Absence of *Loa loa* Microfilaremia among Newly Arrived Congolese Refugees in Texas

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Abstract.

The Centers for Disease Control and Prevention recommends that refugees at risk of *Loa loa* infection be tested for microfilaria before treatment with ivermectin. We report observational results of this approach in African refugees in Texas. Daytime blood smears were performed for microfilaria on at-risk African refugees who arrived in Texas from July 1, 2014 through December 30, 2016. Clinics were asked if there were any adverse events reported among those who received ivermectin. Of the 422 persons screened, 346 (82%) were born in *L. loa*–endemic countries, with 332 (96%) of these being born in the Democratic Republic of Congo. No smears detected microfilaria, and all received presumptive ivermectin with no reports of significant adverse events. In this investigation, the prevalence of significant microfilarial load in sub-Saharan African refugees appeared to be low, and ivermectin treatment was safe and well tolerated.

BACKGROUND

Loa loa infection, sometimes known as the "eye worm," is found in West and Central Africa where competent vectors exist.[1] Ten countries—Angola, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of Congo, Equatorial Guinea, Gabon, Nigeria, and South Sudan—have areas where there are high rates of infection. An estimated 14.4 million people live in these areas of high rates of infection.[1]

Ivermectin is highly effective in the global elimination efforts of onchocerciasis and lymphatic filariasis.[2] However, ivermectin use is generally avoided in areas with *L. loa* infection because life-threatening encephalopathy has been reported when people with high levels of *L. loa* microfilaremia are treated inadvertently with ivermectin.[3] Increasingly, there is interest in greater use of ivermectin for onchocerciasis, filariasis, strongyloidiasis, and scabies for global control programs and in refugees and other displaced populations.[4]

Presumptive treatment of parasitic infections with albendazole began in 1997 in United States-bound refugees, with the subsequent addition of praziquantel for treatment of schistosomiasis for those originating in sub-Saharan Africa. Beginning in 2011, the Centers for Disease Control and Prevention (CDC) implemented a presumptive treatment program for

strongyloidiasis for United States-bound refugees using ivermectin.[5] The CDC recommendations state that refugees who are born in, or have resided in, areas with *L. loa* should not receive presumptive treatment unless a high *L. loa* microfilaremia has been excluded.[5] The current gold standard for *L. loa* microfilaremia diagnosis is identification of the microfilariae on a blood smear made from blood taken from the patient between 10 AM and 2 PM. The logistics of obtaining blood for smears at acceptable times and having qualified interpretation in mobile refugee populations is challenging. Thus, refugees at risk for *L. loa* microfilaremia do not receive ivermectin presumptive treatment before departure to the United States. Instead, these refugees are given a single dose of presumptive therapy with albendazole and praziquantel for other soil-transmitted helminths and schistosomiasis, with management of strongyloidiasis deferred until arrival in the United States.[5]

Of the 69,933 refugees resettled in the United States in 2015, 7,479 (11%) were settled in Texas.[6] The Texas Department of State Health Services (DSHS) performed the daytime blood smears in any at-risk refugee before ivermectin use. We retrospectively reviewed the Texas screening data to determine the prevalence of microfilaria in those born in, or who had lived in, *L. loa* high-risk countries and, subsequently, sought reports of complications associated with ivermectin use.

METHODS

The Refugee Health Program within the Texas DSHS provided refugees a postarrival health assessment within 90 days of arrival as recommended by CDC.[7] We reviewed records of newly arrived African refugees who have resided in any of the 10 *L. loa*–endemic countries[1] before entering the United States and visited one of three Texas refugee health clinics in the jurisdiction of their residence—Tarrant County, City of Amarillo, and City of Austin—during July 1, 2014 through December 31, 2016.

The routine health clinic practice was for venous blood to be collected in an ethylenediaminetetraacetic acid–containing vacuum container tube between 10 AM and 2 PM and shipped to the DSHS Parasitology Laboratory in Austin, Texas. Presence of microfilaria was determined by microscopic examination of Giemsa-stained thick and thin blood smears, as described by the CDC's DPDx—Laboratory Identification of Parasitic Diseases of Public Health Concern.[8] Texas DSHS had arranged to conduct the Knott's Concentration test on positive specimens[8] and send positive samples to the CDC and the National Institutes of Health. Those who tested negative for microfilaremia were offered ivermectin if they had no other contraindications. Clinics were asked if there were any adverse events reported among those who received ivermectin.

The Refugee Health Program of the Texas DSHS provided approval for this nonresearch assessment. Funding was provided by the CDC CK12-1205 Strengthening Surveillance for Diseases among Newly Arrived Immigrants and Refugees.

RESULTS

A total of 422 persons were screened with a daytime blood smear: 212 (50.2%) women; 111 (26.3%) were children younger than 18 years of age (Table 1). Of those who were screened, 346 (82%) were born in *L. loa*–endemic countries, with 332 of these (96%) born in the Democratic Republic of Congo; 18 (4.2%) resided in an endemic country (Table 2); and 10 (2.4%) never lived in an endemic country immediately before arrival in the United States. Also, 12 (2.8%)

resided entirely in one or more *L. loa*–endemic country before arrival. Blood samples were collected a median of 39 days after arrival (range: 36 to 42). All blood smears were negative for microfilaria. All eligible refugees received presumptive ivermectin on the absence of microfilaria; no adverse events were reported.

DISCUSSION

These findings suggest that microfilaremia is rare among this group of newly arrived African, primarily Congolese, refugees in Texas who were born in, or resided in, *L. loa*–endemic countries. Presumptive ivermectin was well tolerated, with no reported medication adverse events on retrospective inquiry.

Despite the Texas program's successful implementation of the postarrival protocol, it can be complex. The protocol requires determining at-risk populations among refugees assessed at the clinic (this inquiry found 5% with no risk were tested); if a refugee has a primary appointment outside the testing hours of 10 AM to 2 PM, they would need to have a separate appointment arranged for daytime blood smear, and a laboratory with familiarity and expertise. Implementation is challenging for most receiving clinics, especially clinics that receive low numbers of at-risk refugees. Given these challenges, predeparture screening and presumptive treatments would be ideal. Future technologies, such as advanced point-of-care testing (e.g., the Loa CellScope),[9] may make predeparture screening and presumptive treatment more feasible in the future.

As *Strongyloides* prevalence is high among sub-Saharan Africans who are also at-risk for *L. loa*,[10] the CDC recommends that refugees arriving from these areas, but who are unable to receive presumptive treatment before departure, be managed at the postarrival health assessment which is typically conducted within the first 30–90 days of arrival in the United States. Such management includes three options: 1) testing for loiasis by performing thick and thin blood smears between 10 AM and 2 PM, with presumptive treatment with ivermectin in those without *L. loa* microfilaria detected; 2) by treatment with a 7-day course of albendazole as an alternative to ivermectin, or, 3) finally, by serologic testing for *Strongyloides* and managing those who are found positive on an individual basis. All three approaches have limitations. Those related to microfilarial testing have been discussed. Treatment of *Strongyloides* with albendazole is currently limited by the exorbitant cost; the listed average wholesale price of albendazole increased 20-fold ($5.92 to $119.58 per typical daily dose) during 2010–2013.[11] Also, the seven-day course of albendazole is inferior to ivermectin.[12] Finally, the serologic tests for *Strongyloides* results are not timely (available in days to weeks) and may lead to false negative in high pretest probability populations.

This evaluation has limitations. The evaluation involved retrospective data review and passive reporting of adverse events, which may have underreported less severe adverse events. We assessed all Congolese refugees in three of seven refugee health clinics arriving in Texas during this time period, and whereas refugees from the Democratic Republic of Congo were well represented, the number of those tested for other populations were low. Thus, the findings here should not be considered generalizable to all refugees or individuals from *L. loa*–endemic areas. Only 4.3% of refugees recently resided in countries that are currently considered *L. loa*–endemic and, thus, these refugees may not be representative. We were not able to determine the home village, district, or migration route of the refugees included in this analysis. Furthermore, *L. loa* is a focal infection and although not found in this population, even populations from a different

geographic area of the same country may have a higher risk. Lastly, Kamgno et al.[13] found amicrofilaremia on day 60 when given 600 mg dose of albendazole. Although the refugees in this assessment received 400 mg of albendazole before arrival in the United States, we were unable to determine the impact of albendazole on our findings. Nonetheless, the data reported here are the first to be reported in managing the risk of ivermectin use in *L. loa* at-risk populations outside endemic areas.

In conclusion, we were unable to detect microfilaria from any of refugees in our cohort from six sub-Saharan countries known to have *L. loa* transmission. This may be due to lack of exposure to the disease because of the focal nature of *L. loa* transmission within endemic countries or due to lack of infection. Either way, no cases of high-level microfilaremia were detected that would have contraindicated the use of ivermectin to treat strongyloidiasis as per the current refugee screening protocol. The screening protocol and use of ivermectin was safe and well tolerated in this setting. Further investigation is needed to determine if widespread *L. loa* screening should be continued in these United States-bound populations before ivermectin use. In addition, more efficient screening, such as point-of-care testing, would be highly desirable and could significantly improve the process—and may make screening and presumptive treatment with ivermectin before departure for the United States feasible.

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TABLE 1

Demographic information for newly arrived refugees screened for microfilaria in Texas—July 2014 to December 2016 (*N* = 422)

	N	**(%)**
Total	**422**	**100**
Sex		
Female	212	50.2
Male	210	49.8
Age group at arrival		
< 4	10	2.4
4–12	56	13.3
13–17	45	10.7
18–24	89	21.1
25–44	163	38.6
≥ 45	59	14.0
Visa status		
Refugees	410	97.2
Asylees	12	2.8
Country of birth		

Loa loa–endemic		
Democratic Republic of Congo	332	78.7
Sudan*	7	1.7
Nigeria	3	0.7
Congo	2	0.5
Cameroon	1	0.2
Central African Republic	1	0.2
Total—*Loa loa*–endemic	**346**	**82**
Loa loa–nonendemic		
Tanzania	31	7.3
Rwanda	18	4.3
Uganda	11	2.6
Eritrea	8	1.9
Other†	8	1.9
Total—*Loa loa*–nonendemic	**76**	**18**
Country of last residence‡		
Loa loa–endemic		
Chad	1	0.2
Congo	14	3.3
Democratic Republic of Congo	1	0.2
Sudan	2	0.5
Total—*Loa loa*–endemic	**18**	**4.2**
Loa loa–nonendemic		
Tanzania	102	24.2
Uganda	91	21.6
Rwanda	82	19.4
Kenya	77	18.2
Other§	41	9.7
Total—*Loa loa*–nonendemic	**393**	**93.1**
Unknown	11	2.6

* Sudan includes South Sudan because it was not distinguishable in the data.

† Other *Loa loa*–nonendemic countries: Burkina Faso, Burundi, Ethiopia, Kenya, Malawi, and Zambia.

‡ Country of last residence is the country of asylum or where the refugee resided before entering the United States.

§ Burundi, Ethiopia, Lebanon, Malawi, Malta, Mozambique, Namibia, Russia, South Africa, and Zambia.

TABLE 2

Residence history of new arrived refugees by countries of endemic and nonendemic for *Loa loa* in Texas ($N = 422$)

	Residence history					
	Birth		Prior residence*		Last residence†	
Loa loa	*n*	%	*n*	%	*n*	%
Endemic‡	346	82	373	88.4	18	4.2
Nonendemic§	76	18	15	3.6	393	93.1
Unknown	0	0	34	8	11	2.6

* Prior residence is the country where the refugee resided before the aslyum country.

† Last residence is the country of asylum or where the refugee resided before entering the United States.

‡ Loa loa–endemic countries include Cameroon, Central African Republic, Chad, Congo, Democratic Republic of Congo, Nigeria, and Sudan. Sudan includes South Sudan because it was not distinguishable in the data.

§ Loa loa–nonendemic countries include Burundi, Eritrea, and Rwanda.