

1 Prevalence of parasitic infections among recent immigrants to Chicago

2 Short title: Parasitic infections in Chicago

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28 were involved in the investigation and recruited and enrolled subjects in the study and
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31 performed the Multi-parallel real-time quantitative PCR (qPCR) conducted on patient
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36

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39

40 Attachments: STROBE statement

41 **ABSTRACT**

42 *Background.* Parasitic infections are likely under-recognized among immigrant
43 populations in the United States (US). We conducted a cross-sectional study to
44 evaluate the frequency of such infections among recent immigrants in Chicago and to
45 identify predictive factors for parasitic infections.

46 *Methodology and principal findings.* 133 recent immigrants were enrolled, filling out a
47 standardized questionnaire regarding medical history and exposures and providing
48 blood and stool samples for evaluation. Fifteen of 125 subjects (12%) who provided a
49 blood or stool sample for testing were found to have evidence of current or prior
50 infection with a pathogenic parasite, of which *Toxocara* spp. (8 subjects, 6.4%) and
51 *Strongyloides stercoralis* (5 subjects, 4%) were most commonly identified. Parasitic
52 infection was more likely among subjects who had immigrated within the previous 2
53 years and those with a self-reported history of ever having seen worms in the stool.
54 Infected individuals were likely to have multiple nonspecific physical complaints;
55 however, classic symptoms of parasitic infections (skin rashes, diarrhea, etc.) were not
56 increased among infected individuals. The most useful surrogate markers identified for
57 parasitic infections were an elevated Immunoglobulin E level (seen in 7/15 subjects with
58 parasitic infections, 46.7% and 22/110 uninfected individuals, 20%, $p=0.04$) and the
59 presence of *Blastocystis hominis* cysts on Ova & Parasite exam (detected in 5/13
60 subjects with parasitic infections who provided a stool sample, 38.5% and 5/98
61 uninfected subjects, 5.1%, $p=0.002$). In contrast, the Absolute Eosinophil Count
62 (typically thought of as an indicator of parasites) was not found to be a good screening
63 test for parasitic infections in this study.

64 *Conclusions.* Our study found that parasitic infections are common in recent US
65 immigrants, which highlights an important health disparity among a vulnerable
66 population. Further, we found that classically used symptoms and laboratory tests had
67 a low predictive value for parasitic infections in this population.

68

69 **AUTHOR SUMMARY** – Parasitic infections, though rare in the United States (US), are
70 common in many areas of the world including the regions of origin of many US
71 immigrants. However, the prevalence rates and health impacts of these infections in
72 immigrant populations are undefined. We conducted a study to identify the frequency of
73 parasitic infections among healthy immigrants in one community, recruiting 133
74 immigrants from 28 countries. Subjects completed a standardized questionnaire
75 regarding symptoms and infection risk-factors and provided blood and stool samples for
76 testing. Twelve percent of subjects in our study had evidence of current or previous
77 pathogenic parasitic infections. Symptoms and risk factors classically thought to be
78 associated with parasitic infection (allergic symptoms, elevated blood eosinophil counts,
79 *etc.*) were common among enrolled subjects, but did not differ significantly between
80 those with and without evidence for infection. Overall, our results suggest that many
81 immigrants, even those who are asymptomatic, may have undiagnosed parasitic
82 infections. These results highlight an important health disparity among a vulnerable
83 underserved population in the US. As most of these infections are easily treatable,
84 more research should be done to further characterize the optimal testing strategies for
85 recent immigrants.

86

87 INTRODUCTION

88 In some regions and among select populations, parasitic diseases are believed
89 to be a significant and under-recognized public health problem within the United States
90 (US).[1-7] However, little is known about the current epidemiology of these
91 infections.[3, 8] Although exact numbers are not available, studies have suggested that
92 within the US there may be up to 300,000 people with Chagas disease,[9-15] 1.3 – 2.8
93 million with serological evidence of exposure to *Toxocara* spp.,[3, 16] 4 million with soil-
94 transmitted helminths,[3, 17, 18] 1.2 million with giardiasis,[19] 41,400 – 169,000 with
95 cysticercosis,[3] and approximately 8,000 with schistosomiasis.[3] These infections
96 represent an important health disparity in the US as higher infection rates for some
97 parasites are believed to occur among those living in poverty in underserved rural and
98 inner-city areas.[2, 3, 20-23]

99 Parasitic infections are believed to be an especially significant health problem
100 within US immigrant populations. Many immigrants come from areas where some
101 parasites are endemic.[3, 24-27] Additionally, recent immigrants may be more likely to
102 have a decreased socioeconomic status and therefore frequently reside in the
103 underserved areas within the US that have an increased prevalence of parasitic
104 infections.[2-4, 22] This population thus possesses a dual risk for parasites.[7]
105 However, published prevalence estimates vary widely and therefore the true prevalence
106 and health impacts of parasitic infections on US immigrant populations is unknown.

107 Both diagnostic and methodologic limitations to research may explain the lack of
108 information regarding parasitic infections among US immigrants. Diagnostic
109 inaccuracies can occur because these infections frequently have nonspecific symptoms

110 or are asymptomatic, and laboratory tests for parasites can have significant limitations.
111 For example, many of the current diagnostic tests for parasitic infections have poor
112 sensitivity. Additionally, these tests are frequently unavailable in the community.[4, 6, 7,
113 17, 25, 28, 29] Serologic testing, the primary method of diagnosis for many parasitic
114 infections, has several important shortcomings, which contributes to the lack of accurate
115 information regarding these infections. These limitations include: an inability to
116 distinguish between active and past infections, the presence of significant cross-
117 reactivity between serologic tests for different parasites, and the fact that some
118 infections (such as many stool helminthiases) do not cause a detectable serologic
119 response.[30-32]

120 Methodologic challenges to research studies may also partly account for the wide
121 variations in reported prevalence estimates of parasitic infections.[1, 3, 4] For example,
122 past estimates of Chagas disease prevalence were based on testing of blood-donors.
123 This method likely underestimated the number of infected individuals due to a “healthy-
124 donor” effect and due to the removal of those with previous positive tests from the pool
125 of potential blood donors.[33] A second commonly used method to obtain prevalence
126 estimates involves multiplying the proportion of people infected with a specific disease
127 within a country by the number of immigrants from that country living in the US.
128 However, within endemic countries there can be large differences in infection risk
129 across different populations and infection risks among those who emigrated may be
130 different from that of the general population within a given country.[10, 11, 24, 34-36]

131 Given the limited data regarding the prevalence of parasitic infections, it is
132 unsurprising that the health impacts imposed by parasites on US immigrant populations

133 are poorly understood. Many of the published studies evaluating health impacts of
134 parasitic infections on immigrants either screened for only a small number of parasites
135 or screened immigrants from a single country, and many were retrospective.[9, 11, 13,
136 14, 25, 26, 37, 38] Improved data regarding the prevalence and impact of these
137 infections are badly needed as parasitic infections can have serious health
138 consequences.[2, 3, 5-7, 17, 20, 39] For example, Chagas disease causes
139 cardiomyopathy and/or esophageal or colonic dilation in up to 20-30% of those
140 infected;[9, 40] those with Toxocariasis may have an increased risk for asthma;[41-44]
141 and intestinal parasite infection has been associated with delayed cognitive
142 development and impaired nutrition in some studies.[45, 46] Parasitic infections have
143 also been shown to increase the severity of illnesses due to other infectious diseases
144 (such as tuberculosis and HIV).[1]

145 Most studies evaluating the impact of parasitic infections in the US have focused
146 on the Southern states because of a warmer climate (facilitating the acquisition of soil-
147 transmitted helminths) and a comparatively high population of immigrants.[5, 12, 13, 22,
148 47] According to US Census reports, however, Illinois is among the states with the
149 highest percentages of immigrants; 10-15% of the state's population is foreign born.[48]
150 Thus, this study was conducted with the overall aim of evaluating the prevalence of
151 parasitic infections among recent immigrants living in Chicago. As many of the
152 symptoms of parasitic infections are nonspecific, an additional objective of our study
153 was to identify any symptoms, signs, or laboratory tests that could be used in this
154 population as predictors of the presence of parasites.

155

156 **METHODS**

157 **Ethics statement.** The study was approved by the Institutional Review Board of the
158 University of Illinois at Chicago and written informed consent was obtained from all
159 participants. Adult subjects signed a consent form, and for enrolled individuals between
160 the ages of 10 and 18, the subject signed an assent form and a parent or guardian
161 signed a parental permission form. For all study activities, study procedures were
162 explained to the participant in their stated language of preference (using an interpreter if
163 needed). Each participant received \$40 to compensate them for their time. Treatment
164 for parasitic infections was not a part of the study, but all subjects were notified of their
165 results and those with positive tests were offered the possibility of seeing one of the
166 study authors (JH) in clinic to discuss treatment options.

167

168 **Study design.** Patients were enrolled for this cross-sectional study between November
169 2014 and July 2016. Subjects were recruited through collaboration with local
170 organizations that provide services to immigrants as well as at English as a Second
171 Language classes, the Mexican consulate in Chicago, through a mass email sent to
172 students enrolled at the University of Illinois at Chicago, and at community health fairs.
173 Subjects were also recruited from community health clinics as long as they were
174 accessing the health care system for reasons clearly unrelated to a parasitic infection
175 (e.g., patients presenting for routine physical exams). Subjects were eligible for
176 inclusion if they were: ages 10-80; willing to undergo a blood draw and provide a stool
177 sample; and an immigrant living in the US mainland for less than 5 years and were
178 originally from Africa, Asia, South America, Central America, Mexico, the Caribbean

179 islands, or Puerto Rico. Although they are U.S. citizens and not immigrants from non-
180 US territories, Puerto Ricans were specifically included in this study because previous
181 research suggested that parasitic infections were common among the Puerto Rican
182 population in Chicago.[49] The five-year time point for living in the US was chosen
183 because immigrants have been shown to have the highest risk for parasitosis in the first
184 5 years after emigration[49] and based on the average expected lifespan of hookworms,
185 *Ascaris lumbricoides* and *Trichuris trichiura*, a primary focus of our investigations.[50]
186 Subjects were excluded from the study if they: 1) were currently pregnant, as the
187 immunosuppression of pregnancy may cause a different presentation of parasitic
188 infection and one of the aims of the study was to identify factors predictive of
189 parasitosis; or 2) they had taken antiparasitic medications since moving to the
190 continental US.

191 Upon enrollment, a standardized questionnaire (Supplemental Appendix) was
192 administered to collect information regarding demographics, risk factors for parasitic
193 infections, and symptoms. Participants then provided clinical samples (blood and stool)
194 to be tested for evidence of parasitic infections as described below.

195

196 **Laboratory testing.** Whole blood for a Complete Blood Count was collected in an
197 Ethylenediaminetetraacetic acid (EDTA) tube and processed in the clinical laboratory at
198 the University of Illinois at Chicago (BXH 800 or BXH 1600, Beckman Coulter, Brea,
199 CA) within 12 hours. Serum samples were collected in a serum separator tube (SST)
200 and centrifuged within 1 hour of collection. A portion of the supernatant was sent for
201 measurement of Immunoglobulin E (IgE) level (Quantitative ImmunoCAP® Fluorescent

202 Enzyme Immunoassay, Arup Laboratories, Salt Lake City, UT). The remainder of the
203 supernatant was stored at -80 °C until samples were shipped as a batch to the Centers
204 for Disease Control and Prevention, where serologic testing was performed for
205 infections endemic to each subject's country of origin (Supplemental Table 1).

206 Antibody responses to cysticercosis, strongyloidiasis, and toxocariasis were
207 determined using a multiplex bead-based assay (MBA).[51-53] For cysticercosis, 3
208 recombinant antigens (rGP50, rT24H, and sTs18var1) were used; one recombinant
209 antigen was used for both strongyloidiasis (Ss-NIE-1) and toxocariasis (rTc-CTL-1).
210 Briefly, the antigens were coupled to carboxylated magnetic particles, and then
211 incubated with sera (diluted 1:100 in PBS/0.3% Tween-20/5% milk) for 30 minutes. After
212 two washes with PBS/0.3% Tween-20, the complex was detected by a biotinylated
213 conjugate which then reacted with streptavidin-phycoerythrin. The mean fluorescence
214 intensity was measured using the MagPix instrument (Luminex corporation, Austin, TX).
215 Positivity for each antibody response was determined using specific cut-off points for
216 each antigen (which had been previously defined[51-53]).

217 Antibody against *T. cruzi* antigens was detected using a commercial kit (Weiner
218 Lab, Argentina) and following the company protocol instructions.[54-56] After adding
219 serum, the plate was incubated for 30 min while shaking at room temperature. After the
220 conjugate was added, the reaction ran for an additional 30 minutes. Substrate (TMB)
221 was added and color development was stopped by adding 1N H₂SO₄ according to the
222 kit instructions[55]. The optical density at 450nm was detected using the Versamax
223 system.

224 All serum specimens were initially tested by FAST-ELISA using *Schistosoma*
225 *mansoni* adult microsomal antigen and then by a species-specific immunoblot
226 appropriate to the subject's country of origin. These procedures and the methods used
227 to interpret results have been discussed in previous publications.[57-59]

228 Patients also provided a stool sample for standard Ova & Parasite (O&P) direct
229 microscopy (Arup Labs Qualitative Concentration/Trichrome Stain/Microscopy, Salt
230 Lake City, UT), and a multi-parallel quantitative polymerase chain reaction (qPCR)
231 which tests for eight common gastrointestinal pathogens (*Ancylostoma*, *Ascaris*,
232 *Cryptosporidium*, *Entamoeba*, *Giardia*, *Necator*, *Strongyloides*, and *Trichuris*). Only one
233 stool sample was requested for O&P due to our desire to compare O&P directly with
234 qPCR and because the yield of collecting multiple samples for O&P exam has been
235 shown to be low in immigrant populations.[60] The stool samples for qPCR were frozen
236 without fixatives at -80 °C and shipped as a batch to the Baylor College of Medicine
237 where DNA was extracted and the qPCR was conducted according to previously
238 published methods.[61-63]

239
240 **Statistical analysis.** Statistical analyses were performed using Prism 7 (GraphPad,
241 San Francisco, CA) and SAS (Cary, NC). Data were summarized by using frequency
242 with percentage for categorical variables. For continuous variables, geometric mean
243 with standard deviation or median with range or interquartile range were used (medians
244 were used as measures of central tendency for highly skewed variables). For
245 categorical variables, prevalence ratios (PR) were used to evaluate relationships
246 between covariates and the main outcome (the presence of a parasitic infection) and

247 Fisher's Exact test or Chi-squared test were used to determine significance. Mann-
248 Whitney U test was used to evaluate for associations between continuous variables and
249 the presence of a parasite. Correlations were calculated using Spearman's rank
250 correlation coefficient. Kappa values were used to compare results from stool O&P
251 exam to qPCR testing.

252

253 **RESULTS**

254 **Patient characteristics.** Seven hundred and thirty-eight people were approached
255 about the study, and 133 were enrolled (Supplemental Figure 1). All enrolled subjects
256 filled out the study questionnaire (unedited results shown in Supplemental Table 2); 125
257 (94%) of enrolled subjects provided blood and 113 (85%) provided stool samples to be
258 tested for parasitic infections (however, for 2 of the 113 subjects, only qPCR could be
259 performed as they did not return samples for O&P exam). The mean age of enrolled
260 subjects was 32 years, and 60/133 (45.1%) were male (Table 1). Participants came
261 from 28 different countries. Most subjects (95/133, 71.4%) reported an annual
262 household income of less than \$20,000 per year. As shown in Table 1, few subjects
263 (25/133, 18.8%) had been raised in a rural environment. Despite this, many subjects
264 reported having been exposed to animals (65/133, 48.9%), well-water (65/133, 48.9%),
265 and bathing in ponds or streams (58/133, 43.6%) in their country of origin.

266

267 Table 1. Demographics, symptoms, and laboratory results of 133 enrolled subjects

| Characteristic | Results ^a |
|--------------------------------------|----------------------|
| Age, mean years (standard deviation) | 32 (17.3) |

| | |
|--|-----------------------------|
| Gender, male:female, N (% male) | 60:73 (45.1) |
| Country/region of origin, N (%) | |
| Asia (excluding India) | 33 (24.8) |
| Mexico | 30 (22.6) |
| India | 26 (19.5) |
| Central/South America | 22 (16.5) |
| Africa | 13 (9.8) |
| Middle East | 5 (3.8) |
| US (Puerto Rico) | 4 (3) |
| Mean number of years in school (standard deviation) | 9.9 (5.2) |
| Annual household income in US dollars, N (%) | |
| < 20,000 | 95 (71.4) |
| 20,000 - 40,000 | 30 (22.6) |
| 40,000 - 60,000 | 5 (3.8) |
| 60,000 - 100,000 | 2 (1.5) |
| > 100,000 | 1 (0.8) |
| Length of time living in the continental United States ^b , mean years (range, standard deviation in years) | 2 (10 days–5 years, 1.6) |
| Raised in rural environment, N (%) | 25 (18.8) |
| Exposure history prior to immigration, number yes (%) | |
| Frequently walked barefoot | 76 (57.1) |

| | |
|--|----------------------------|
| Close contact with animals | 65 (48.9) |
| Used a well as source of drinking water | 65 (48.9) |
| Bathed in streams or ponds | 58 (43.6) |
| Lived in a house with a thatched roof | 25 (18.8) |
| Treatment with antiparasitic medication prior to emigration, number yes (%) | 46 (34.6) |
| Symptoms reported by the patient on the day of study enrollment ^c , N (%) | |
| Gastrointestinal | 32 (24.1) |
| Constitutional | 25 (18.8) |
| Musculoskeletal | 25 (18.8) |
| Dermatologic | 13 (9.8) |
| Pulmonary | 12 (9) |
| Cardiovascular | 10 (7.5) |
| Allergic | 3 (2.3) |
| Immunoglobulin E (IgE) results | |
| Subjects with elevated Immunoglobulin E, N (%) | 29/125 ^d (23.2) |
| Immunoglobulin E level, IU/mL, median (range, standard deviation) | 57 (3-7732, 706) |
| Absolute eosinophil count (AEC) results | |

| | |
|---|---------------------------|
| Subjects with elevated absolute eosinophil count, N (%) | 12/123 ^e (9.8) |
| Absolute eosinophil count, median cells/microliter (range, standard deviation) | 200 (0-1600, 240) |
| Pathogenic parasitic infection, N (%) | 15/125 ^f (12) |

268 a - unedited results from all enrolled subjects are shown in Supplemental Table 2; N –
269 number of subjects; b - potential range (due to enrollment criteria) 0-5 years; c –
270 gastrointestinal symptoms included: heartburn, difficulty or pain with swallowing,
271 abdominal pain, diarrhea, nausea/vomiting; constitutional symptoms included: weight
272 loss, fatigue, fevers, and weakness; musculoskeletal symptoms included pain and
273 stiffness in the joints or myalgias; dermatologic: itching, hives, or rash; pulmonary
274 symptoms: wheezing, shortness of breath, cough; cardiovascular: chest pain,
275 palpitations, or irregular heart beat; and allergic symptoms included: those who
276 responded “yes” to the question “do you currently have any symptoms of seasonal
277 allergies;” d – of the 125 subjects who underwent a blood draw, normal value of IgE
278 defined as <696 IU/mL for subjects 10-12 years old, <629 for those ages 13-15, < 537
279 for those ages 16-17, and < 214 IU/mL in adults; e – for two of the 125 subjects who
280 underwent a blood draw, a complete blood count was unable to be performed due to
281 clotting of the blood sample, normal AEC defined as < 500 cells/UL; f – of 125 subjects
282 who provided a clinical sample (blood or stool) for testing

283

284 **Laboratory testing.** The median IgE among the 125 subjects from whom blood
285 samples were obtained was 57 IU/mL (range 3-7732); 29 (23.2%) subjects had elevated
286 IgE levels. Twelve subjects (9.8%) were found to have eosinophilia, and the median

287 absolute eosinophil count (AEC) level was 200 cells/UL (range 0-1600 cells/UL, Table
288 1). There was a weak correlation between IgE and AEC levels in adults ($r=0.23$,
289 $p=0.02$; children were excluded from this correlation as they have different normal
290 ranges for IgE).

291
292 **Parasitic infections.** Fifteen of 125 subjects (12%) who provided a clinical sample for
293 testing were found to have evidence of current or prior infection with a pathogenic
294 parasite species. As shown in Table 2, the most common infections identified were
295 *Toxocara* spp., seen in 8 subjects (6.4%), followed by *Strongyloides stercoralis* (5
296 subjects, 4%). Of subjects found to have evidence of parasitic infection, 3 subjects
297 (3/15, 20%) had positive tests for more than one pathogenic parasitic species (Table 2).

298
299 Table 2. Parasitic infections diagnosed among recent immigrants living in Chicago

| Parasitic infections | Number of subjects infected (%) |
|---|---------------------------------|
| Soil-transmitted helminths | |
| <i>Toxocara</i> spp. | 8 (6.4) ^a |
| <i>Strongyloides stercoralis</i> | 5 (4) ^b |
| <i>Trichuris trichiura</i> | 2 (1.8) ^c |
| <i>Ascaris lumbricoides</i> | 1 (0.9) ^c |
| Protozoa | |
| <i>Giardia duodenalis</i> | 4 (3.5) ^d |
| Non-pathogenic or disputed pathogenicity species^e | |
| <i>Blastocystis hominis</i> | 10 (9) |
| <i>Endolimax nana</i> | 4 (3.6) |
| <i>Dientomoeba fragilis</i> | 3 (2.7) |

| | | |
|---|----------------------|----------------------|
| <i>Iodamoeba bütschlii</i> , <i>Entamoeba coli</i> , <i>Entamoeba hartmanii</i> | 1 each (0.9) | |
| Number of subjects with multiple pathogens | 3 (2.4) ^f | |
| Comparison of Ova and Parasite Exam to qPCR for pathogenic species^g | qPCR positive | qPCR negative |
| Ova & Parasite positive | 1 | 0 |
| Ova & Parasite negative | 7 | 107 |

300 N – number of subjects; a – of 125 subjects who provided blood samples for testing, all
301 eight subjects were diagnosed based on a positive serologic test; b – of 125 subjects
302 who provided blood and/or stool samples for testing: one subject tested negative on O&P
303 but positive on both serology and stool qPCR, three subjects had a positive serologic test
304 but negative O&P and qPCR, and one subject had a positive serology but did not provide
305 a stool sample for testing; c – of 113 subjects who provided a stool sample for qPCR
306 testing, pathogenic species diagnosed based on a positive stool qPCR test; d – of 113
307 subjects who provided a stool sample for testing: one subject tested positive on both
308 qPCR and O&P tests and three subjects tested positive on qPCR but negative on O&P; e
309 – of 111 subjects who returned a stool sample for O&P testing, all infections diagnosed
310 based on a positive on O&P exam as these nonpathogenic or disputed pathogenicity
311 organisms were not tested for on qPCR; f - of 125 subjects who provided blood and/or
312 stool samples for testing: one subject had positive stool qPCR tests for both *Ascaris* and
313 *Trichuris* and a positive serologic test for *Toxocara*, one subject had positive stool qPCR
314 tests for *Trichuris* and *Giardia* as well as positive serologic testing for *Toxocara*, and the

315 third subject had positive serologic testing and stool qPCR for *S. stercoralis* and positive
316 serologic testing for *Toxocara*; g - p-value=0.07, sensitivity of O&P compared to qPCR
317 12.5%, specificity 100%, positive predictive value (PPV) 100%, negative predictive value
318 (NPV) 93.9%, kappa 0.21.

319

320 **Outcome assessment.** With the exception of constitutional symptoms, which were
321 slightly more likely to be present in subjects diagnosed with *Giardia* (p=0.01), there were
322 no significant differences in any of the evaluated symptoms, exposures, or laboratory
323 results between those found to be mono-infected with each of the different parasite
324 species detected (e.g. *Toxocara* spp., soil-transmitted helminths, or *Giardia*).
325 Consequently, for our primary analysis we compared uninfected individuals to subjects
326 with evidence for any pathogenic parasitic infection, with infected subjects treated as a
327 single group.

328 A large number of subjects (10/111 subjects who provided a sample for O&P
329 testing, 9%) were found to have *Blastocystis hominis*. Although the pathogenicity of *B.*
330 *hominis* remains controversial,[64, 65] infection with this organism in our sample was
331 not associated with any significant differences in symptoms or laboratory values
332 compared to the uninfected group. Accordingly, in our analysis *Blastocystis* was not
333 included as a pathogenic parasitic infection.

334

335 **Demographic characteristics of subjects with parasitic infections.** Nearly all
336 of the subjects found to have evidence of a pathogenic parasite (14/15, 93.3%) had
337 lived in the continental US for 2 years or less (compared to 70/110 of those who were

338 uninfected, 63.6%, PR 6.8, p=0.02, Table 3). This history was therefore a very
 339 sensitive, though not specific, marker for parasitic infections (sensitivity 93.3%,
 340 specificity 36.4%, PPV 16.7%, NPV 97.6%). No other demographic variables, including
 341 age, gender, recruitment site, or region of origin differed significantly between those with
 342 and without infections. As shown in Table 3, there was a trend (though not statistically
 343 significant) towards a greater likelihood of parasitic infections in subjects of Asian origin,
 344 subjects who had not completed high school, and subjects with an annual household
 345 income of less than \$20,000 per year.

346

347 Table 3. Findings associated with the presence of a parasitic infection

| Demographics | Uninfected N=110 | Parasitic Infection ^a N=15 | Prevalence ratio ^b (95% Confidence Interval) | p- value |
|--|---------------------|---|---|-------------|
| Length of time living in the United States, N (%) | | | | |
| > 2 years | 40 (36.4) | 1 (6.7) | Reference | 0.02 |
| ≤ 2 years | 70 (63.6) | 14 (93.3) | 6.8 (0.9-50.2) | |
| Mean age (standard deviation) | 31 (16.4) | 37.5 (21.6) | 1.0 (1.0-1.1) | 0.2 |
| Gender, N (%) | | | | |

| | | | | |
|--|------------------------|-----------|----------------|------|
| Female | 58 (52.7) | 8 (53.3) | Reference | 0.99 |
| Male | 52 (47.3) | 7 (46.7) | 1.0 (0.4-2.5) | |
| Country/Region of origin, N (%) | | | | |
| Mexico | 26 (23.6) | 2 (13.3) | Reference | 0.28 |
| Asia (excluding India) | 24 (21.8) | 8 (53.3) | 3.5 (0.8-15.1) | |
| India | 21 (19.1) | 2 (13.3) | 1.2 (0.2-8) | |
| Central/South America | 18 (16.4) | 2 (13.3) | 1.4 (0.2-9.1) | |
| Africa | 12 (10.9) | 1 (6.7) | 1.1 (0.1-10.8) | |
| Middle East | 5 (4.5) | 0 (0) | Undefined | |
| USA (Puerto Rico) | 4 (3.6) | 0 (0) | Undefined | |
| Years of schooling | | | | |
| >12 | 56 (51.9) ^c | 5 (33.3) | Reference | 0.27 |
| 9-12 | 28 (25.9) | 4 (26.7) | 1.5 (0.4-5.7) | |
| ≤8 | 24 (22.2) | 6 (40) | 2.4 (0.7-7.9) | |
| Annual household income, US dollars | | | | |
| ≥20,000 | 34 (30.9) | 2 (13.3) | Reference | 0.2 |
| <20,000 | 76 (69.1) | 13 (86.7) | 2.6 (0.6-11.1) | |

| Childhood Exposures (in country of origin) | Uninfected, number yes, (%) N=110 | Parasitic infection, number yes, (%) N=15 | Prevalence ratio ^b (95% confidence interval) | p-value |
|--|--------------------------------------|--|---|--------------|
| Self-reported history of seeing worms in the stool | 18 (16.4) | 8 (53.3) | 4.4 (1.7-10.9) | 0.003 |
| Used a well as source of drinking water | 49 (44.5) | 11 (73.3) | 3.0 (1.0-8.9) | 0.05 |
| Raised in rural environment | 19 (17.3) | 3 (20) | 1.2 (0.4-3.8) | 0.73 |
| Frequently walked barefoot | 60 (54.5) | 11 (73.3) | 2.1 (0.7-6.2) | 0.27 |
| Close contact with animals | 51 (46.4) | 7 (46.7) | 1.0 (0.4-2.6) | 0.99 |
| Bathed in streams or ponds | 47 (42.7) | 7 (46.7) | 1.2 (0.4-3.0) | 0.79 |
| Lived in a house with a thatched roof | 20 (18.2) | 3 (20) | 1.1 (0.3-3.6) | 0.99 |
| Treated with antiparasitic medication (prior to emigration) | 38 (34.5) | 7 (46.7) | 1.6 (0.6-4.0) | 0.4 |
| Symptoms reported by the patient on the day of study enrollment ^d | Uninfected, number yes, (%) N=110 | Parasitic infection, number yes, (%) | Prevalence ratio ^b (95% confidence interval) | p-value |

| | | N=15 | | |
|------------------|-----------|----------|---------------|-------------|
| Gastrointestinal | 26 (23.6) | 3 (20) | 0.8 (0.3-2.7) | 0.99 |
| Constitutional | 17 (15.5) | 6 (40) | 3 (1.2-7.5) | 0.03 |
| Musculoskeletal | 18 (16.4) | 6 (40) | 2.8 (1.1-7.1) | 0.04 |
| Dermatologic | 11 (10) | 1 (6.7) | 0.7 (0.1-4.7) | 0.99 |
| Pulmonary | 10 (9.1) | 1 (6.7) | 0.7 (0.1-5.1) | 0.99 |
| Cardiovascular | 7 (6.4) | 2 (13.3) | 2 (0.5-7.5) | 0.29 |
| Allergic | 2 (1.8) | 0 (0) | Undefined | 0.99 |

348
349 N – number of subjects; a – Not including non-pathogenic or disputed pathogenicity
350 organisms; b – prevalence ratio comparing the frequency of the listed demographic
351 variable, symptom, or exposure in those with versus those without evidence of a
352 parasitic infection; c – 108 of the 110 subjects without parasitic infections responded to
353 this question; d - gastrointestinal symptoms included: heartburn, difficulty or pain with
354 swallowing, abdominal pain, diarrhea, nausea/vomiting; constitutional symptoms
355 included: weight loss, fatigue, fevers, and weakness; musculoskeletal symptoms
356 included pain and stiffness in the joints or myalgias; dermatologic: itching, hives, or
357 rash; pulmonary symptoms: wheezing, shortness of breath, cough; cardiovascular:
358 chest pain, palpitations, or irregular heart beat; and allergic symptoms included: those
359 who responded “yes” to the question “do you currently have any symptoms of seasonal
360 allergies.”

361
362 **Exposure history and symptoms in subjects with evidence of parasitic infection.**

363 A self-reported history of ever having seen worms in the stool was strongly associated
364 with evidence of current or prior parasitic infection (8/15, 53.3% in the infected group

365 reported this history versus 18/110, 16.4%, in the uninfected group, $p=0.003$, PR 4.4,
366 Table 3). This history appeared to be a nonspecific marker of risk for any parasitic
367 infection and was equally common among those diagnosed with enteric parasites
368 compared to those with non-enteric parasites (p -value=0.8). Although it did not reach
369 significance, there also appeared to be a trend towards increased parasitic infections in
370 subjects who recalled drinking well water in their country of origin (11/15, 73.3%)
371 compared to those who did not (49/110, 44.5%, $p=0.05$, PR 3). Other classic risk
372 factors for parasitic infections (close contact with animals, *etc.*), although commonly
373 reported among study participants, did not differ between those with and without
374 evidence of parasitic infections (all p -values ≥ 0.05 , Table 3).

375 In the year prior to study enrollment, subjects with evidence of parasitic infections
376 had experienced an overall increased number of physical complaints (median 8)
377 compared to those with no evidence of parasites (4, $p=0.02$). However, symptoms
378 typically thought of as indicative of parasitic infections, such as rash, pruritus, or
379 diarrhea, did not differ significantly between the groups (all p -values >0.05 for symptoms
380 experienced both the day of study enrollment and within the previous year).

381
382 **Laboratory values in subjects with evidence of parasitic infections.** Both the
383 median IgE level (249 IU/mL) and the proportion of subjects with an increased IgE level
384 (7 of 15 subjects, 46.7%) were significantly increased in subjects with evidence for
385 parasitic infections compared to those who were uninfected (median IgE 52 IU/mL,
386 22/110, 20%, subjects with elevated IgE level, both p -values <0.05 , Table 4). In
387 contrast, subjects who reported a history of seasonal allergies and/or asthma were not

388 found to have increases in IgE (p-value=NS). The difference in median IgE levels
 389 between groups remained statistically significant when subjects <18 years old were
 390 excluded from analysis (as normal values for IgE are higher in this group). Although an
 391 elevated IgE level was a relatively specific finding for parasitic infections (specificity
 392 80%, NPV 92%), this finding was not a sensitive marker of infection (sensitivity 47%,
 393 PPV 24%).

394

395 Table 4. Laboratory results in uninfected versus infected individuals

| Laboratory results | Uninfected N=110 | Parasitic infection ^a N=15 | p-value |
|--|---------------------|---|--|
| Immunoglobulin E (IgE), Median (IQR), IU/mL | 52 (26 - 177) | 249 (67 - 480) | 0.005 |
| Infected with 1 parasite | | 111 (50.5–311) | |
| 2+ parasitic infections | | 662 (267–1097) | |
| Absolute Eosinophil Count (AEC), Median (IQR), cells/UL | 200 (100 - 200) | 200 (100 - 400) | 0.1 |
| Hemoglobin, mg/dL, mean (standard error) | 14.4 (0.2) | 14.1 (0.3) | 0.6 |
| Number of subjects with abnormal laboratory test | Uninfected, | Parasitic | Prevalence ratio (95% confidence |

| | N (%) | infection, N (%) | interval), p-value |
|---|-----------------------|------------------------|---------------------------------|
| IgE, Number elevated ^b (%) | 22 (20) | 7 (46.7) | 3.5 (1.4-8.8), 0.04 |
| AEC, Number elevated ^c (%) | 9 (8.3) ^d | 3 (20) | 2.4 (0.8-7.2), 0.2 |
| <i>Blastocystis hominis</i> cysts present on O&P exam | 5 (5.1 ^e) | 5 (38.5 ^f) | 6.3 (2.5-15.7), 0.002 |

396 N – number; a – excluding non-pathogenic or disputed pathogenicity species; IQR –
397 interquartile range; b - normal value of IgE <696 IU/mL for subjects 10-12 years old,
398 <629 for those ages 13-15, < 537 for those ages 16-17, and < 214 IU/mL in adults; c -
399 normal AEC < 500 cells/UL; d – of 108 subjects in the uninfected group who were tested
400 for a CBC (as for two patients who underwent a blood draw the CBC was unable to be
401 performed due to clotting of blood in the tube); e - of 98 subjects in the uninfected group
402 who provided a stool sample for O&P exam; f – of 13 subjects in this group who
403 provided a stool sample for O&P exam.

404

405 The median AEC did not differ between those with and without evidence of a
406 parasitic infection (Table 4). Eosinophilia in our sample was also not associated with a
407 reported history of allergies, asthma, or taking medications known to cause
408 eosinophilia.[66, 67] Despite a low sensitivity for parasites (20%, PPV 25%), however,
409 eosinophilia was relatively specific to subjects with evidence of parasitic infection

410 (specificity 91.8%, NPV 89.4%). The sensitivity of AEC as a marker for parasitic
411 infection did not improve appreciably when only parasitic infections known to cause
412 chronic eosinophilia (*Strongyloides* and *Toxocara*[28, 67-69]) were compared to those
413 who were uninfected.

414 The presence of cysts of *B. hominis* on O&P exam was strongly associated with
415 infection with a pathogenic parasite species. Five of the 13 subjects in the parasite
416 positive group who returned a stool sample had a positive O&P for *Blastocystis*, 38.5%,
417 compared to 5/98 tested for O&P exam in the uninfected group, 5.1%, $p=0.002$,
418 PR=6.3.

419

420 **DISCUSSION**

421 Despite the fact that many US immigrants come from areas where parasitic
422 infections are endemic, data about the prevalence and risks for parasites among
423 immigrants are sparse. In response to this deficit, we conducted a comprehensive
424 evaluation for the presence of a broad array of parasitic infections in recent immigrants
425 in Chicago. We found that 12 percent of recent immigrants in our sample had evidence
426 of prior or current infection with a pathogenic parasite species.

427 Our study found a few key factors which were significantly more likely in subjects
428 with evidence of parasites: a self-reported history of having previously observed worms
429 in the stool, having immigrated within the past 2 years, and reporting a relatively high
430 number of nonspecific physical ailments within the previous year. Our results also
431 highlight that clinical risk factors (such as contact with animals and frequently walking
432 barefoot), symptoms (including urticaria, rash, and diarrhea), and laboratory findings

433 (eosinophilia) traditionally thought to be associated with parasites were commonly found
434 but not predictive of infection in this study population. If confirmed in a larger sample,
435 these results suggest that practitioners should have a high degree of suspicion for
436 parasitic infections when evaluating recent immigrants regardless of the presence or
437 absence of symptoms or laboratory abnormalities.

438 Our results highlight the limitations of current diagnostic tests for parasitic
439 infections. For example, the sensitivity of O&P exam compared to qPCR testing (which
440 is not yet universally available) for pathogenic parasites was very poor. While this could
441 represent false positive qPCR tests, previous use of these tests in other studies has
442 indicated a low rate of false positives.[8, 49, 61, 62] Further, the O&P exam has been
443 shown to have serious limitations, in part because some parasitic infections are
444 characterized by intermittent shedding in the stool.[70] The lack of adequate diagnostic
445 tests for parasitic infections was also evident in the fact that, for many of the parasites
446 screened for in this study, the primary method of diagnosis is serologic testing.
447 Serologic tests can have significant limitations as they often have cross-reactivity
448 among multiple parasites and these tests cannot distinguish between prior and current
449 infections.[3, 6, 8, 17, 28, 37, 71, 72]

450 Similar to prior studies of immigrant populations,[28, 68] we found that a
451 relatively high percent of subjects in our study had eosinophilia and/or elevated IgE
452 levels. IgE appeared to be a slightly better marker for chronic parasitic infection in this
453 sample than eosinophilia. However, neither test had an adequate sensitivity to merit
454 recommending its use for routine screening purposes. For some parasitic infections,
455 eosinophilia has been shown to be absent or mild with longstanding infection,[73, 74]

456 and therefore the poor sensitivity of AEC for parasitic infections in our sample could
457 reflect a lack of acute parasitic infections among these subjects. Although eosinophilia
458 has long been thought of as a hallmark of helminth infection, several previous studies
459 have also failed to show any correlation between the two.[75, 76] However, the high
460 specificity of eosinophilia for parasitosis seen in our study suggests that, when this
461 finding is present in a recent immigrant, a workup for parasitic infections should be
462 initiated.

463 A large number of subjects in our study demonstrated cysts of *Blastocystis*
464 *hominis* on O&P exam. The association between *Blastocystis* and clinical disease has
465 been controversial. Various studies have shown that subjects with *B. hominis* may have
466 an increased likelihood of irritable bowel syndrome and that symptomatic patients with
467 this parasite may experience a beneficial effect from treatment with antiparasitic
468 medications.[64, 77] In our study, however, infection with *Blastocystis* did not appear to
469 be associated with any increase in symptoms in the preceding year or on the day of
470 enrollment. Interestingly, the presence of *Blastocystis* cysts on an O&P exam was
471 strongly associated with the presence of positive tests for pathogenic parasitic
472 infections. Therefore, our results agree with those of several recent studies and suggest
473 that the primary import of *B. hominis* infection may be from a public health perspective
474 by serving as a surrogate marker for the presence of fecal-oral transmission.[65, 77, 78]

475 Our study results showed that a high percentage of recent immigrants had
476 evidence of current or prior infection with a few key pathogenic parasites, including
477 *Strongyloides*, *Toxocara*, and *Giardia*. Positive serologic testing for *Strongyloides* has
478 been shown to be associated with a high likelihood of active ongoing infection and a risk

479 for developing disseminated disease or hyperinfection syndrome.[17, 79] The rate of
480 seropositivity for strongyloidiasis in our sample was 4%. This may have clinical
481 implications because a study evaluating the cost-effectiveness of empiric treatment
482 versus a test-and-treat strategy found that, if the prevalence of *Strongyloides* infection is
483 greater than 2% in a community, then the presumptive treatment strategy is more cost-
484 effective.[80]

485 Our study had several limitations. The small number of subjects found to have
486 parasitic infections limited our ability to identify risk-factors associated with these
487 infections. However, our sample size was necessitated by the extensive testing
488 performed on each subject and was also similar to those of previous studies of
489 immigrant health.[8, 81] Furthermore, the fact that our sample was very heterogeneous
490 and subjects enrolled in the study came from many different countries could have
491 reduced our ability to find associations between clinical factors and the presence of
492 infection. Our recruitment of some subjects from English as a Second Language
493 classes and at the Mexican consulate in Chicago could have skewed the study towards
494 immigrants from non-English-speaking countries and Mexico. A significant limitation to
495 this study, as for all studies evaluating parasitic infections (as well as to care of patients
496 at risk for parasitic infection), is the lack of adequate diagnostic tests for parasitosis.

497 Despite these limitations, however, our study is one of the only recent studies to
498 evaluate the prevalence of parasites in immigrants and provides a strong argument for
499 further investigation of the health impacts of these infections in the immigrant
500 community. Although our sample size was limited, a strength of our study is that we
501 conducted a comprehensive evaluation for parasitic infections including testing of both

502 stool and serum samples. Our results suggest that as many as 12% of recent
503 immigrants in the community may have evidence of current or previous infection with a
504 pathogenic parasitic species. From a public health perspective, it is important to note
505 that the infections identified in the current patient sample are not typically spread from
506 person to person. However, if confirmed in a larger study, these results present an
507 important health disparity among a vulnerable underserved population in the US. This
508 health disparity has persisted despite the presence of effective, safe, and well-tolerated
509 antiparasitic medications capable of treating each of the identified pathogens in our
510 sample.[17, 80]

511

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739 **Supporting Information:**

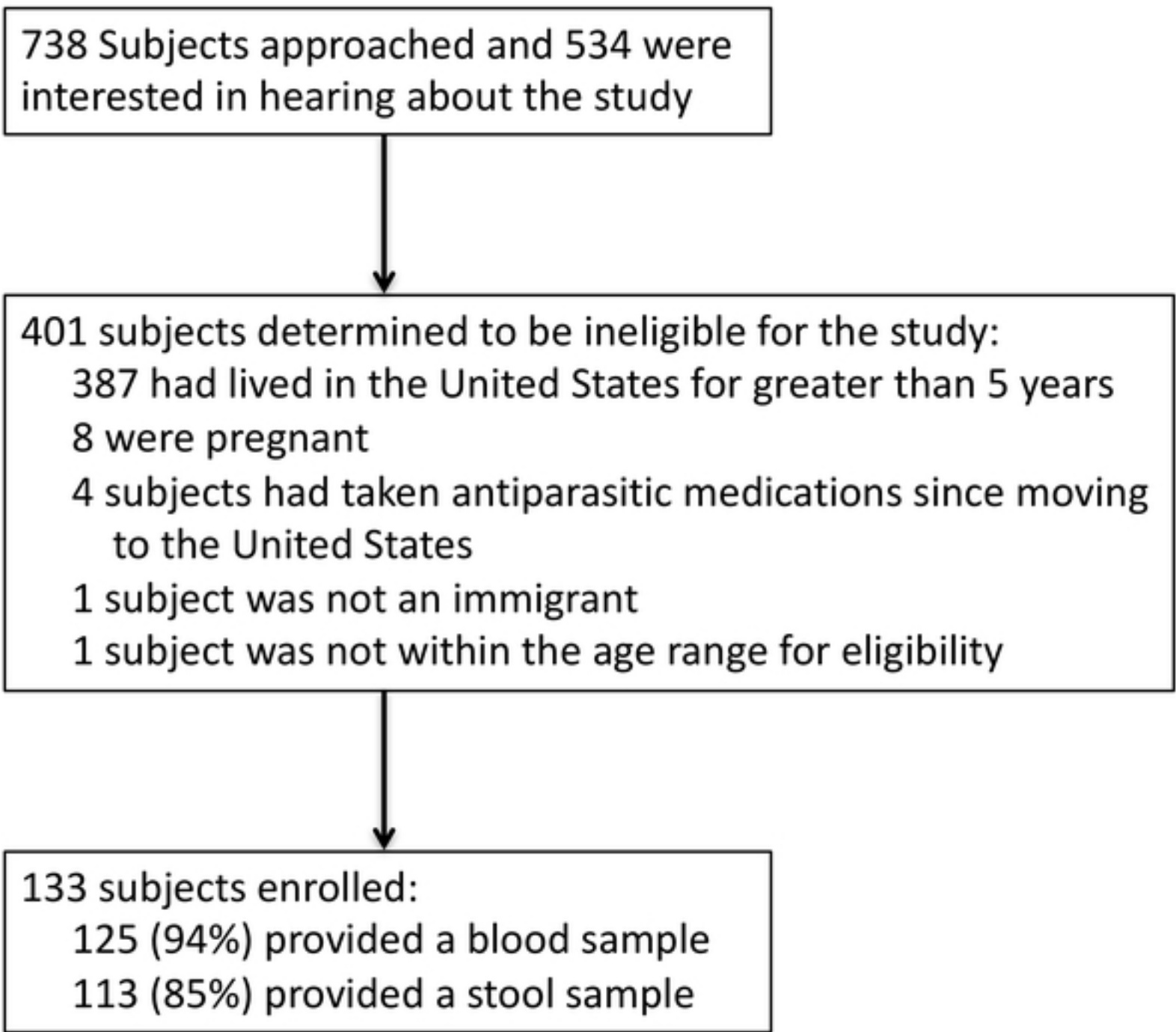
740 **S1 Supplemental Appendix. Closed-answer questionnaire.** This questionnaire was
741 filled out by each participant to obtain information about their demographics, symptoms,
742 and exposure histories.

743 **S2 Supplemental Table 1. Serologic testing performed based on subjects'**
744 **countries of origin.**

745 **S3 Supplemental Figure 1. Study recruitment and enrollment.**

746 **S4 Supplemental Table 2. Responses to closed-answer questionnaire and**
747 **laboratory results.** This table contains the complete individual responses subjects
748 provided to the symptom and demographic questionnaire as well as the raw results from
749 all laboratory tests performed.

750



Figure