

3.6 PARASITIC INFECTIONS

PARASITIC INFECTIONS (Stool O & P): Record treatment in the "Medications Prescribed" section.					
<input type="checkbox"/> None Identified	<input type="checkbox"/> Ascaris	<input type="checkbox"/> Giardia	<input type="checkbox"/> Strongyloides	Giardia FAb: <input type="checkbox"/> Neg <input type="checkbox"/> Pos	
	<input type="checkbox"/> Blastocystis	<input type="checkbox"/> H.nana	<input type="checkbox"/> Trichuris	Cryptosporidium FAb: <input type="checkbox"/> Neg <input type="checkbox"/> Pos	
	<input type="checkbox"/> E.histolytica	<input type="checkbox"/> Hookworm	<input type="checkbox"/> Other		

PURPOSE

To identify and treat intestinal parasite infections

BACKGROUND

The worldwide prevalence of parasitoses is staggering. It is estimated that one quarter of the world's population may be infected by soil-transmitted nematodes such as round worms, hookworm, and whipworm.¹⁵ Over one billion persons worldwide are estimated to be carriers of *Ascaris*. Approximately 480 million people, or 12% of world population, are infected with *Entamoeba histolytica*.¹⁶ At least 500 million carry *Trichuris* (whipworm). At present, 200 to 300 million people are infected with one or more of *Schistosoma* species, and it is estimated that more than 20 million persons throughout the world are infected with *H. nana*.¹⁷ *Giardia lamblia* infects between 2 – 8% of the developing world's population.¹⁸ The enormous morbidity from parasitoses is a reflection of the number of people infected. Consequences of parasitic infection include anemia due to blood loss and iron deficiency, malnutrition, growth retardation, invasive disease, and death.

Parasitic infections are frequently detected in refugees; however, the types of organisms found will vary with the geographic origin of the refugee. It is important to note, however, that most refugees are asymptomatic carriers of parasites. Consequently, the imperative for testing and treating refugees is to prevent long-term sequelae to the refugee and prevent transmission in the U.S. Refugees from tropical countries typically have mixed helminth and protozoan infections, while refugees from the former socialist countries of Eastern Europe and the former Soviet Union typically have protozoan infections.

In 2001, the CDC implemented a program of pre-departure empiric treatment for refugees in Sub-Saharan Africa. This

¹⁵ Chan MS. The global burden of intestinal nematode infections – fifty years on. *Parasitol Today*. 1997;13:438-448.

¹⁶ Bruckner D. Amebiasis. *Clinical Microbiology Reviews*. 1992;5:356-369.

¹⁷ Katz M, Et al. *Parasitic Diseases, Second edition*. Springer-Verlag, 1989. p 96.

¹⁸ Gardner TB, Hill DR. Treatment of giardiasis. *Clinical Microbiology Reviews*. 2001;14:114-128.

treatment entails a single 600 mg oral dose of albendazole. Since implementation of this program, RIHP has documented dramatically decreased prevalences of intestinal parasites (particularly helminths) among African refugees.¹⁹ Prior to this program, the most common pathogens found in refugees resettled in Massachusetts were *Giardia* (45% of pathogenic parasites identified), *Trichuris* (whipworm, 33%), *E.histolytica* (9%), and *Ascaris* and hookworm (each 5%). Subsequent to the empiric treatment program, overall prevalence of helminth infections declined from 24% to 4% among African refugees. The odds of having a helminth infection in African refugees who have had pre-departure treatment with albendazole is now only 15% that of refugees who arrived prior to the program implementation.

In 2008, CDC developed new guidelines for [overseas presumptive treatment of intestinal parasites](#) and [domestic evaluation](#). The overseas recommendations are summarized:

- All South and Southeast Asian refugees [some exceptions noted] should receive presumptive therapy with a single dose of albendazole (400 mg, 200 mg for children 12-23 months) and ivermectin, 200 µg/kg orally once a day for two days, prior to departure to the United States.
- All African refugees who are not at risk of *Loa loa* infection [some exceptions noted] should receive presumptive therapy with a single dose of albendazole (400 mg for adults and children older than 23 months, 200 mg for children 12-23 months) and ivermectin, 200 µg/kg orally once a day for two days, and praziquantel, 40 mg/kg divided in two doses, prior to departure to the United States.
- All African refugees who are at risk of *Loa loa* infection [some exceptions noted] should receive presumptive therapy with a seven-day course of albendazole (400 mg orally twice a day) and praziquantel, 40 mg/kg divided in two doses, prior to departure to the United States.

The domestic guidance is based on implementation of the overseas treatment recommendations.

Finally, malaria is increasingly an important issue among refugees resettled in the U.S. Recent literature^{20,21} has documented a high prevalence of malaria among recent

¹⁹ Geltman PL, Cochran J, Hedgecock C. Intestinal parasites among African refugees resettled in Massachusetts and the impact of an overseas pre-departure treatment program. *Am J Trop Med Hyg.* 2003;69:657-662.

²⁰ Maroushek SR, Aguilar EF, Stauffer W, Abd-Alla MD. Malaria among refugee children at arrival in the United States. *Pediatr Infect Dis J.* 2005;24:450-452.

²¹ Ndao M, Bandyayera E, Kokoskin E, Gyorkos TW, MacLean JD, Ward BJ. Comparison of blood smear, antigen detection, and nested-PCR methods for screening refugees from regions where malaria is endemic after a malaria outbreak in Quebec, Canada. *Journal of Clinical Microbiology.* 2004;42:2694-2700.

refugee arrivals from Africa. Among symptomatic cases, the triad of fever, splenomegaly, and thrombocytopenia were highly specific for malaria. Of note, a fairly high proportion of children with malaria were asymptomatic. In the report by Maroushek et al., 29% of those with malaria were asymptomatic. Because of the predominance of *P. falciparum* in most of Africa, individuals often will develop some immunity over time, thus reducing symptoms. This is not the case with other forms of malaria that predominate in other parts of the world, in particular Southeast Asia. Pre-departure treatment with Fansidar is likely to be ineffective due to high rates of resistance to that drug.²²

CDC recommended pre-departure presumptive treatment against *P. falciparum* malaria using artemisinin-based combination therapy (ACT) with artemether-lumefantrine for refugees from sub-Saharan Africa. The 2008 CDC guidelines for [overseas](#) and [domestic](#) presumptive treatment of malaria are available from the Division of Global Migration and Quarantine.

PROGRAM REQUIREMENTS

In brief, the RHAP requires the following of providers:

1. Collect a single stool sample from each refugee.
 - ⇒ For those refugees returning for TST reading in 48-72 hours, provide the stool collection kit at the first visit and request return at the time of the TST reading.
 - ⇒ Order O&P and fluorescent antibody testing for *Giardia* and *Cryptosporidium*.
2. Consider presumptive treatment for strongyloides, schistosomiasis or malaria per recommendations detailed below.
3. Review positive findings in the context of families; consider presumptive treatment of negative individuals.
4. Provide needed anti-parasitic medication at the second visit; earlier if clinically indicated.
5. Report positive *Cryptosporidium*, *Giardia*, *E. histolytica* and other reportable enteric results to the Massachusetts Department of Public Health (fax lab report to 617.983.6813) or local health department.

First visit

Because of the continued risk of protozoan infections, all refugees should have a single stool sample screened for ova and parasites (O&P) and fluorescent antibody testing for *Giardia* and *Cryptosporidium*. Instruct the refugee on actual specimen collection and give kits to patients. Instruct the

²² Centers for Disease Control. Malaria in refugees from Tanzania -- King County, Washington, 2007. *MMWR*. 2008;57:869-872.

refugee patient to bring back stool in 2-3 days, preferably when she/he is coming for the PPD reading. The stool results should be available for the second visit.

Because of reports of high prevalence of asymptomatic parasitemia among African refugees, in FY2007, RIHP required malaria smears for all refugee arrivals from Sub-Saharan Africa. This testing failed to detect unsuspected cases of malaria and was discontinued for FY2008. Instead, clinicians should assess refugees from Sub-Saharan Africa and other regions with endemic malaria for signs or symptoms suggestive of acute or chronic malaria (e.g. fever, splenomegaly, and thrombocytopenia). Consider ordering malaria thick and thin blood smears for these patients. RIHP encourages clinicians to test refugees liberally as the Maroushek study found that no symptom, either alone or in combination with another symptom, was predictive of the presence or absence of malaria. Results of the malaria smear should be reported on the targeted testing form. Documentation should include treatment as well.

As always, RIHP requires RHAP clinical sites to obtain and provide anti-parasitic medication to refugee patients deemed eligible for outpatient treatment of uncomplicated malaria. Treatment should not be deferred until the second visit, as may be done for asymptomatic intestinal parasites. Guidelines for treatment of malaria are in Appendix 6.3 and include criteria for determining severity level and eligibility for outpatient treatment.

24-hour malaria consultation is available from the Centers for Disease Control and Prevention at 770-488-7788 during weekday business hours and by page at 770-488-7100 after hours and on weekends and holidays.

Alternatively, clinicians may consult local infectious disease specialists with expertise in the treatment of malaria.

Empiric Treatment of Strongyloides and Schistosome

Because surveillance data suggest a high prevalence of occult infection with *Strongyloides stercoralis* and *Schistosoma* species among Somali Bantu and Southern Sudanese refugees, the CDC has issued guidance regarding presumptive treatment of recently arrived Sudanese and

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Somali Bantus for strongyloidiasis and schistosomiasis. The full text of this guidance can be found on the [website](#) of the CDC's Division of Global Migration and Quarantine.

The CDC guidance recommends that in the absence of evidence of cysticercosis; history of seizures not evaluated for neurocysticercosis; pregnancy; or lactation; the preferred treatments are as follows:

Strongyloidiasis:

- **Somali Bantu:** If ≥ 15 kg, treat with ivermectin 200 mcg/kg, by mouth, once; if < 15 kg but ≥ 1 year of age, treat with albendazole 400 mg, by mouth, two times per day, for 7 days.
- **Sudanese:** if ≥ 1 year of age, treat with albendazole as above.

Schistosomiasis:

- **Somali Bantu and Sudanese:** If ≥ 4 years of age, treat with praziquantel in two doses of 20 mg/kg, by mouth, given 6-8 hours apart.

For Sudanese refugees, the CDC guidance recommends use of the alternative regimen of albendazole for the presumptive treatment of strongyloidiasis because Southern Sudan falls within the geographic distribution of *Loa loa* infection. Rarely, individuals with concurrent loiasis may develop encephalopathy after taking ivermectin.

RHAP clinicians are encouraged to follow these recommendations until the CDC implements a pre-departure treatment program overseas. RIHP will reimburse RHAP sites for these three medications for new arrivals.

Clinicians may also opt to test newly arrived refugees for evidence of these infections. Most academic and commercial reference laboratories can perform accurate serologic testing for *Strongyloides*; however the estimated prevalence in these populations is high enough for the CDC to recommend treatment without testing. **Presumptive treatment is particularly appropriate for strongyloidiasis because the surveillance data are derived from serologic testing that indicates an active infection.** Occult infection could place a refugee at risk of developing disseminated strongyloidiasis under certain circumstances.

Unlike for *Strongyloides*, a positive serologic test for *Schistosoma* is not specific for active infection; therefore,

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rather than treating patients presumptively, clinicians may prefer to test patients with clinical findings suggestive of active schistosomiasis (e.g. hematuria or eosinophilia). Testing for *Schistosoma* infection can be unreliable however. Clinicians wishing to test for schistosomiasis should arrange for specimens to be sent to the CDC through the State Laboratory Institute.

Lastly, because these infections are endemic throughout most of tropical Sub-Saharan Africa, RIHP recommends implementation of this guidance with other refugees from Africa, such as Liberians, other West Africans, and majority-clan ethnic Somalis. **RIHP encourages clinicians to consider presumptive treatment of all new arrivals from Sub-Saharan Africa until pre-departure treatment programs are implemented overseas.** The choice of treatment regimen is at the clinician's discretion. A list of countries with endemic loiasis follows below as a guide for clinicians to determine which treatment regimen is appropriate based on whether the refugee's country of origin has a high prevalence of loiasis:

Countries Endemic for *Loa loa* Infection

Angola, Benin, Cameroon, Central African Republic, (Chad, southern half of country), Congo, Democratic Republic of Congo (formerly Zaire), Equatorial Guinea, Gabon, Nigeria, Sudan (Western and Southwestern parts of Darfur, Bahr El Ghazal, and Equatoria Provinces).

Countries with Isolated Cases of Loiasis:

Ethiopia, Guinea, Ivory Coast, Liberia, Malawi, Sierra Leone, Uganda, Zambia

Between visits

Review lab results. Write and pre-fill prescriptions for medications to treat pathological intestinal parasites. Prescribe through a pharmacy affiliated with your program to ensure that the patient is not billed for antiparasitic medications.

Second visit

Describe the findings to the patient. If test results are positive for a pathological parasite, discuss treatment with your patient. Give the pre-filled medication to the patient and describe how to take medications. Single dose medications should be taken at the clinic visit whenever possible. Discuss the need for follow-up. In addition, clinicians have the option of testing up to 2 additional O & P's and serologic testing for helminths and filaria for patients with eosinophilia or other clinical findings suggestive of parasitoses.

EVALUATING FINDINGS

The health assessment program requires examination of stool to detect parasites. If parasites other than those listed on the health assessment form are identified, please list by name under “*Other.*”

Decisions concerning management of an individual patient require experience with the different clinical characteristics of the various parasitic infections. The usual sites of the parasite infection in the host are often apparent, but certain parasites’ life cycles will take them to other parts of the human body where they may or may not cause symptoms. The existence of a tissue-invasive parasite should be considered in patients with peripheral eosinophilia.

The geographic distribution of parasitic infections is varied, and knowledge of distributions is of great value to knowing what to look for in a patient. Information such as refugee migration, food habits, lack of shoes, lack of potable water, quality of sanitation, and history of insect bites are helpful in ruling-out or -in parasitic infections. Tissue invasion may produce fever, headache, pain, chills, nausea and vomiting. Pressure from growing parasites may give rise to pain. In the brain, parasitic infection might cause various motor and sensory abnormalities, including seizures. Parasites may obstruct the intestine, bile ducts, lymph channels, and capillaries of the brain and other organs causing serious problems. Extensive anemia may be produced by red cell destruction, blood loss, or suppression of hematopoiesis.

Clinicians are reminded to comply with the Commonwealth’s regulations regarding reporting of certain diseases to either local or state public health officials as required by state regulations (105 CMR 300.00).

The [list](#) of infectious diseases reportable by law as well as other resources related to reporting are on the DPH web site.

The following is a brief guide to the life cycle, pathology, symptomatology, and treatment of parasites most commonly seen in refugee populations:

Ascaris***Ascaris lumbricoides*** (Roundworm)

Ascaris is the largest intestinal roundworm in humans (8-12 inch in length). Infections are common world-wide, but mostly in the tropics, in areas with poor sanitation, and wherever human feces are used as fertilizer. Nonspecific gastrointestinal symptoms are reported in some patients. If

the infection goes untreated, adult worms can live for as long as 12 to 18 months. **Patients with multiple parasites including *Ascaris* should always receive treatment for *Ascaris* first, due to the risk of migration of the worm in response to noxious stimuli.**²³

Blastocystis

Blastocystis hominis (Protozoan)

Blastocystis is present in many healthy, asymptomatic individuals with stool microscopy showing fewer than three trophozoites per high powered field. It is often considered non-pathogenic. Infrequently, any of the following symptoms may occur: mild diarrhea (two to four soft stools per day), abdominal pain, nausea, anorexia, fatigue, bloating, cramps, or alternating diarrhea and constipation.²⁴ Treatment should be reserved for immunocompromised patients who are symptomatic and in whom no other pathogen or process is found to explain gastrointestinal symptoms.

Clonorchis

Clonorchis sinensis (Fluke)

Clonorchis is commonly known as the Oriental liver fluke. Humans get infected by eating uncooked fish containing infectious metacercariae and by ingestion of cysts in drinking water. The parasites live in the distal bile ducts and irritate them by mechanical force and toxic secretions. Depending on the severity of the infection (may be up to thousands of worms), the liver may become enlarged and tender. The bile ducts gradually thicken, becoming dilated and tortuous. Adenomatous transformation of the biliary epithelium develops. Light infections, however, may produce only mild symptoms or go unrecognized. As additional worms are acquired, indigestion and epigastric discomfort (unrelated to meals), weakness, and weight loss become noticeable. In heavy infection, anemia, liver enlargement, slight jaundice, edema, ascites, and diarrhea also develop. In late stages, tachycardia, palpitations, vertigo and mental depression may ensue.²⁵

E. histolytica

Entamoeba histolytica (Protozoan)

Entamoeba histolytica occurs in both pathogenic and non-pathogenic strains. Pathogenic strains may penetrate the epithelial tissue of the colon causing ulceration (amebic dysentery). In some cases, organisms that reach the liver by the portal bloodstream produce abscesses (hepatic

²³ Red Book 2006. pp 218-219.

²⁴ Red Book 2006. pp 231-232.

²⁵ Brown, pp 222-225.

amebiasis). The onset of symptoms of amebic liver abscesses can be abrupt or insidious. Fever and localized abdominal pain are almost always present. Right shoulder pain usually indicates referred pain from diaphragmatic irritation. The liver is usually tender to palpation. In a fraction of these cases, amoebae may spread to other organs such as the lungs, brain, kidney or skin, with a high fatality rate.²⁶

Giardia*Giardia lamblia (intestinalis)* (Protozoan)

Giardia is a flagellate protozoan that exists in trophozoite and cyst forms; the cyst form is resistant to drying and other environmental effects and is infectious. Infection is limited to the small intestine and/or biliary tract. It is transmitted through food and water contaminated by sewage, food handlers with poor hygiene, and through other fecal-oral routes. Infection is more common in children than in adults, particularly in the 6-10 year age group. Patients with clinical illness may develop acute watery diarrhea with abdominal pain, or they may experience a protracted, intermittent, disease which is characterized by passage of foul-smelling diarrhea or soft stool associated with flatulence, abdominal distention, and anorexia.²⁷

Hookworms*Ancylostoma duodenale* and *Necator americanus*

Hookworm eggs are passed in the stool and then hatch in warm, moist soil, releasing rhabditiform larvae that develop within a few days into filariform larvae. No free-living adult forms exist. Filariform larvae invade the skin and migrate through venous blood to the heart and then the lungs, where they penetrate into alveoli and migrate via the trachea into the gastrointestinal system. Once the larvae reach the small intestine, they mature into adults that attach themselves to the duodenal and jejunal mucosa where they suck blood. The worms produce an anticoagulant that causes blood to ooze around the feeding worm, leading to blood in the stool and ongoing blood loss. Clinical manifestations are complaints of hunger and nondescript abdominal pain. Severe cases can lead to anemia. Children with significant worm loads may experience growth retardation and inanition.²⁸

H. nana*Hymenolepis nana* (Dwarf tapeworm)

Tapeworms, or cestodes, are hermaphroditic flatworms composed of a scolex, or head, that attaches itself to the

²⁶ Red Book 2006, pp 204-206.

²⁷ Red Book 2006, pp 296-301.

²⁸ Brown, pp 119-125 and Red Book 2006, pp 374-375.

intestinal mucosa where a chain of progressively mature segments (proglottids) containing the reproductive parts produce ova. Adults live in the gut lumen of the definitive host. These worms have no gut and absorb nutrients across their integument. Larval forms encyst in the tissues of intermediate hosts. *H. nana* uses the human as both definitive and intermediate host. It is transmitted directly from hand to mouth and, less frequently, by contaminated food or water, and, possibly, by insect intermediate hosts. The unhygienic habits of children favor the prevalence of the parasites in the younger age groups. The worm's habitat is in the upper two-thirds of the ileum with a life span of several weeks.

The ability of *H. nana* to autoinoculate may lead to very heavy worm loads (as many as 2000 worms) and to cramping pain, diarrhea, nausea and vomiting, and headache. Intestinal erosions may occur. In children, heavy *H. nana* infestation may be associated with lack of appetite, abdominal pain with or without diarrhea, anorexia, vomiting, irritability, and rarely, seizures. These neurologic manifestations have been ascribed to absorption of toxic substances produced by the worms.²⁹

Schistosoma

Schistosoma species

Schistosomiasis encompasses three distinct phases of clinical manifestations and on a worldwide scale is one of the most common causes of hematuria. Individuals exposed to various *Schistosoma* sp. trematodes will initially experience a pruritic papular dermatitis after penetration of the skin by cercariae. With non-human pathogen species, this is referred to as "swimmer's itch," and can be contracted from fresh and salt water. Human pathogenic species include the following: *S. mansoni*, *S. japonicum*, *S. haematobium*, *S. mekongi*, and *S. intercalatum*. These species rely on the presence of a fresh water snail as vector and have various geographic distributions. *S. mansoni* is found mainly in tropical Africa, Latin America, the Caribbean, and the Arabian peninsula. *S. haematobium* is found mainly in Africa and the eastern Mediterranean area. *S. mekongi* and *japonicum* are found mainly in the Mekong River delta and in parts of China, the Philippines, and Indonesia respectively.

After skin penetration, the organism migrates through the blood stream via the lungs before ultimately lodging in the venous plexus draining the bladder (*haematobium*) or the colon. Following a period of 4-6 weeks, an acute illness (characterized by fever, malaise, cough, rash, abdominal pain,

²⁹ Brown H, Neva F. *Basic Clinical Parasitology*. Appleton-Century-Crofts, 1983. pp 179-181; and *Red Book 2006*, pp 646-648.

nausea, diarrhea, lymphadenopathy, and eosinophilia) ensues and is termed “Katayama fever.” With heavy gastrointestinal infestations, bloody diarrhea and tender hepatomegaly may occur. Chronic disease reflects the worm burden and fibrosis with inflammation at the sites of deposited eggs. Infected individuals may be asymptomatic with light infestations. Heavy colon involvement may cause chronic bloody, mucoid diarrhea, abdominal pain, hepatosplenomegaly, ascites, and esophageal varices (due to portal hypertension). Bladder symptoms related to inflammation and fibrosis may include dysuria, terminal hematuria (microscopic or gross), secondary UTIs, and pelvic pain.

Infections by *S. mansoni* and other species affecting the GI tract are diagnosed by microscopy of concentrated stool specimens. Infections by *S. haematobium* are diagnosed by microscopy of filtered urine. Egg excretion peaks at 12-3:00 PM. Mucosal biopsies may be necessary for diagnosis, and serologic testing is available.

Strongyloides

***Strongyloides stercoralis* (Roundworm)**

S. stercoralis is usually excreted in the stool as a rhabditiform larva. The rhabditiform larva molts into an infective filariform larva (about 700 µm) after a couple of days in the soil. The filariform larvae may penetrate the human skin and migrate in the same manner as the hookworms. When larvae reach the upper part of the small intestine, they develop into adults. The rhabditiform larvae also may develop into sexually mature free-living males and females in the soil. This indirect cycle appears to be associated with the optimal environmental conditions for a free-living existence in tropical countries. Autoinfection and maintenance of the disease may occur (despite removal of the host from an endemic area) when rhabditiform larvae develop into filariform larvae in the gut lumen.³⁰

Most patients with strongyloidiasis are asymptomatic. A heavy worm load can lead to epigastric pain, weakness, malaise and watery diarrhea, perhaps due to an absorptive defect. Upper gastrointestinal radiographic studies may show duodenal and jejunal mucosal edema. Ulceration, and even intestinal perforation may occur. The hyperinfection syndrome can be an overwhelming systemic disease and is often fatal. Extensive migration of larvae can lead to derangement of multiple organs, secondary bacterial abscesses in the liver and other organs, and development of adult worms in the bronchial tree. Strongyloidiasis can be diagnosed by demonstrating

³⁰ Brown, pp 115-119; and *Red Book 2006*, pp 629-631.

larval forms in the stool or parasites in duodenal aspirates or biopsies and is suggested by blood tests that show hypereosinophilia of greater than 30% without obvious clinical correlation.³¹

Trichuris*Trichuris trichiura* (Whipworm)

Prior to the CDC's overseas empiric treatment program, *Trichuriasis* was the second most common intestinal parasitosis diagnosed during the RHAP. The embryonic development of *Trichuris* takes place outside the host. An unhatched, infectious first stage larva is produced in three weeks in a warm, moist, and shaded soil environment. When the egg is ingested by humans, the activated larva escapes from the weakened egg shell in the upper small intestine and penetrates an intestinal villus. *Trichuris* lives primarily in the human cecum, but is also found in the appendix and lower ileum. Clinical manifestations are usually absent in light infections; in heavy or chronic infections, abdominal pain and tenderness, frequent blood-streaked diarrheal stools, nausea and vomiting, weight loss and anemia may occur.³²

Common Non-Pathogenic Parasites

Blastocystis hominis (see above)

Dientamoeba fragilis (may treat with Paromomycin if symptomatic and no other etiology – see table for

Entamoeba histolytica treatment)

Endolimax nana

Entamoeba coli

Entamoeba hartmanni

Iodamoeba butschlii

**Other Common Parasites
Lice, Scabies**

Lice and scabies are two common arthropod parasites often found in refugee populations. MassHealth covers both over-the-counter permethrin and lindane; in addition, if prescribed by a RHAP provider, the RHAP will reimburse sites and affiliated pharmacies for permethrin for refugees who have not yet received their MassHealth cards. Preferred treatment of lice is permethrin 1% cream rinse ("Nix")³³ with removal of nits. Scabies also should be treated but with permethrin 5% lotion ("Elimite")²⁷ in a single overnight application with instructions about careful hygiene and simultaneous household cleaning. Symptomatic treatment of pruritus is

³¹ Jain M, DeMaria A Jr. Parasitic and tropical diseases and advice for travelers. In: Noble J, Gantz N, eds. *Primary Care and General Medicine, Second Edition*. p 4.

³² *Red Book 2006*, pp 674-675.

³³ Use of brand name is for identification purposes only and does not imply product endorsement.

essential for relief from the allergic response to scabies infection, with anti-histamines and/or topical steroids for up to two weeks after permethrin treatment.

PHARMACOLOGIC TREATMENT OF PARASITIC DISEASES

Clinicians at RHAP clinical sites should become familiar with the treatment of common, uncomplicated parasitic infections. Most common among these are trichuriasis, giardiasis, intestinal amoebiasis, and ascariasis. The following tables summarize medications that are reimbursed by RHAP for the treatment of intestinal parasites. In addition to these, RHAP will reimburse for permethrin to treat scabies and lice. RHAP clinics are expected to have a relationship with a local or on-site pharmacy for obtaining anti-parasitic (and other) medications for patients in advance of the second visit. At the time of the second visit, clinicians should review dosing with patients (via an interpreter) and observe consumption of the medication (at least the first dose if part of a multi-dose course).

Note: Clinicians may consider empiric treatment of refugees with negative O & P tests in the following situations:

- Multiple family members with similar intestinal parasites. For example, if two family members have trichuriasis, the clinician may consider treating the patient with mebendazole or albendazole.
- A patient (from a country with endemic parasitoses) with a high-risk medical condition which predisposes to complications from parasitoses. For example, a patient with asthma or rheumatic disease who may be likely to be placed on steroids. In these instances, the clinician should consider empiric treatment with albendazole, 400 mg po bid for 3 days.

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RECOMMENDED AND REIMBURSED DRUGS FOR MAJOR PARASITES*

Parasite	Drug (generic/trade) <i>In Order of Preference:</i>	Adult Dosage	Pediatric Dosage
<i>Ascaris</i>	Mebendazole/Vermox	500 mg once or 100mg bid x 3d.	Same
	Albendazole/Albenza	400 mg once	Same
<i>Clonorchis</i>	Praziquantel/Biltricide	25 mg/kg q 6° x 3 doses	Same
	Albendazole/Albenza	10 mg/kg x 7 days	Same
<i>E. histolytica</i> ³⁴	Paromomycin/Humatin	25-35 mg/kg/day ÷ tid x 7 days	Same
	Iodoquinol/Yodoxin	650 mg tid x 20 days	30-40 mg/kg/day ÷ tid x 20 days (max. 2 gm)
<i>Giardia</i>	Metronidazole/Flagyl	250 mg tid x 5 days	15 mg/kg/day ÷ tid x 5 d.
	Nitazoxanide/Alinia		100 mg bid x 3d. (1-3 yrs) 200 mg bid x 3d. (4-11 yrs)
Hookworm	Mebendazole/Vermox	500 mg once or 100mg bid x 3d.	Same
	Albendazole/Albenza	400 mg once	Same
<i>Hymenolepis</i>	Praziquantel/Biltricide	25 mg/kg x 1 dose	Same
Lice	Permethrin 1% cream rinse/Nix	Apply x 1; repeat after 2 wks prn	Same
Scabies	Permethrin 5% lotion/Elimite	Apply qhs and rinse in AM once	Same
<i>Schistosoma</i>	Praziquantel/Biltricide	20 mg/kg bid-tid x 1 day ³⁵	Same
<i>Strongyloides</i>	Ivermectin/Stromectol ³⁶	200 µg/kg/day x 1-2 days	Same
	Thiabendazole/Mintezol	25 mg/kg bid x 7 days	Same
Tape worms ³⁷	Praziquantel/Biltricide	5-10 mg/kg x 1 dose	Same
<i>Toxocara canis</i>	Albendazole/Albenza	400 mg bid x 5 days	Same
	Mebendazole/Vermox	100-200 mg bid x 5 days	Same
<i>Trichuris</i>	Mebendazole/Vermox	500mg once or 100mg bid x 3d.	Same
	Albendazole/Albenza	400 mg once ³⁸	Same

*The Medical Letter on Drugs and Therapeutics. August 2004;1-12.

Note: Nitazoxanide/Alinia is only reimbursed for children under 12 years of age.

Note: Patients with *Ascaris* as well as another parasite should always be treated for *Ascaris* first due to the risk of migration of the worm.

Note: Albendazole is only available as a film-coated tablet and may not be suitable for use in young children.

Note: Paromomycin is not absorbed and may be useful for treatment of amoebiasis and giardiasis during pregnancy.

³⁴ Asymptomatic carriage only. Obtain consultation for symptomatic case treatment.

³⁵ TID dosing for *S. japonicum* and *S. mekongi*.

³⁶ Ivermectin not FDA approved for use in disseminated strongyloidiasis.

³⁷ *Diphyllobothrium latum*, *Taenia saginata/solium*, and *Dipylidium* only. Consult reference for others.

³⁸ In heavy infection, may need to treat with 400 mg bid x 3 days.

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FORMULATIONS:

- Albendazole/Albenza: 200 mg film-coated tablets
- Iodoquinol/Yodoxin: 210 and 650 mg tablets
- Ivermectin/Stromectol: 3 mg unscored and 6 mg scored tablets
- Mebendazole/Vermox: 100 mg chewable tablets
- Metronidazole/Flagyl: 250 & 500 mg tablets, 100 mg/5cc suspension (specially prepared)
- Nitazoxanide/Alinia: 500 mg tablets, 100mg/5cc suspension
- Paromomycin/Humatin: 250 mg capsules
- Permethrin/Elimite/Nix: 5% cream (60gm) /1% cream rinse (59cc)
- Praziquantel/Biltricide: 600 mg triscored tablets, 150 mg/section
- Thiabendazole/Mintezol: 500 mg chewable tablets, 500mg/5cc suspension

MAJOR SIDE EFFECTS*:

Drug	Common	Rare
Albendazole	Abd. pain, reversible alopecia, transaminase elevation, <i>Ascaris</i> migration	Leukopenia, rash, renal toxicity
Iodoquinol	Rash, acne, goiter, nausea, anal pruritus, diarrhea, cramps	Optic neuritis/atrophy, loss of vision, peripheral neuropathy, iodine sensitivity
Ivermectin	Mazzotti-type reaction in onchocerciasis: fever, pruritus, lymphadenopathy, headache, arthralgia	Hypotension, edema, tachycardia, possible ophthalmological changes
Mebendazole	Diarrhea, abdominal pain, <i>Ascaris</i> migration	Leukopenia, alopecia, hepatotoxicity, agranulocytosis, hypospermia
Metronidazole	Nausea, dry mouth, metallic taste, headache, GI disturbance, insomnia, vertigo, tinnitus, weakness, stomatitis, dark urine, disulfiram-like rxn., paresthesia, rash, urethritis	Seizures, encephalopathy, pseudomembranous colitis, ataxia, leukopenia, pancreatitis, peripheral neuropathy
Nitazoxanide	Abdominal pain, diarrhea, headache, nausea	(No rare side effects listed)
Paromomycin	GI disturbance, eighth nerve toxicity, nephrotoxicity if IV administration, vertigo, pancreatitis	(No rare side effects listed)
Permethrin	Burning, stinging, numbness, increased pruritus, edema, erythema, rash	(No rare side effects listed)
Praziquantel	Malaise, headache, dizziness, sedation, GI upset, fever, sweating, nausea, eosinophilia, fatigue	Pruritus, rash
Thiabendazole	Nausea, vomiting, vertigo, headache, drowsiness, pruritus, leukopenia, crystalluria, rash, hallucinations and psychological reactions, visual/olfactory disturbance, erythema multiforme	Shock, tinnitus, intrahepatic cholestasis, seizures, angioneurotic edema, Stevens-Johnson Syndrome

*This table is not meant to be a definitive list of side effects and contraindications. Clinicians are responsible for familiarizing themselves with prescribed anti-parasitic drugs.

**DISEASE SYNDROMES
IN TRAVELERS AND
REFUGEES**

Diarrhea, eosinophilia, fever, mass lesions, respiratory infections, and skin lesions are the most common disease syndromes in travelers and immigrant (refugee) populations. RHAP's targeted testing includes common first line tests used in the evaluation of eosinophilia. Included in these are up to two stool microscopy tests in addition to the one in the core protocol and serologic tests for *Schistosoma*, *Strongyloides*, and filaria. Targeted testing is described in Section 3.11. The following tables about the etiologies of eosinophilia are from: Jain M, DeMaria, A Jr. Parasitic and tropical diseases and advice for travelers. In: *Primary Care & General Medicine, Second Edition*.³⁹

**CAUSES OF SIGNIFICANT
PERIPHERAL BLOOD
EOSINOPHILIA**

Peripheral blood eosinophilia is defined as more than 450 eosinophils per cubic millimeter of blood. It occurs with allergic reactions and a number of disease processes but, on a worldwide basis, it is a common laboratory finding associated with parasitic infection.

Helminthic parasites:

Angiostrongylus cantonesis and *A. costaricensis*

Anisakiasis

Ascaris lumbricoides (invasive larval stage)

Capillaria philippinensis

Echinococcus

Fasciolopsis buski

Filariasis

Animal hookworms

Hookworms (invasive larval stage)

Liver flukes

Paragonimus westermani

Schistosomiasis

Strongyloides stercoralis (initial inf. and autoinf.)

Toxocara species

Trichinosis

Tropical eosinophilia

(Unidentified microfilariae)

Other infections/infestations:

Pulmonary aspergillosis

Severe scabies

Wiscott-Aldrich syndrome

³⁹ Jain, p 35.

Allergies:

Asthma

Hay fever

Drug reactions

(Eosinophilic myalgia syndrome-tryptophan, toxic oil syndrome)

Other:

Addison's disease

Inflammatory bowel disease

Dermatitis herpetiformis

Atopic dermatitis

Toxic/chemical syndrome

Autoimmune and related disorders:

Hypereosinophilia syndrome (unknown etiology)

Polyarteritis nodosa

Necrotizing fasciitis

Eosinophilic vasculitis

Pemphigus

Mucin-secreting adenocarcinomas

Immunodeficiency states:

Hyperimmunoglobulin E with
recurrent infection

Neoplastic diseases:

Hodgkin's disease

Mycosis fungoides

Chronic myelocytic leukemia

Eosinophilic leukemia

Polycythemia vera

Section 3: CLINICAL PROGRAM**EVALUATION OF FEVER**

The differential diagnosis of fever in a refugee can be narrowed by a good history (travel history, food/water exposure, insect bites, and animal contacts in particular), a physical examination (looking specifically for rash, lymphadenopathy and hepatosplenomegaly), and appropriate laboratory testing (particularly a CBC to identify anemia and eosinophilia). A differential diagnosis of some selected systemic febrile illnesses to consider in refugees is listed below.

DIAGNOSIS	REGION	VECTORS [] and CLINICAL CHARACTERISTICS { }
COMMON		
Acute respiratory infection	Worldwide	
Gastroenteritis	Worldwide	[Food, water, fecal-oral]
Enteric fever, incl. typhoid	Worldwide	[Food, water, fecal-oral]
Urinary tract infection	Worldwide	
Drug reactions	Worldwide	[Antibiotics, prophylactic agents, other] {Rash frequent}
Malaria	Tropics, mainly	[Mosquitoes] {Fever, hepatosplenomegaly}
Arboviruses	Asia, Carib., Afr.	[Mosquitoes]
Viral Hepatitis	Worldwide	{Fever, malaise, jaundice}
Hepatitis A	Worldwide	[Food, water, fecal-oral]
Hepatitis B	Worldwide, esp. Asia, Africa	[Body fluids] {Long incubation}
Hepatitis C	Worldwide	[Body fluids]
Tuberculosis	Worldwide	[Airborne, milk] {Long incubation}
STD	Worldwide	[Sexual contact]
LESS COMMON		
Filariasis	Asia, Afr., S.Amer.	[Biting insects] {Long incubation}
Measles	Worldwide	[Airborne]
Amebiasis +/- abscess	Worldwide, tropics	[Food, water, fecal-oral]
Brucellosis	Worldwide	[Milk, cheese, food, animal contact]
Listeriosis	Worldwide	[Foodborne] {Meningitis}
Leptospirosis	Worldwide	[Animals, fresh water] {Jaundice, Meningitis}
Strongyloidiasis	Tropics	[Soil contact] {Eosinophilia}
Toxoplasmosis	Worldwide	[Undercooked meat, cat feces, congenital]
RARE		
Relapsing fever	West Americas, Asia, N. Afr.	[Ticks, lice]
Hemorrhagic fevers	Worldwide	[Arthropod and non-arthropod transmitted]
Yellow fever	Tropics	[Mosquitoes] {Hepatitis}
Hemorrhagic fever with renal syndrome	Europe, Asia	[Rodent urine] {Renal impairment}
Hantavirus	Western N. Amer.	[Rodent urine] {Resp. Distress Syndrome}
Lassa fever	Africa	[Rodent excreta, person to person] {Often severe}
Other		

MALARIA⁴⁰

Malaria, caused by the *Plasmodium sp.* parasites, is one of the most prevalent diseases in the world, with disastrous social consequences and a heavy burden on economic development. Malaria accounts for 10% to 30% of all hospital admissions worldwide. The total cost of malaria-related health care, treatment, and lost economic productivity was estimated to be nearly \$1 billion for tropical Africa alone.

The deterioration of social and economic conditions, dislocation of populations, and armed conflicts in Africa and Southeast Asia have exacerbated control of malaria. With disrupted public and clinical health services, malaria control efforts are limited, putting underserved rural populations at greater risk. In the absence of adequate health services, incomplete treatment and inappropriate use of prophylaxis increases drug resistance of the *Plasmodia* parasites.

Annually, 300 – 500 million cases and 1.5 – 2.7 million deaths are estimated to occur. Eighty percent of the cases occur in tropical Africa, and malaria is the cause of 15% to 25% of all deaths of children under the age of five. Around 800,000 children under the age of five die from malaria every year. Pregnant women who contract malaria are at risk of miscarriage and *in utero* growth retardation. Refugees from non-endemic areas may also be at risk if they have had to migrate through or into an endemic zone.

Refugees from sub-Saharan Africa likely received pre-departure presumptive treatment for malaria. If an individual from sub-Saharan Africa did not receive treatment before travelling to the United States, please consider presumptive treatment.

Malaria is an infection caused by protozoa of the genus *Plasmodium* in which the asexual cycle (schizogony) takes place in the red blood cells of vertebrates and the sexual cycle (sporogony) takes place in mosquitoes. The *Anopheles* mosquito is the arthropod vector for transmission outside the human host. Four *Plasmodia* species are most common in infections of human beings: *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*. Diagnosis relies on identification of the parasite on stained thick blood smears.

Acute illness is characterized by non-specific symptoms such as fever, malaise, myalgia, headache, photophobia, diarrhea, anorexia and nausea. Fever may last up to three weeks and gradually come in the classic cyclic paroxysms. Complications may include meningoencephalitis, arthralgia/arthritis, orchitis,

⁴⁰ Red Book 2006; pp. 435-441.

shock, and respiratory symptoms (including pulmonary edema). Laboratory findings include anemia, hypoglycemia, evidence of acidosis or renal failure, and leukopenia. Hepatosplenomegaly, pallor, and jaundice are common physical findings. Perinatal and congenital infections of mother and fetus may be severe. Chronic infection may result in tropical splenomegaly syndrome, characterized by hemolysis and splenomegaly with elevated titers of antiplasmodium antibodies.

The CDC recently has revised its recommended regimen for pre-departure presumptive treatment for refugees departing from Sub-Saharan Africa (i.e. the region of endemic falciparum malaria). The current recommendation is for artemisinin-based combination therapy (ACT) with artemether-lumefantrine. Malaria pre-departure presumptive therapy is administered and documented as directly-observed therapy, and this documentation must be carried by the refugee. To be considered valid the presumptive therapy must be completed no sooner than 3 days prior to departure.

Special populations including pregnant or lactating women and children <5 kilograms require directed treatment after diagnostic testing and thus do not receive presumptive therapy. Individuals in these groups who lack signs and symptoms of malaria but have laboratory-diagnosed *Plasmodium falciparum* infection are treated with either a combination of oral quinine and clindamycin (preferred) or a longer course of oral quinine.

Refugees from Sub-Saharan African who have received pre-departure treatment with a recommended antimalarial drug or drug combination do not need further evaluation or treatment for malaria once in the U.S. unless they have clinical symptoms.

Refugees from Sub-Saharan Africa who have not received the recommended presumptive or directed pre-departure treatment should either receive presumptive treatment on arrival (preferred) or have laboratory screening to detect *Plasmodium* infection.

Given the low prevalence of infection in most other areas from which refugees arrive, the prolonged course of treatment, potential adverse effects of medication, and the lack of useful

laboratory screening tools, the CDC does not currently recommend that newly arriving refugees from regions other than Sub-Saharan Africa receive presumptive treatment for non-falciparum malaria or laboratory diagnostic evaluation on arrival to the United States. The CDC will monitor non-falciparum prevalence rates among future arriving refugee populations, and will update their guidance if indicated.

The CDC's website contains detailed guidance on dosing of atovaquine-proguanil for presumptive treatment in the U.S.:

http://www.cdc.gov/ncidod/dg/refugee/rh_guide/malaria/domestic.htm#table2

Other than presumptive outpatient treatment, any treatment of refugees for malaria should be done in consultation with an infectious disease specialist.

The Centers for Disease Control offer 24-hour consultation at 770-488-7788 during weekday business hours and by page at 770-488-7100 after hours and on weekends and holidays.

Treatment guidelines are available at:
http://www.cdc.gov/malaria/diagnosis_treatment/clinicians.htm

RESOURCES

[Division of Parasitic Diseases, NCID](#)

CDC

404-488-4050

[CDC Malaria Guidelines](#)