## Cryptic Parasite Infection in Recent West African Immigrants with Relative Eosinophilia

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Relative eosinophilia (defined as an eosinophil percentage >5% but an eosinophil count <450 cells/ $\mu$ L) is significantly associated with helminth infection in recently arrived West African immigrants (odds ratio, 20.5; 95% confidence interval, 2.7–154). The main parasitic causes related to relative eosinophilia are geohelminthic diseases (specifically, hookworms) and schistosomiasis.

Absolute eosinophilia is usually defined as an increase in peripheral blood eosinophilic leukocytes to >450 cells/ $\mu$ L of blood [1]. Imported absolute eosinophilia (occurring in travelers or immigrants from tropical areas) is frequently associated with parasitic diseases (mainly helminthic diseases) [1–5]. However, the significance of relative eosinophilia is an unresolved question. Relative eosinophilia can be defined as an elevated percentage of eosinophilis (>5%) in individuals whose peripheral blood eosinophilic leukocyte count remains <450 cells/ $\mu$ L. In nontropical areas, it is usually caused by drug hypersensitivity reactions [6] or adrenal insufficiency [7]

The aim of this work was to investigate the presence of a cryptic parasitic infection in immigrants from sub-Saharan areas who had relative eosinophilia. We prospectively studied 187 asymptomatic African immigrants without absolute eosino-

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Clinical Infectious Diseases 2008;46:e48–50 © 2008 by the Infectious Diseases Society of America. All rights reserved. 1058-4838/2008/4606-00E1\$15.00 DOI: 10.1086/528865 philia who had recently arrived in Gran Canaria, Spain. Participants were classified into 2 groups according to the percentage of blood eosinophils (table 1). A defined set of demographic, clinical, and laboratory data was collected for each patient.

Written consent was obtained from all of the participants. The study was reviewed and approved by the ethical committee of the Hospital Insular de Las Palmas (Las Palmas de Gran Canaria, Spain).

Direct parasitological tests included 3 examinations of stool samples for ova and parasites using the Kato-Katz and Ritchie techniques and, in selected cases, the agar culture method [8]; microscopic examination of urine samples on terminal specimen; and Knott's test for detection of microfilaremia. The immune chromatographic test (ICT Filariasis; Binax) for the detection of *Wuchereria bancrofti* antigens, skin snips, and the Mazotti test were used in selected cases.

Serological assays were performed using ELISA. Crude extracts of adult *Dirofilaria immitis* worm [9], *Schistosoma bovis* adult worm [1], *Fasciola hepatica* excretion/secretion [10], and *Trichinella spiralis* L1 worm [11] antigens were used for detection of filariasis, schistosomiasis, fascioliasis, and trichinellosis.

Statistical tests were performed using the SPSS statistical package, version 11.5 (SPSS), and HDS Epimax Table Calculation (Health Decision Strategies). Fisher's exact test was used for evaluation of the association between demographic or laboratory data and the presence or absence of relative eosinophilia. The Student's t test was used for comparison of mean values between the 2 groups studied.

The demographic and clinical characteristics of the patients are shown in table 1. The majority of patients were male and came from sub-Saharan Africa (mainly from West Africa). All of the patients were asymptomatic during clinical evaluation.

No significant differences were found when we compared demographic data (age, sex, and geographic area) and laboratory abnormalities (except the presence of microhematuria, which was more prevalent in the relative eosinophilia group).

Thirty-nine (20.8%) of the immigrants included in the study received a diagnosis of at least 1 parasitic disease (1 patient had an eosinophil percentage <5%, and the rest of the patients had relative eosinophilia; P < .001). Thirty-one (16.5%) of the subjects with relative eosinophilia had only 1 parasite, 6 (3.2%) had 2 parasites, and 1 (0.5%) had 3 parasites. The more frequent causes of relative eosinophilia were geohelminths (accounting for 25 [54.3%] of the parasitic infections) and *Schistosoma* species (accounting for 17 [36.9%]) (table 2). No

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	Eosinophil percentage		percentage	
Variable	All subjects	≥5%	<5%	Ρ
No. of patients	187	134	53	
Age, mean years $\pm$ SD	$26.3~\pm~6.3$	$26.0~\pm~6.2$	$27.3~\pm~6.5$	.696
Male sex	87.8	87.3	90.6	.662
West African origin,	91.5	94	86	.133
Country				
Nigeria	27.7	29.1	24.5	
Ghana	19.1	17.2	24.5	
Sierra Leone	13.3	16.4	5.7	
Mali	5.9	7.5	3.8	
Cameroon	4.3	6.0	0.0	
Liberia	3.7	3.0	5.7	
Other	25.4	20.8	35.8	
Laboratory data				
Liver cytolysis	22.5	27.6	19.0	.311
Cholestasis	8.6	11.8	4.8	.243
Microhematuria	18.1	27.3	10.9	.034
Eosinophil count, mean cells/ $\mu$ L $\pm$ SD	281 ± 112.4	$334~\pm~69$	146 ± 83	<.001
Eosinophil percentage, mean value $\pm$ SD	$5.3 \pm 2.3$	$6.5\ \pm 1.3$	$2.3\ \pm 1.1$	<.001

 Table 1. Demographic and clinical data for recent West African immigrants with relative eosinophilia.

NOTE. Data are percentage of patients, unless otherwise indicated.

significant differences were found between different parasitic diagnoses. Absolute mean eosinophil counts ( $\pm$ SD) were 337  $\pm$  84 in patients with geohelminthic infection, 343  $\pm$  67 in patients with schistosomiasis, and 277  $\pm$  109 in patients with filarial infection (P = .43). Relative mean eosinophil percentages ( $\pm$ SD) were 6.1  $\pm$  1.9 in geohelminthic infection, 6.8  $\pm$  0.9 in schistosomiasis, and 6.4  $\pm$  1.8 in filarial infection (P = .54). Only 3 filarial infections were detected by serological

methods in the relative eosinophilia group. In this setting, relative eosinophilia is significantly associated with helminthic infection (OR, 20.5; 95% CI, 2–154). Positive predictive value and negative predictive value of relative eosinofilia for a parasitic infection were 28% (95% CI, 25%–29%) and 98% (95% CI, 89%–99%), respectively.

It seems well established that the presence of absolute eosinophilia in immigrants coming from tropical zones is attrib-

Table 2. Final diagnosis according to the presence of relative eosinophilia.

	No. of parasites (% of patients), by eosinophil percentage		
Parasite	≥5%	<5%	
Schistosoma species			
All	17 (12.6)	0(0)	
Schistosoma mansoni	5 (3.7)		
Schistosoma haematobium	5 (3.7)		
Schistosoma intercalatum	1 (0.7)		
Other Schistosoma species	6 (4.4)		
Hookworm	16 (11.9)	O (O)	
Trichuris trichura	6 (4.4)	0(0)	
Ascaris lumbricoides	3 (2.2)	O (O)	
Filarial species <sup>a</sup>	3 (2.2)	1 (1.9)	
Fasciola species	1 (0.7)	0(0)	
All parasitic infections	48 (28.3 <sup>b</sup> )	1 (1.9)	

<sup>a</sup> Diagnosis made by serological methods.

<sup>b</sup> Thirty-eight of 134 patients.

utable, in a high percentage of cases, to the presence of helminthic infection [1-5]. Nevertheless, the significance of relative eosinophilia (which is frequent in this population) has not been reported.

Therefore, we used the same method to evaluate the presence of parasitic infection in asymptomatic individuals without absolute eosinophilia from sub-Saharan Africa. In the group of people with relative eosinophilia, it was demonstrated that there was at least 1 helminthic infection in >20% of the population, which was a clearly significant difference from the rate for people with a normal percentage of eosinophils. Thus, we can suggest that the detection of relative eosinophilia in this population is suggestive of cryptic helminthic infection, which must be evaluated using direct and indirect methods. Our data confirm the need of evaluation of parasitic infection in immigrants, although absolute eosinophilia was not present [12].

Another point of interest of our study is the difference in the type of helminth more frequently found in subjects with relative eosinophilia (mainly geohelminths and, to a lesser extent, schistosomes), compared with the type more frequently found in subjects with absolute eosinophilia (who principally have filarial disease) [1]. It is possible that these differences are caused by the association of filariasis with greater degrees of eosinophilia [1]. Finally, some cases of relative eosinophilia could be related to other helminthic infections for which the patients were not evaluated (e.g, infection due to cestodes), although the parasitological study has been extensive.

In summary, an eosinophil percentage >5% is significantly associated with helminthic infection among a population of asymptomatic immigrants recently arrived from West Africa. The main diagnoses are geohelminthic diseases and/or schistosomiasis.

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## References

- Pardo J, Carranza C, Muro A, et al. Helminth-related eosinophilia in African immigrants, Gran Canaria. Emerg Infect Dis 2006; 12:1587–9.
- Libman MD, MacLean JD, Gyorkos TW. Screening for schistosomiasis, filariasis, and strongyloidiasis among expatriates returning from the tropics. Clin Infect Dis 1993; 17:353–9.
- Nutman TB, Ottesen EA, Ieng S, et al. Eosinophilia in Southeast Asian refugees: evaluation at a referral center. J Infect Dis 1987; 155:309–13.
- Schulte C, Krebs B, Jelinek T, Nothdurft HD, von Sonnenburg F, Loscher T. Diagnostic significance of blood eosinophilia in returning travelers. Clin Infect Dis 2002; 34:407–11.
- Seybolt LM, Christiansen D, Barnett ED. Diagnostic evaluation of newly arrived asymptomatic refugees with eosinophilia. Clin Infect Dis 2006; 42:363–7.
- Johnson DH, Cunha BA. Drug fever. Infect Dis Clin North Am 1996;10: 85–91.
- Beishuizen A, Vermes I, Hylkema BS, Haanen C. Relative eosinophilia and functional adrenal insufficiency in critically ill patients. Lancet 1999; 353:1675–6.
- Siddiqui AA, Berk SL. Diagnosis of *Strongyloides stercoralis* infection. Clin Infect Dis 2001; 33:1040–7.
- Perera L, Pérez Arellano JL, Cordero M, Simón F, Muro A. Utility of antibodies against a 22 kDa molecule of *Dirofilaria immitis* in the diagnosis of human pulmonary dirofilariosis. Trop Med Int Health 1998; 3:151–5.
- Hillyer GV, Soler de Galanes M. Identification of a 17-kDa Fasciola hepatica immunodiagnostic antigen by enzyme-linked immunoelectrotransfer blot technique. J Clin Microbiol 1988; 26:2048–53.
- Alcántara P, Correa D. Human humoral immune response against Trichinella spiralis. Int J Parasitol 1993;23:657–60.
- Caruana SR, Kelly HA, Ngeow JY, et al . Undiagnosed and potentially lethal parasite infections among immigrants and refugees in Australia. J Travel Med 2006; 13:233–9.