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The changing aetiology of eosinophilia in migrants and returning travellers in the Hospital for Tropical Diseases, London 2002—2015: An observational study

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Summary *Introduction:* Determining the cause of eosinophilia in patients returning from the tropics continues to present a diagnostic challenge. The history, symptoms and degree of eosinophilia are often poor predictors of eventual diagnosis, but helminths are an important cause. The current British Infection Association recommendations use travel history to guide investigation of eosinophilia. However the global burden of helminth disease and travel patterns have changed over the last 3 decades and guidelines based on previous epidemiology need to be reviewed in the light of current data.
Methods: Consecutive patients presenting with, or referred for, investigation of eosinophilia were identified prospectively. Case notes, laboratory results and electronic records were reviewed for demographic and clinical data. Patients with an eosinophil count $\geq 0.50 \times 10^9$/L were included, and grouped based on lifetime history of travel to: West Africa, elsewhere in Africa, and the rest of the world. Results were compared to published data from 1997 to 2002 collected at the same centre.

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Results: Of 410 patients who met the inclusion criteria, 407 had a documented travel history. Average yearly referrals for eosinophilia fell from 58 per year between 1997 and 2002, to 33 per year (2002–2015). The proportion of eosinophilia cases diagnosed with a parasitic cause fell from 64% to 50%, and yields for all parasitological investigations fell, the largest reduction in stool microscopy (20% yield to 9%) and day bloods for microfilariae (14% yield to 3%). *Strongyloides stercoralis* was the commonest diagnosis overall in our cohort, accounting for 50% of the total parasites diagnosed, and was present in 38% of patients from West Africa, 19% from rest of Africa, and 34% from rest of world; a relative increase compared to previous data. Schistosomiasis is slightly less common in those who had travelled to West Africa than the rest of Africa, and overall point prevalence has fallen from 33% (1997–2002) to 17% (2002–2015). Travellers were significantly less likely than patients who had immigrated to the UK to be diagnosed with any parasite (OR 0.54 95% CI 0.378–0.778 $p = 0.0009$).
Discussion: A parasitic cause will still be found in half of people returning from the tropics with an eosinophilia, but we observed a fall in the overall prevalence of parasitic diagnoses when compared with the earlier data. This may, in part, be explained by the impact of control programmes on the prevalence of parasites globally, especially filarial disease. *S. stercoralis* now represents the majority of parasites diagnosed in our cohort from all continents. We identified significantly higher rates of strongyloidiasis in immigrants than returning travellers. Despite the falling yields of stool microscopy and filarial serology the current guidelines based on travel history remain relevant with adequate yield.

Introduction

Determining the aetiology of eosinophilia in travellers remains a diagnostic challenge for physicians working in the field of infectious diseases and haematology. Making the correct diagnosis is important, not only to avoid wasting resources on undirected investigations and empirical therapy, but also to avoid the rare but serious sequelae that may follow a missed diagnosis of the more dangerous causes of eosinophilia, whether helminthic, or non-infectious causes such as haematological malignancy.[1] Diagnostic dilemmas may arise as history, examination and eosinophil levels are often poor predictors of underlying disease.[2–4] Whilst numerous microbiological and serological tests are available, untargeted testing is time-consuming, expensive and frustrating.[5]

Many strategies have been suggested to rationalise the approach to patients with eosinophilia, including microscopy of multiple stool samples for ova, cysts and parasites (OCP), serological screening in selected patient groups,[2,6,7] screening based on geographic area of travel[3,5,8,9] and even empirical treatment amongst refugee populations.[2,10–13]

It is important to note that many of these approaches are based on studies of unselected groups of refugees or returning travellers, and thus may not have validity for focused investigation of eosinophilia in the wider populations.

The current British Infection Association (BIA) eosinophilia recommendations 2010[14] were based in part on data collected from 261 people investigated for eosinophilia between 1997 and 2002 at our unit, a specialist hospital for tropical diseases in London.[5] These data were used to develop a system to guide investigations by geographical area of travel: West Africa, rest of Africa and the rest of the world (see Box 1). The patients included in that analysis by Whetham et al. were neither exclusively immigrants nor returned travellers, and the BIA guideline does not distinguish between the two groups within the eosinophilia investigation algorithm.

In the last 25 years, the World Health Organisation (WHO) has orchestrated mass drug administration programmes targeted at lymphatic filariasis, onchocerciasis and schistosomiasis.[15–18] It is not known whether this has altered the prevalence of parasitic causes of eosinophilia in travellers to the extent that the BIA recommendations on a geographically driven diagnostic algorithm are still relevant. Here we compare data from 2002 to 2015 with equivalent data from 1997 to 2002 to establish whether the yields of investigations and prevalence of parasitic causes identified in travellers and migrants attending our unit have changed over the past twenty years, and thus

Box 1. Guide to investigate cause of tropical eosinophilia by region of travel.

All areas: Microscopy of concentrated stool, strongyloides culture and serology.
All Africa: Additional schistosomal serology, terminal urine microscopy and filarial serology.
West Africa*: Additional day bloods for filtration and examination for microfilaria. Skin snips/Mazzoti only done if indicated by symptoms, positive filarial serology or persisting eosinophilia.
*Benin, Congo, Gabon, Ghana, Guinea, Guinea Bissau, Cote d'Ivoire, Nigeria, Togo, Burkina Faso, Gambia, Liberia, Mali, Mauritania, Equatorial Guinea, Senegal, Sierra Leone, Central African Republic, Cameroon, Niger, Chad.