia solium
Latin America	Taenia solium Schistosoma mansoni Opisthorchis guayaquilensis (Ecuador)
Middle East	Echinococcus
Eastern Europe	Diphyllobothrium latum Opisthorchis felineus

In the previous sections of this chapter, we have detailed the presumptive therapy which newly arrived immigrants should undergo prior to or at time of arrival to the United States. It is important to realize that eosinophilia can take up to 3–6 months to return to normal after treatment. Therefore, in patients who have been treated, a recheck of the peripheral eosinophil count should be performed three to six months afterward to ensure resolution. If the eosinophil count remains elevated, a more detailed workup should be pursued, with emphasis on the most common causes—*Strongyloides*, soil-transmitted helminths, and *Schistosoma* species. During the workup of eosinophilia, it is important to consider the geographic region where the patient originates, as this can to help guide the differential diagnosis. If 6 months after presumptive treatment the eosinophil count is still elevated, the differential must be broadened to include other infectious and noninfectious causes.

In the setting of parasitic infection, eosinophilia typically develops when the parasite is migrating through tissues. Many parasites that cause eosinophilia can have a long duration of infection. The most extreme example of this is *Strongyloides*, as the duration of infection can last the entire life of the patient due to the parasite's capability for autoinfection. Without the ability for autoinfection, the duration of eosinophilia will last the life span of the parasite in question. Other parasites with a long duration of infection are *Schistosoma* (up to 32 years), *Loa loa* (16–24 years), and *Onchocerca* (15 or more years). Hookworm and *Ascaris* are examples of parasites with relatively shorter life spans (3–5 and 1–1.5 years, respectively); therefore the duration of eosinophilia is much shorter [30]. Treatment should be directed at the parasite identified during eosinophilia evaluation. However, despite a thorough investigation, it is possible that an etiology may not be identified, in which case presumptive therapy may be warranted. In this scenario, single-dose therapy with ivermectin and/or albendazole has been proposed [30].

Summary

Parasitic infections continue to be a cause of morbidity in newly arrived refugees. While pre-departure presumptive treatment has reduced parasitic infection burden, some parasites remain of concern, especially those that have a long duration of infection. CDC provides screening recommendations for refugees based on geographic risk factors, and following these guidelines can detect a majority of parasitic infections. Since screening and treatment recommendations are updated periodically, providers are encouraged to access CDC resources for guidance on management.

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