

In order to provide our readers with timely access to new content, papers accepted by the American Journal of Tropical Medicine and Hygiene are posted online ahead of print publication. Papers that have been accepted for publication are peer-reviewed and copy edited but do not incorporate all corrections or constitute the final versions that will appear in the Journal. Final, corrected papers will be published online concurrent with the release of the print issue.

SERRE DELCORE AND OTHERS

INFECTIOUS DISEASES IN SUB-SAHARAN AFRICANS

Infectious Diseases in Sub-Saharan Immigrants to Spain

Núria Serre Delcor,* Begoña Treviño Maruri, Antoni Soriano Arandes, Isabel Claveria Guiu, Hakima Ouvarab Essadik, Mateu Espasa Soley, Israel Molina Romero, and Carlos Ascaso

Investigadors del Programa de Salut Internacional de l'Institut Català de la Salut (PROSICS), Tropical Medicine and International Health Unit Drassanes–Vall d'Hebron, Hospital Vall d'Hebron, Institut Català de la Salut, Barcelona, Spain; Microbiology Department, Hospital Vall d'Hebron, Institut Català de la Salut, Barcelona, Spain; Infectious Diseases Department, Hospital Vall d'Hebron, Institut Català de la Salut, Barcelona, Spain; Public Health Department, Hospital Clínic, Barcelona, Spain

* Address correspondence to Núria Serre Delcor, PROSICS, Tropical Medicine and International Health Unit Drassanes–Vall d'Hebron, Hospital Vall d'Hebron, Institut Català de la Salut, Avinguda Drassanes 17-21, 08001 Barcelona, Spain. E-mail: n.serre@vhebron.net

Abstract.

Immigrants may be carriers of infectious diseases because of the prevalence of these diseases in their country of origin, exposure during migration, or conditions during resettlement, with this prevalence being particularly high in sub-Saharan Africans. We performed a retrospective review of 180 sub-Saharan immigrants screened for infectious diseases at an International Health Center from January 2009 to December 2012. At least one pathogenic infectious disease was diagnosed in 72.8% patients: 60.6% latent tuberculosis infection, 36.8% intestinal parasites (intestinal protozoa or helminths), 28.1% helminths, 14.8% hepatitis B surface antigen positive, 1.2% anti-hepatitis C virus positive, 1.2% human immunodeficiency virus–positive, and 1.2% malaria. Coinfections were present in 28.4%. There was significant association between eosinophilia (absolute count or percentage) or hyper-IgE and the presence of helminths ($P < 0.001$). Relative eosinophilia and hyper-IgE were better indicators of helminth infection than absolute eosinophilia, particularly for schistosomiasis and strongyloidiasis. We found a high prevalence of infectious diseases in sub-Saharan immigrants, which could lead to severe health problems (in the absence of prompt treatment), representing a high cost to the public health system and possible transmission in the host country. Accurate screening and tailored protocols for infectious diseases are recommended in sub-Saharan immigrants.

INTRODUCTION

The economical and social situations in low-resource countries have led to a global increase of migratory movements to developed countries. According to official data, the number of legal foreign residents in Spain has increased from 748,953 in 1999 to 4,677,059 in 2014.¹ Some official sources indicate a reduction in the number of legal immigrants in Spain in recent years; however, the Spanish press has reported that in 2014 the number of illegal immigrants crossing the southern borders of Spain had doubled, with most being from Africa.²

Some infectious diseases may be diagnosed in immigrants living in developed countries as a result of the burden of the disease in their country of origin, exposure during migration, and conditions experienced during resettlement in the host country.^{3–5} Most undocumented sub-Saharan immigrants take high-risk land and maritime routes to reach Europe.⁶ In fact, the prevalence of some of these infections has been estimated to be particularly high among sub-Saharan immigrants, especially among the more vulnerable cases requiring social help.^{4,7,8} Several studies have described a higher prevalence of latent tuberculosis infection (LTBI) (46–

71%) and positive hepatitis B surface antigen (HBsAg; 10–14%) in sub-Saharan immigrants than in Latin American (LTBI, 19–47%; HBsAg, 0–7%) or Asian immigrants (LTBI, 30–51%; HBsAg, 0–3%).^{7–11} Coinfections should also be taken into account as some of these infections have a similar geographical distribution. Prompt diagnosis and treatment of these infections are important, since, for example, in the case of LTBI, 5–10% of cases may develop active tuberculosis (TB), and a quarter of the cases with HBsAg may develop cirrhosis and/or liver cancer.^{12,13} Some helminth infections such as schistosomiasis and strongyloidiasis may be asymptomatic in the early stages, but without prompt treatment these infections may lead to severe disease including bladder cancer, hepatocellular carcinoma, or disseminated infection in immunosuppressed subjects.^{14,15} Furthermore, without early proper screening and treatment, some of these infections could represent a public health risk for local transmission in the host country.^{16,17} Previous studies have considered relative and absolute eosinophilia and hyper-IgE as good indicators to facilitate the diagnosis of helminth infections in immigrants and travelers.^{18–21} Some countries have launched screening protocols for immigrants including clinical history, physical examination, and laboratory screening.^{22–24}

This situation may be exacerbated by administrative problems such as the lack of legal documentation, difficulties to obtaining access to health care, and the attitude of not seeking medical treatment held by many immigrants.²⁵ One study in Madrid of 988 immigrants (79.9% from sub-Saharan Africa) found that 72% of them were undocumented.⁷ Furthermore, the living conditions in the host country may facilitate the transmission of some infectious diseases. This situation may be more notable among sub-Saharan than Latin American immigrants because of historical reasons and political agreements among the different countries. Migratory movements of Latin American to Spain began much earlier, consequently these people usually have an already established social network (immigrant associations, friends, family, work, etc.). To improve this situation, some public and private institutions offer shelter centers for homeless immigrants.

The aim of this study was to describe infectious diseases in newly arrived sub-Saharan immigrants after a standardized health visits at an International Health Center in Barcelona, Spain.

MATERIALS AND METHODS

We performed a retrospective observational study with general assessment of the presence of infectious diseases in sub-Saharan immigrants (with or without symptoms) living in shelters attended at the Unit of International Health Drassanes-Vall d'Hebron (UIHDV), Barcelona (Spain), from January 2009 to December 2012.

The following infectious diseases were considered in the study: endemic infections from tropical areas (malaria, schistosomiasis, filariasis, and intestinal parasites) and worldwide international infections with a high prevalence in some areas (TB, human immunodeficiency virus [HIV], hepatitis B, hepatitis C, and syphilis).

Data collection included the following variables: sex, date of birth, country of origin, migratory route, date of arrival to Spain, date of first visit at the International Health Center, clinical symptoms, eosinophilia levels (absolute count and percentage), IgE level, and diagnosis of infectious diseases. The time from the arrival in Spain to the first consultation was calculated using the date of arrival in Spain and the date of the first visit. All the data remain confidential and have never been used for legal action against any immigrant.

Ethical approval was obtained from the Ethical Committee of the Hospital Vall d'Hebron and was conducted in accordance with good clinical practice guidelines. A referral agreement was made between the shelters and the UIHDV for all newly arrived immigrants. Oral informed consent was obtained from all the patients before the performance of any test.

Standardized health visits and analysis were based on international guidelines.^{22–24} These included the clinical history, a complete physical examination, and the laboratory analyses according to clinical presentation and geo-epidemiological data (Table 1). LTBI was defined as a tuberculosis skin test (TST) ≥ 10 mm and normal chest X-ray.¹²

Eosinophilia was defined as > 500 eosinophil/mm³ or $> 7\%$ and hyper-IgE > 500 IU/mL.^{21,26–28} When high eosinophilia and/or hyper-IgE was observed in the blood tests, but negative results were obtained in the first parasitological studies, further laboratory tests for helminths were performed (Table 2).

Other tests were conducted depending on the clinical symptoms reported by the patient (Table 3). Treatment was given following The Medical Letter Guidelines.²⁹

Direct parasitological tests included fresh stool studies, formalin–ether concentration, iodine stain, thick and thin blood smears, leuko-concentrations using saponin, urine sedimentation, the Graham test, skin snips for cutaneous filariae, modified Ziehl–Neelsen staining, charcoal fecal culture, and stool antigen detections for *Entamoeba histolytica*, *Giardia intestinalis*, and *Cryptosporidium*.³⁰

Categorical variables were described using frequencies, and quantitative variables were expressed with median and interquartile range (IQR). Categorical variables were compared using the χ^2 or the Fisher's test when necessary. To compare continuous variables, the Student's *t* or the Mann–Whitney *U* test was used. Contrast of hypothesis was done with a 5% alpha risk and 95% confidence intervals. The SPSS 21.00[®] was used for statistical analysis.

RESULTS

A total of 180 patients were reviewed. Some tests, albeit less than 13% (19% in IgE), were not performed in all the subjects. On comparison of the demographic data (gender and age) and the presence of clinical symptoms, no statistically significant differences were observed between the lost and tested cases.

The median age of the subjects included was 17.0 years (range = 12.0–49.0), with 76.7% being < 18 years old, and 178/180 (98.9%) males. Table 4 shows the countries of origin. The median time from arrival in Spain to consultation was 4 months (IQR = 1.0–9.0). Of 175 immigrants, 160 (91.4%) took a land-maritime route to reach Europe and 15 (8.6%) came directly by flight.

A total of 119/180 (66.1%) subjects were clinically asymptomatic while the following symptoms were reported in the remaining cases: gastrointestinal in 15/180 (8.3%), musculoskeletal in 11/180 (6.1%), neurological in 10/180 (5.6%), cutaneous in 9/180 (5.0%), fever in 5/180 (2.8%), genitourinary in 4/180 (2.2%), respiratory in 3/180 (1.7%), and other symptoms in 4/180 (2.2%).

In 131/180 (72.8%) patients, infection by at least one pathogen was diagnosed. Of 180, 51 (28.4%) presented coinfection: 39/180 (21.7%) with two infections, 9/180 (5.0%) with three infections, and 3/180 (1.7%) with four infections. Table 5 shows the imported infectious diseases

diagnosed. There was no association between the presence of clinical symptoms and the diagnosis of an infectious disease ($P = 0.40$). The prevalence of infectious diseases was 121/160 (75.6%) in patients taking land-maritime routes and 7/15 (46.7%) in patients arriving by plane. These differences were statistically significant ($P = 0.02$). The results of the blood analyses showed high absolute eosinophilia in 32/156 (20.5%), high relative eosinophilia in 49/157 (31.2%), and hyper-IgE in 40/146 (27.4%).

Two (1.3%) cases of malaria by *Plasmodium falciparum* were diagnosed, both of which were 17 years of age. One had come from Ghana 8 days before consultation and the other had arrived from Guinea Conakry 1 month before; neither reported previous clinical symptoms.

In 48/171 (28.1%), at least one helminth (in blood, urine, or feces) was diagnosed and 9/171 (5.3%) showed coinfection by two helminths. The most common parasitic infections were: schistosomiasis in 19 cases (16 diagnosed by microscopic examination and three by serology), hookworm in 16, giardiasis in 10, and strongyloidiasis in nine (three diagnosed by microscopic examination and six by serology) (Table 6).

On comparison of subjects with helminths 19/31 (61.3%) cases showed absolute eosinophilia versus 25/120 (20.8%) with normal levels, 31/48 (64.6%) cases presented relative eosinophilia versus 14/104 (13.5%) with normal levels, and 24/38 (63.2%) cases showed hyper-IgE versus 17/103 (16.5%) with normal levels. A statistically significant association was found between eosinophilia (absolute count or percentage) or hyper-IgE and the presence of helminths ($P < 0.001$). Relative eosinophilia and hyper-IgE were better indicators of helminth infection than absolute eosinophilia, particularly for hookworms, schistosomiasis, and strongyloidiasis.

DISCUSSION

Most of the cases in this study were young males from west Africa. Indeed, 99% of the subjects in our study were male, being a higher percentage compared with the ratio of the general immigrant population in Spain in 2011 (53%).¹ However, this gender predominance has been associated with immigrants from Asia and Africa (61% and 65% males, respectively).¹ With respect to country of origin, according to official data, the general immigrant population in Spain in 2011 was mainly from Romania, Morocco, the United Kingdom, Ecuador, Colombia, and Bolivia.³¹ Therefore, in terms of country of origin, our sample does not represent the general immigrant population in Spain.

Although many cases presented infectious disease, most were asymptomatic (66%), with previous studies showing slightly higher rates (69–87%).^{10,11,18,32} Similar to previous studies, no relationship was found between having symptoms and the presence of imported infectious diseases, suggesting that screening protocols should be carried out regardless of clinical status.^{9,33} The prevalence of pathogenic infectious disease was high (73%). This prevalence was reportedly lower (45%) in studies including other areas of origin.¹⁰ The prevalence of either infections or noninfectious diseases was 84% in previous studies.⁷ According to our data, sub-Saharan immigrants coming through a land-maritime routes are more vulnerable to infectious diseases.

Latent TB infection.

The prevalence of LTBI (61%) in this study was similar to that of other studies (46–71%), being higher than the general prevalence in the world (one-third of the world's population is

estimated to be infected) and in that of other immigrant groups.^{7–10,12,34} Nonetheless, the prevalence of LTBI in this study may be overestimated, since false-positive TST result may be observed in subjects who have received the Bacillus Calmette–Guérin vaccine or are infected with other mycobacterias.¹² This is important to take into account because the side effects of chemoprophylaxis for LTBI are not negligible.³⁵ Nevertheless, the use of new interferon-gamma assays (IGRAs) could solve this limitation, although its high cost has precluded its widespread use in some resource-strained public health settings by the World Health Organization.^{12,34,36} In a previous study in Almeria, molecular analyses detected the transmission of TB between immigrants and the autochthonous population.¹⁷ Therefore, as recommended in international guidelines, TB screening protocols (including IGRAs if possible) are recommended in newly arrived immigrants from areas with a high prevalences of TB (≥ 20 cases per 100,000 inhabitants) to achieve early diagnosis and treatment of active or latent infection.^{22,37}

Hepatitis B surface antigen.

In this study, the prevalence of HBsAg in sub-Saharan immigrants (15%) was similar to that described in other studies (10–19%), being higher compared with other immigrant groups.^{7–10,38} International guidelines recommend screening in populations in which the prevalence is estimated to be greater than 2%.³⁹ On the other hand, although the prevalence of HbsAg in sub-Saharan immigrants remains as high as 10% in some areas in Africa, it has decreased in recent years probably due to expanded immunization programs in these countries.⁴⁰ Nonetheless, this situation is particularly worrisome in our population since apartments and rooms in shelters are often shared making protective measures a necessity to household contacts.^{13,39} Therefore screening for hepatitis B and vaccination in nonimmune persons living in shelters is important to offer follow-up and treatment of cases, to screen for hepatitis B in possible contact cases and vaccinate them if necessary.

Malaria.

We detected two cases of malaria both of which were asymptomatic. Asymptomatic malaria by *P. falciparum* has been previously described.⁴¹ Malaria may be fatal without treatment and thus, its detection in asymptomatic sub-Saharan subjects is needed, especially taking into account that this infection may remain asymptomatic in semi-immune individuals for more than 28 months.^{41,42} In addition, nontreated cases of malaria may be a risk for the host country, as they can facilitate transmission by mosquito bites, blood transfusion or congenital transmission. Indeed, although Greece had remained malaria free since 1974, locally acquired *Plasmodium vivax* cases have been reported annually since 2010, thereby reinforcing the risk of reintroduction. However, fortunately, mosquito vectors in Europe today are rarely infected by *P. falciparum*.⁴¹ Therefore, we recommend that screening for malaria should be considered in asymptomatic sub-Saharan immigrants. The use of microscopic examination currently remains the gold standard for malaria diagnosis, however, real-time polymerase chain reaction could be a good option as it has shown to have a higher sensitivity in asymptomatic patients and requires less time for technicians to perform.⁴³

Parasites, eosinophilia, and hyper-IgE.

The prevalence of pathogenic intestinal parasites (22%) in our study was similar to that of others (21–25%).^{7,10,38} On the other hand, some studies have reported lower prevalences (3–11%)

than what we found, which may be explained by different reasons: experience and type of laboratory test used for the diagnosis, the difficulties to complete screening protocols in this population, the short time of arrival to Spain in our population, the area of origin, and different migratory processes.^{8,9} Helminths were present in 28% of our cases. Previous studies in immigrants have described lower prevalences of helminths (6–16%), showing a trend to being higher in studies in which most cases were from sub-Saharan Africa.^{7,11,33,44,45}

Schistosomiasis and strongyloidiasis are potentially serious diseases and were common in this group. The prevalence of schistosomiasis (9%) by microscopic examination in this study was higher compared with other studies (0.3%).⁴ However, the use of serology tests may present a higher prevalence of schistosomiasis (0.8–41%).^{7–10,38} Unfortunately, serology test results remain positive indefinitely after treatment, and thus, resolved and active infection cannot be distinguished.⁴⁶ In addition, serology may give false-negative results, especially in cases with *Schistosoma haematobium* infection.⁴⁷ Schistosomiasis is a chronic, parasitic disease that could produce severe urinary or gastrointestinal damage.¹⁴ The geographical distribution of schistosomiasis is particularly high in sub-Saharan Africa and is mainly determined by the presence of snail vectors that need specific climatic conditions. Nonetheless, several studies have described the establishment of *Biomphalaria tenagophila* snails in Europe (the intermediate host of *Schistosoma mansoni*), and *S. haematobium* was diagnosed in a family living in Corsica a few years ago, having been transmitted by *Bulinus* spp. snails. Thereafter, other cases were diagnosed, constituting a public health problem for Corsica and Europe.^{16,48,49} Climatic change, the establishment of an intermediate host, and the presence of nontreated schistosomiasis patients could facilitate the transmission of schistosomiasis in Europe and lead to an important public health problem. Therefore, we recommend direct examination in urine and feces in these cases to screen for schistosomiasis. Serology could be considered in places with little experience in microscopic examination or on high suspicion of schistosomiasis and the first parasitological tests are negative.

The presence of strongyloidiasis in this study was not negligible. In most cases diagnosis was made by serology, similar to previous studies.⁸ Serology for strongyloidiasis has usually higher sensitivity than microscope examination.⁵⁰

The range of high eosinophilia (21–31%) found in this study was similar to that of other studies (9–27%).^{7,8,10,51,52} The prevalence of helminths was higher in cases with eosinophilia or hyper-IgE (61–65% versus 14–21%). These results were slightly higher in previous studies (64–77%). However, the diagnoses in some of these studies were based on serological tests that may give false-positive results.^{18,27,52} A significant association was found between absolute and relative eosinophilia and hyper-IgE with the presence of helminths, similar to what has been described in other studies.^{52,53} In our study, relative eosinophilia and hyper-IgE were better indicators of helminth infection than absolute eosinophilia, particularly for hookworms, schistosomiasis and strongyloidiasis, the most pathogenic helminths. In a study carried out in Kenya to establish reference intervals for hematology parameters in the local population, the authors found differences compared with other regions, highlighting the importance of defining normal reference values, such as for eosinophilia, for populations in Africa.⁵⁴ Several previous studies and health guidelines for imported diseases in immigrants use absolute eosinophilia as single indicator of helminth infection. Taking into account our results, relative eosinophilia and hyper-IgE should be considered as better indicators of the presence of helminths in sub-Saharan immigrants. To our knowledge, no other study has shown these results. Nonetheless, further

studies are needed in this regard. However, these helminth infections were also diagnosed in subjects with normal eosinophil levels or IgE. Thus, we recommend helminth screening in newly arrived sub-Saharan immigrants according to the area of origin (coproparasitological, uroparasitological, and hemoparasitic microscopic examination). In cases with high relative eosinophilia or hyper-IgE and with the first results being negative, further studies should be considered (three or more coproparasitological studies, charcoal fecal culture, and parasitological serologies), paying particular attention to possible schistosomiasis and strongyloidiasis.

Coinfections.

More than one-quarter of our study population presented coinfection by different imported infectious diseases, being similar to previous studies reporting from 9% to 35% of coinfection.^{7,10,32} The presence of coinfection should always be considered since a delay in treatment may, in some cases, lead to serious consequences in both the short term (malaria) and the long term (HIV, TB, HBsAg, schistosomiasis, and strongyloidiasis) with respect to the health of the subject involved as well as the public health system. Furthermore, coinfection may alter the normal course of some infections, such as schistosomiasis and viral hepatitis, HIV and viral hepatitis, or HIV and strongyloidiasis.^{55–57}

Compliance.

Only 10% of the study population did not complete all of the tests, similar to what has been reported in other retrospective studies.^{10,58} Gender, age, and the presence of clinical symptoms were homogeneous on comparison of lost versus tested cases, and thus it seems reasonable to assume that these losses did not generate a large bias in the results. However, taking into account the high prevalence of some infectious diseases in this population, special care should be taken to avoid losses to follow-up.

In conclusion, our results demonstrate a high prevalence of pathogenic imported infectious diseases (73%) in newly sub-Saharan immigrants compared with other immigrant groups, particularly for LTBI, HBsAg, and schistosomiasis. In addition, over a quarter of our subjects presented coinfection. Some of these infections may lead to the development of severe health problems, representing a high cost for public health systems in the absence of prompt treatment, and may be a growing menace for the risk of transmission in host countries. Relative eosinophilia and hyper-IgE are better indicators of helminth infection than absolute eosinophilia, particularly the more pathogenic helminths such as schistosomiasis and strongyloidiasis. According to our results, these infections were present in two of three cases when relative eosinophilia was present.

According to our results, for the benefit of the individuals and the public health system, it is advisable to perform accurate screening and tailored protocols—particularly TST or IGRAs, hepatitis B screening, malaria tests, schistosomiasis (microscopic examination if possible), strongyloidiasis (at least serology) in newly sub-Saharan immigrants (particularly patients coming through land-maritime routes, regardless of the clinical symptoms), with great attention to helminths in case of relative eosinophilia or hyper-IgE. Referral agreements should be strengthened between shelters for sub-Saharan immigrants and International Health Centers in the search for new strategies to ensure compliance to medical visits.

Received August 11, 2015.

Accepted for publication December 8, 2015.

Authors' addresses: Núria Serre Delcor, Begoña Treviño Maruri, Antonio Soriano Arandes, Isabel Claveria Guiu, and Hakima Ouaraab Essadik, PROSICS, Tropical Medicine and International Health Unit Drassanes–Vall d'Hebron, Hospital Vall d'Hebron, Institut Català de la Salut, Barcelona, Spain, E-mails: n.serre@vhebron.net, mtrevino@vhebron.net, asoriano@vhebron.net, iclaveria@vhebron.net, and houaarab@vhebron.net. Mateu Espasa Soley, Microbiology Department, PROSICS, Hospital Vall d'Hebron, Institut Català de la Salut, Barcelona, Spain, E-mail: mespasa@vhebron.net. Israel Molina Romero, Infectious Diseases Department, PROSICS, Hospital Vall d'Hebron, Institut Català de la Salut, Barcelona, Spain, E-mail: imolina@vhebron.net. Carlos Ascaso, Public Health Department, Hospital Clinic Barcelona, Spain, E-mail: carlosascaso@ub.edu.

REFERENCES

- <eref>1. INE, 2015. *Anuario estadístico de España, 2011*. Available at: http://www.ine.es/prodyser/pubweb/anuarios_mnu.htm. Accessed November 20, 2015.</eref>
- <eref>2. Agencia EFE, 2015. *EN 2014 casi se duplicaron los inmigrantes que entraron en España por el Sur de forma irregular*. La Vanguardia, Andalucía, February 6, 2015. Available at: <http://www.lavanguardia.com/local/sevilla/20150206/54426930592/duplicar-inmigrantes-espana.html>. Accessed June 29, 2015.</eref>
- <jrn>3. Stauffer WM, Weinberg M, 2009. Emerging clinical issues in refugees. *Curr Opin Infect Dis* 22: 436–442.</jrn>
- <eref>4. ECDC, 2015. *TB in Vulnerable Populations*. Available at: http://ecdc.europa.eu/en/activities/diseaseprogrammes/programme_tuberculosis/Pages/tuberculosis_vulnerable_populations.aspx. Accessed November 18, 2015.</eref>
- <jrn>5. Harris AR, Rusell RJ, Charters AD, 1984. A review of schistosomiasis in immigrants in western Australia demonstrating the unusual longevity of *Schistosoma mansoni*. *Trans R Soc Trop Med Hyg* 78: 385–388.</jrn>
- <eref>6. News BBC, 2007. *Key Facts: Africa to Europe Migration*. Available at: <http://news.bbc.co.uk/2/hi/europe/6228236.stm>. Accessed November 18, 2015.</eref>
- <jrn>7. López-Vélez R, Huerga H, Turrientes MC, 2003. Infectious diseases in immigrants from the perspective of a tropical medicine referral unit. *Am J Trop Med Hyg* 69: 115–121.</jrn>
- <jrn>8. Monge-Maillo B, López-Vélez R, Norman FF, Ferrere-González F, Martínez-Pérez Á, Pérez-Molina JA, 2015. Screening of imported infectious diseases among asymptomatic sub-Saharan African and Latin American immigrants: a public health challenge. *Am J Trop Med Hyg* 92: 848–856.</jrn>
- <jrn>9. Monge-Maillo B, Jiménez BC, Pérez-Molina JA, Norman F, Navarro M, Pérez-Ayala A, Herrero JM, Zamarrón P, López-Vélez R, 2009. Imported infectious diseases in mobile populations, Spain. *Emerg Infect Dis* 15: 1745–1752.</jrn>
- <jrn>10. Bocanegra C, Salvador F, Sulleiro E, Sánchez-Montalvá A, Pahissa A, Molina I, 2014. Screening for imported diseases in an immigrant population: experience from a teaching hospital in Barcelona, Spain. *Am J Trop Med Hyg* 91: 1277–1281.</jrn>

- <jrn>11. Lifson AR, Thai D, O'Fallon A, Mills WA, Hang K, 2002. Prevalence of tuberculosis, hepatitis B virus, and intestinal parasitic infections among refugees to Minnesota. *Public Health Rep* 117: 69–77.</jrn>
- <eref>12. CDC, 2014. *Diagnosis of Latent TB Infection*. Available at: <http://www.cdc.gov/tb/publications/LTBI/diagnosis.htm#3>. Accessed May 31, 2015.</eref>
- <eref>13. World Health Organization, 2015. *Hepatitis B*. Available at: <http://www.who.int/mediacentre/factsheets/fs204/en/>. Accessed May 31, 2015.</eref>
- <eref>14. World Health Organization, 2015. *Schistosomiasis*. Available at: <http://www.who.int/topics/schistosomiasis/en/>. Accessed May 31, 2015.</eref>
- <eref>15. World Health Organization, 2015. *Strongyloidiasis*. Available at: http://www.who.int/neglected_diseases/diseases/strongyloidiasis/en/. Accessed May 31, 2015.</eref>
- <eref>16. ECDC, 2015. *Local Transmission of Schistosoma haematobium in Corsica, France*. Available at: http://ecdc.europa.eu/en/publications/Publications/risk-assessment-Schistosoma%20haematobium-Corsica-update_TOR1N6.pdf. Accessed November 18, 2015.</eref>
- <jrn>17. Martínez-Lirola M, Alonso-Rodríguez N, Sánchez ML, Herranz M, Andrés S, Peñafiel T, Rogado MC, Cabezas T, Martínez J, Lucerna MA, Rodríguez M, Bonillo Mdel C, Bouza E, García de Viedma D, 2008. Advanced survey of tuberculosis transmission in a complex socioepidemiologic scenario with a high proportion of cases in immigrants. *Clin Infect Dis* 47: 8–14.</jrn>
- <jrn>18. Pardo J, Carranza C, Muro A, Angel-Moreno A, Martín A-M, Martín T, Hernández-Cabrera M, Pérez-Arellano JL, 2006. Helminth-related eosinophilia in African immigrants, Gran Canaria. *Emerg Infect Dis* 12: 1587–1589.</jrn>
- <jrn>19. Cooper PJ, Ayre G, Martin C, Rizzo JA, Ponte EV, Cruz AA, 2008. Geohelminth infections: a review of the role of IgE and assessment of potential risks of anti-IgE treatment. *Allergy* 63: 409–417.</jrn>
- <jrn>20. Checkley AM, Chiodini PL, Dockrell DH, Bates I, Thwaites GE, Booth HL, Brown M, Wright SG, Grant AD, Mabey DC, Whitty CJ, Sanderson F; British Infection Society and Hospital for Tropical Diseases, 2010. Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management. *J Infect* 60: 1–20.</jrn>
- <jrn>21. Pate MB, Smith JK, Chi DS, Krishnaswamy G, 2010. Regulation and dysregulation of immunoglobulin E: a molecular and clinical perspective. *Clin Mol Allergy* 8: 3.</jrn>
- <eref>22. CDC, 2012. *General Refugee Health Guidelines*. Available at: <http://www.cdc.gov/immigrantrefugeehealth/guidelines/general-guidelines.html>. Accessed May 31, 2015.</eref>

- <jrn>23. Pottie K, Greenaway C, Feightner J, Welch V, Swinkels H, Rashid M, Narasiah L, Kirmayer LJ, Ueffing E, MacDonald NE, Hassan G, McNally M, Khan K, Buhrmann R, Dunn S, Dominic A, McCarthy AE, Gagnon AJ, Rousseau C, Tugwell P; coauthors of the Canadian Collaboration for Immigrant and Refugee Health, 2011. Evidence-based clinical guidelines for immigrants and refugees. *Can Med Assoc J* 183: E824–E925.</jrn>
- <jrn>24. Barnett ED, 2004. Infectious disease screening for refugees resettled in the United States. *Clin Infect Dis* 39: 833–841.</jrn>
- <jrn>25. López Lázaro L, 2008. Commentary: immigration, health status, and use of primary care services. *Atencion Primaria Soc Esp Med Fam Comunitaria* 40: 232–233.</jrn>
- <jrn>26. Churchill DR, Chiodini PL, McAdam KP, 1993. Screening the returned traveller. *Br Med Bull* 49: 465–474.</jrn>
- <jrn>27. Whetham J, Day JN, Armstrong M, Chiodini PL, Whitty CJM, 2003. Investigation of tropical eosinophilia; assessing a strategy based on geographical area. *J Infect* 46: 180–185.</jrn>
- <jrn>28. Schulte C, Krebs B, Jelinek T, Nothdurft HD, von Sonnenburg F, Löscher T, 2002. Diagnostic significance of blood eosinophilia in returning travelers. *Clin Infect Dis* 34: 407–411.</jrn>
- <eref>29. The Medical letter, 2015. *Drugs for Parasitic Infections*. Available at: <http://secure.medicalletter.org/para>. Accessed May 31, 2015.</eref>
- <eref>30. World Health Organization, 1991. *Basic Laboratory Methods in Medical Parasitology*. Available at: [http://whqlibdoc.who.int/publications/9241544104_\(part1\).pdf](http://whqlibdoc.who.int/publications/9241544104_(part1).pdf). Accessed May 31, 2015.</eref>
- <eref>31. INE, 2012. *Extranjeros en la Unión Europea y en España*. Available at: http://www.ine.es/ss/Satellite?L=es_ES&c=INECifrasINE_C&cid=1259938022122&p=1254735116567&pagename=ProductosYServicios%2FPYSLayout. Accessed November 20, 2015.</eref>
- <jrn>32. Manganelli L, Berrilli F, Di Cave D, Ercoli L, Capelli G, Otranto D, Giangaspero A, 2012. Intestinal parasite infections in immigrant children in the city of Rome, related risk factors and possible impact on nutritional status. *Parasit Vectors* 5: 265.</jrn>
- <jrn>33. Geltman PL, Cochran J, Hedgecock C, 2003. Intestinal parasites among African refugees resettled in Massachusetts and the impact of an overseas pre-departure treatment program. *Am J Trop Med Hyg* 69: 657–662.</jrn>
- <eref>34. World Health Organization, 2015. *New WHO Recommendations on Use of Commercial TB Interferon-Gamma Release Assays (IGRAs) in Low- and Middle-Income Countries*. Available at: http://www.who.int/tb/features_archive/igra_policy24oct/en/. Accessed May 31, 2015.</eref>
- <eref>35. CDC, 2013. *Treatment of Latent TB Infection*. Available at: <http://www.cdc.gov/tb/publications/ltbi/treatment.htm>. Accessed May 31, 2015.</eref>
- <jrn>36. Salinas C, Ballaz A, Díez R, Aguirre U, Antón A, Altube L, 2015. Tuberculosis screening program for undocumented immigrant teenagers using the QuantiFERON[®]-TB Gold In-Tube test. *Med Clin (Barc)* 145: 7–13.</jrn>

- <eref>37. WHO, 2014. *Estimated TB Incidence Rates, 2013*. Available at: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_TBincidence_2013.png. Accessed June 29, 2015.</eref>
- <jrn>38. Gibney KB, Mahrshahi S, Torresi J, Marshall C, Leder K, Biggs B-A, 2009. The profile of health problems in African immigrants attending an infectious disease unit in Melbourne, Australia. *Am J Trop Med Hyg* 80: 805–811.</jrn>
- <eref>39. CDC, 2008. *Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection*. Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm>. Accessed May 31, 2015.</eref>
- <jrn>40. Ott JJ, Stevens GA, Groeger J, Wiersma ST, 2012. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. *Vaccine* 30: 2212–2219.</jrn>
- <jrn>41. Monge-Maillo B, Norman F, Pérez-Molina JA, Díaz-Menéndez M, Rubio JM, López-Vélez R, 2012. *Plasmodium falciparum* in asymptomatic immigrants from sub-Saharan Africa, Spain. *Emerg Infect Dis* 18: 356–357.</jrn>
- <jrn>42. Krajden S, Panisko DM, Tobe B, Yang J, Keystone JS, 1991. Prolonged infection with *Plasmodium falciparum* in a semi-immune patient. *Trans R Soc Trop Med Hyg* 85: 731–732.</jrn>
- <jrn>43. Matisz CE, Naidu P, Shokoples SE, Grice D, Krinke V, Brown SZ, Kowalewska-Grochowska K, Houston S, Yanow SK, 2011. Post-arrival screening for malaria in asymptomatic refugees using real-time PCR. *Am J Trop Med Hyg* 84: 161–165.</jrn>
- <jrn>44. Abu-Madi MA, Behnke JM, Doiphode SH, 2010. Changing trends in intestinal parasitic infections among long-term-residents and settled immigrants in Qatar. *Parasit Vectors* 3: 98.</jrn>
- <jrn>45. Garg PK, Perry S, Dorn M, Hardcastle L, Parsonnet J, 2005. Risk of intestinal helminth and protozoan infection in a refugee population. *Am J Trop Med Hyg* 73: 386–391.</jrn>
- <eref>46. CDC, 2012. *Schistosomiasis*. Available at: http://www.cdc.gov/parasites/schistosomiasis/health_professionals/. Accessed May 31, 2015.</eref>
- <jrn>47. Kinkel H-F, Dittrich S, Bäumer B, Weitzel T, 2012. Evaluation of eight serological tests for diagnosis of imported schistosomiasis. *Clin Vaccine Immunol* 19: 948–953.</jrn>
- <eref>48. World Health Organization, 2015. *Schistosomiasis, Countries or Areas at Risk, 2014*. Available at: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_ShistoPrevalence_ITHRiskMap.png?ua=1. Accessed June 29, 2015.</eref>
- <jrn>49. Majoros G, Fehér Z, Deli T, Földvári G, 2008. Establishment of *Biomphalaria tenagophila* snails in Europe. *Emerg Infect Dis* 14: 1812–1814.</jrn>
- <jrn>50. Requena-Mendez A, Chiodini P, Bisoffi Z, Buonfrate D, Gotuzzo E, Muñoz J, 2013. The laboratory diagnosis and follow up of strongyloidiasis: a systematic review. *PLoS Negl Trop Dis* 7: e2002.</jrn>

- <jrn>51. Caruana SR, Kelly HA, Ngeow JYY, Ryan NJ, Bennett CM, Chea L, Nuon S, Bak N, Skull SA, Biggs BA, 2006. Undiagnosed and potentially lethal parasite infections among immigrants and refugees in Australia. *J Travel Med* 13: 233–239.</jrn>
- <jrn>52. Belhassen-García M, Pardo-Lledías J, Pérez del Villar L, Muro A, Velasco-Tirado V, Blázquez de Castro A, Vicente B, García García MI, 2014. Relevance of eosinophilia and hyper-IgE in immigrant children. *Medicine (Baltimore)* 93: e43.</jrn>
- <jrn>53. Carranza-Rodriguez C, Pardo-Lledías J, Muro-Alvarez A, Pérez-Arellano JL, 2008. Cryptic parasite infection in recent west African immigrants with relative eosinophilia. *Clin Infect Dis* 46: e48–e50.</jrn>
- <jrn>54. Odhiambo C, Oyaro B, Odipo R, Otieno F, Alemnji G, Williamson J, Zeh C, 2015. Evaluation of locally established reference intervals for hematology and biochemistry parameters in western Kenya. *PLoS One* 10: e0123140.</jrn>
- <jrn>55. Kamal SM, Graham CS, He Q, Bianchi L, Tawil AA, Rasenack JW, Khalifa KA, Massoud MM, Koziel MJ, 2004. Kinetics of intrahepatic hepatitis C virus (HCV)-specific CD4⁺ T cell responses in HCV and *Schistosoma mansoni* coinfection: relation to progression of liver fibrosis. *J Infect Dis* 189: 1140–1150.</jrn>
- <jrn>56. Gatanaga H, Yasuoka A, Kikuchi Y, Tachikawa N, Oka S, 2000. Influence of prior HIV-1 infection on the development of chronic hepatitis B infection. *Eur J Clin Microbiol Infect Dis* 19: 237–239.</jrn>
- <jrn>57. Siegel MO, Simon GL, 2012. Is human immunodeficiency virus infection a risk factor for *Strongyloides stercoralis* hyperinfection and dissemination. *PLoS Negl Trop Dis* 6: e1581.</jrn>
- <jrn>58. Chang AH, Perry S, Du JNT, Agunbiade A, Polesky A, Parsonnet J, 2013. Decreasing intestinal parasites in recent northern California refugees. *Am J Trop Med Hyg* 88: 191–197.</jrn>

TABLE 1

Standardized analysis for infectious diseases in sub-Saharan immigrants attended at the Unit of International Health Drassanes, Vall d'Hebron, Barcelona (Spain), from January 2009 to December 2012

Complete blood count with white cell differential and IgE
Creatinine level, liver function tests, and cholesterol and glucose levels
Basic urine test
Serologies: HBsAg, anti-HBc, HCV, TPHA, RPR, and HIV
Tuberculosis: TST (if ≤ 35 years old and ≤ 5 years since arrival in Spain) and chest X-ray
Helminths and intestinal protozoa: one stool and one urine sample for direct microscopic examination
Microfilaremia: detection of hemoparasites by microscopic examination
Malaria: thick and thin blood smear

anti-HBc = antibodies to hepatitis B core antigen; HBsAg = hepatitis B surface antigen; HCV = antibodies to hepatitis C; HIV = human immunodeficiency virus; TPHA and RPR = syphilis serology; TST = tuberculosis skin test.

TABLE 2

Study protocol for sub-Saharan immigrants with high absolute or relative eosinophilia or hyper-IgE and negative results for helminths in first screening protocol

Three stool samples for coproparasitological study and charcoal fecal culture
If previous microscopic examinations are negative, serologies according to epidemiological background: <i>Echinococcus granulosus</i> IgG (EIA); <i>Fasciola hepatica</i> IgG + IgM (indirect HA); <i>Taenia solium</i> IgG (EIA); <i>Toxocara cani</i> IgG (EIA); <i>Onchocerca volvulus</i> IgG, IgG1, IgG2, IgG3, and IgG4 (ELISA); <i>Wuchereria bancrofti/Brugia malayi</i> IgG, IgG1, IgG2, IgG3, and IgG4 (ELISA); <i>Strongyloides stercoralis</i> IgG (ELISA); and <i>Schistosoma mansoni</i> (ELISA)

EIA = enzyme immunoassay; ELISA = enzyme-linked immunosorbent assay; HA = hemagglutination.

TABLE 3

Other test for sub-Saharan immigrants according to epidemiologic background

Chronic skin itching: skin snips for cutaneous filariae
Anal itching: Graham test
Diarrhea: fresh stool studies, formalin–ether concentration, stool antigen detection for <i>Entamoeba histolytica</i> , <i>Giardia intestinalis</i> , and <i>Cryptosporidium</i> , coproculture, modified Ziehl–Neelsen staining
Fever: QBC (and consider other test for imported fever)
Prolonged cough and fever: Ziehl–Neelsen of sputum

QBC = quantitative buffy coat.

TABLE 4

Country of origin in sub-Saharan immigrants living in shelter centers (N = 180)

Country of origin	Patients (%)
Ghana	71 (39.4)
Gambia	37 (20.6)
Senegal	23 (12.8)
Guinea Conakry	23 (12.8)
Nigeria	9 (5.0)
Mali	6 (3.3)
Burkina Faso	3 (1.7)
Guinea Bissau	2 (1.1)
Angola, Cameroon, Congo, Democratic Republic of Congo, Liberia, and Sierra Leona	1 (0.6) each

TABLE 5

Infectious diseases in sub-Saharan immigrants

Imported infections	Number of patients that performed the test	Positive cases	Positive cases in patients arriving in Europe by land-maritime route	Positive cases in patients arriving in Europe by plane	Fisher's test
	Cases (%)	Cases (%)	Cases (%)	Cases (%)	<i>P</i> value
LTBI	142 (78.9)	86 (60.6)	78/128 (60.9)	5/10 (50.0)	0.51
Active TB	160 (88.9)	0.0 (0)	0.0 (0)	0.0 (0)	–
HbsAg+	169 (93.9)	25 (14.8)	23/149 (15.4)	1/15 (6.7)	0.69
Anti-HBc+	168 (93.3)	124 (73.8)	108/148 (73.0)	13/15 (86.7)	0.35
HCV	167 (92.8)	2 (1.2)	2/149 (1.3)	0/13 (0)	1
Latent syphilis	164 (91.1)	9 (5.5)	9/146 (6.2)	0/13 (0)	1
HIV	167 (92.8)	2 (1.2)	2/148 (1.4)	0/14 (0)	1
<i>Plasmodium falciparum</i>	157 (87.2)	2 (1.3)	2/139 (1.4)	0/13 (0)	1
Intestinal parasites	171 (95.0)	63 (36.8)	62/151 (41.1)	4/15 (26.7)	0.40
Pathogenic intestinal parasites	171 (95.0)	38 (22.2)	37/160 (23.1)	0/15 (0)	0.04*
Pathogenic intestinal poliparasitosis	171 (95.0)	12 (7.0)	12/160 (7.5)	0/15 (0)	0.57
Helminths	171 (95.0)	48 (28.1)	45/151 (29.8)	2/15 (13.3)	0.23
Absolute eosinophilia	156 (86.7)	32 (20.5)	45/139 (32.4)	3/13 (23.1)	0.75
Relative eosinophilia	157 (87.2)	49 (31.2)	30/138 (21.7)	2/13 (15.4)	0.73
Hyper-IgE	146 (81.1)	40 (27.4)	36/130 (27.7)	3/12 (25.0)	1
Infectious disease	180 (100)	131 (72.8)	121/160 (75.6)	7/15 (46.7)	0.028*
Coinfections	180 (100)	51 (28.4)	48/160 (30.0)	2/15 (13.3)	0.23

anti-HBc: antibodies to hepatitis B core antigen; HBsAg = hepatitis B surface antigen; HCV = antibodies to hepatitis C virus; HIV = human immunodeficiency virus; LTBI = latent tuberculosis infection; TB = tuberculosis. Absolute eosinophilia > 500 eosinophil/mm³; relative eosinophilia > 7%; hyper-IgE > 500 UI/mL; intestinal parasites: all intestinal protozoa and helminths regardless of pathogenicity.

TABLE 6

Helminths and intestinal protozoa in sub-Saharan immigrants (*N* = 180)

Helminths and intestinal protozoa	Cases (%)	95% CI	Absolute eosinophilia	Relative eosinophilia	Hyper-IgE	Eosinophilia and/or hyper-IgE
			Cases (%)	Cases (%)	Cases (%)	Cases (%)
Number of patients	180 (100%)	–	32/156 (20.5)	49/157 (31.2)	40/146 (27.4)	66/157 (42.0)
Coprop. and urop. test*	171/180 (95.0)	–	31/32 (96.9)	48/49 (98.0)	38/40 (95.0)	63/66 (95.5)
Microscopic examination for filarias*	157/180 (87.2)	–	31/32 (96.9)	48/49 (98.0)	38/40 (95.0)	63/66 (95.5)
Parasitological serologies*	45/180 (25.0)	–	23/32 (71.9)	36/49 (73.5)	28/40 (70.0)	45/66 (68.2)
Hookworm	16/171 (9.4)	4.7–14.1	6/31 (19.4)	10/48 (20.8)	9/38 (23.7)	12/63 (19.0)
<i>Schistosoma mansoni</i>	10/171 (5.9)	2.0–9.7	3/31 (9.7)	5/48 (10.4)	5/38 (13.2)	7/63 (11.1)
<i>Schistosoma haematobium</i>	6/171 (3.5)	0.5–6.7	6/31 (19.4)	6/48 (12.5)	5/38 (13.2)	6/63 (9.5)
<i>Schistosoma</i> serology	3/45 (6.7)	1.4–18.3	0/23 (0.0)	2/36 (5.6)	1/28 (3.6)	2/45 (4.4)
<i>Giardia duodenalis</i>	10/171 (5.9)	2.0–9.7	2/31 (6.5)	2/48 (4.2)	2/38 (5.3)	2/63 (3.2)
<i>Schistosoma stercorali</i>	3/171 (1.8)	0.4–5.0	0/31 (0.0)	1/48 (2.1)	1/38 (2.6)	1/63 (1.6)
<i>S. stercoralis</i> serology	6/45 (13.3)	2.3–24.4	4/23 (17.4)	6/36 (16.7)	4/28 (14.3)	6/45 (13.3)
<i>Mansonella perstans</i>	7/157 (4.5)	0.9–8.1	4/31 (12.9)	4/48 (8.3)	3/38 (7.9)	5/63 (7.9)
<i>Toxocara serology</i>	2/45 (4.4)	0.5–15.1	1/23 (3.6)	2/36 (7.1)	1/28 (3.6)	2/45 (4.4)
<i>Ascaris lumbricoide</i>	1/171 (0.6)	0.0–3.2	0	0	0	0
<i>Trichuris trichiura</i>	1/171 (0.6)	0.0–3.2	0	0	0	0
<i>Hymenolepis nana</i>	1/171 (0.6)	0.0–3.2	0	0	0	0
Cases with helminths	48/171 (28.1)	21.1–31.1	19/31 (61.3)	31/48 (64.6)	24/38 (63.2)	36/63 (57.0)

CI = confidence interval; Coprop. = coproparasitological; Urop. = uroparasitological.

* Number of patients undergoing the test. Absolute eosinophilia > 500 eosinophil/mm³; relative eosinophilia > 7%; hyper-IgE > 500 UI/mL.