The investigation of eosinophilia

Anna M Checkley

Abstract

Eosinophilia is a common problem in travellers and migrants returning from the tropics. It usually signifies an underlying helminth infection, although it is still important to bear in mind the possibility of a non-infectious cause in this group of patients.

It is frequently asymptomatic, but deserves investigation to prevent significant disease in the future. The presentation of helminth infections may differ between those who have migrated from endemic areas — who can have heavy infections with a subacute course — and travellers, in whom acute presentations are usual. Negative tests should be repeated if they were performed within 3 months of return from the tropics.

Here, we consider the most common and potentially serious causes of eosinophilia in returned travellers. The diagnosis of eosinophilia may be incidental, so we first consider when and how to investigate asymptomatic eosinophilia. We then consider the symptomatic presentation of eosinophilia, organized in syndromes that the physician is likely to encounter (fever and respiratory, gastrointestinal, genitourinary, neurological and dermatological presentations).

Keywords diagnosis; eosinophilia; filariasis; helminth; migrant; schistosomiasis; *Strongyloides*; traveller

Introduction

Eosinophilia is defined as an eosinophil count greater than 0.45×10^9/litre. It is a well-recognized feature of allergic disorders, drug reactions, connective tissue disease and malignancy (Table 1). However, in migrants and travellers returning from the tropics, eosinophilia most commonly signifies an underlying helminth infection.[1–4] This article focuses on the investigation of eosinophilia in this population; recent UK guidelines provide more detail.[5]

Which infectious agents cause eosinophilia?

Many helminths cause eosinophilia, most commonly nematodes (roundworms, e.g. *Ascaris*) and trematodes (flukes, e.g. *Schistosoma*). Eosinophilia is often greatest during the tissue migration phase of the parasite before eggs can be detected, for example, in the stool. It is often higher in travellers, many of whom have been infected recently, than in chronically infected migrants.[6,18] However, not all cases of helminth infection result in eosinophilia.

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Why, when and with what tests should we investigate asymptomatic eosinophilia?

A considerable proportion (21–33%) of travellers and migrants with eosinophilia have no symptoms.[1,3] The commonest pathogens identified in this group are intestinal helminths, schistosomes, *Strongyloides* and *Filaria*.[1] Schistosomiasis and strongyloidiasis can have serious consequences so it is important to investigate eosinophilia in returning travellers and migrants, even if it is asymptomatic. Investigations performed in early infection can be negative. It usually takes several weeks before eggs appear in stool, urine or sputum samples, and serological tests become positive after 4–12 weeks. It is therefore recommended that initially negative investigations be repeated at 3 months. Moreover, serological tests often cross-react, especially in *Strongyloides* and filarial infections. Expert advice should therefore be sought when the diagnosis is not clear (Box 1).

Helminth distribution varies, with some species having widespread distribution (e.g. *Ascaris*) and some very focal (e.g. *Loa loa*). In addition, certain activities may predispose individuals to infection. A detailed travel history should therefore be taken, including the regions visited and exact timings of possible exposures, such as swimming in fresh water lakes in Africa, walking barefoot, and drinking water and foods consumed (e.g. salads, raw fish).

Investigations should be based on the geographical area visited.[5] All patients returning from the tropics should have concentrated stool microscopy and *Strongyloides* serology, and *Strongyloides* stool culture, and an HIV test should also be considered. Concentrated stool microscopy, available in all hospital microbiology departments, identifies most soil-transmitted helminths (*Ascaris lumbricoides*, *Trichuris trichiura*, hookworm sp.) but has a low sensitivity in detecting *Strongyloides*. Other screening investigations vary depending on the region visited. Terminal urine microscopy (for ova) and serology for schistosomiasis should be performed in those returning from Africa. The filarial parasites, *L. loa*, *Onchocerca volvulus* and *Wuchereria bancrofti*, are relatively common in West Africa, so filarial serology should additionally be requested. Figure 1 shows a flow chart outlining the investigation of asymptomatic eosinophilia. Note that some of the drugs used to treat helminth infections are not licensed in the UK and other non-endemic countries, and may need to be obtained from specialist centres.

What clinical syndromes can accompany eosinophilia? How should they be managed?

Fever and/or respiratory symptoms

Katayama syndrome: this occurs during acute schistosomiasis infection. It comprises fever and high-grade eosinophilia ($>5 \times 10^9$/litre), dry cough, urticarial rash and, sometimes, pulmonary infiltrates on chest radiograph.[7] Serology, and stool and terminal urine microscopy are often negative during this early stage of infection. When this presentation is accompanied by a history of fresh water exposure in Africa, empirical treatment should comprise praziquantel 40 mg/kg (single dose) and oral prednisolone 20 mg/day for 5 days. Praziquantel is relatively ineffective against immature stages of schistosomiasis, so treatment should be repeated at 6–8 weeks. Swimmer's itch and a papular pruritic

Non-infectious causes of peripheral eosinophilia

Atopy	Haematological	Vasculitis	Dermatological	Drug	Other
Asthma	Hodgkin's and non-Hodgkin's lymphoma	Eosinophilic granulomatosis with polyangiitis (Churg—Strauss syndrome)	Immunobullous disorders: dermatitis herpetiformis and pemphigoid	NSAIDs	Allergic bronchopulmonary aspergillosis
Eczema	Chronic eosinophilic leukaemia	Polyarteritis nodosa	Atopic dermatitis	β-Lactam antibiotics	Sarcoidosis
Hay fever	Systemic mastocytosis	Granulomatosis with polyangiitis (Wegener's granulomatosis)		Sulpha-containing antibiotics	Addison's disease
	Chronic myelomonocytic leukaemia	Other connective tissue diseases and vasculitides		Tetracycline	Eosinophilic myocarditis
	Chronic myeloid leukaemia			Acetylsalicylic acid	Familial eosinophilic syndromes
	Acute myeloid leukaemia			Carbamazepine	Heavy metal poisoning
	Myelodysplastic syndrome			Colchicine	Idiopathic eosinophilic pneumonias
				Nitrofurantoin	
				Dapsone	
				Minocycline	

NSAIDs, non-steroidal anti-inflammatory drugs.
From Checkley AM et al. Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management. *J Infection* 2010; **60**:1—20. Reproduced with permission.

Table 1

eruption may also occur immediately following cercarial penetration of the skin.

Loeffler's syndrome: this is caused by larvae of helminths such as *Ascaris*, hookworm and *Strongyloides* migrating through the lungs during acute infection. It presents similarly to Katayama syndrome, with fever, urticaria, wheeze, dry cough and eosinophilia. Migratory pulmonary infiltrates are sometimes seen on the chest radiograph. Diagnosis is clinical as symptoms occur before eggs can be detected in the stool. Albendazole 400 mg/day for 3 days is recommended.

Paragonimiasis: this is most commonly caused by the lung fluke *Paragonimus westermani*, and South East Asia accounts for 90% of imported cases. It is acquired by eating raw fresh water crab and crayfish. Abdominal pain, diarrhoea and urticaria are followed by pleuritic chest pain, eosinophilic pleural effusions, then chronic cough with haemoptysis.[8]

Diagnosis is clinical, and may be confirmed by sputum microscopy and serology. Chest radiograph may show pleural effusions, consolidation or cavitation. Treatment is with praziquantel 25 mg/kg three times daily for 2 days or triclabendazole 10 mg/kg/day for 3 days.

Gastrointestinal/genitourinary symptoms

Strongyloidiasis: this is widely distributed throughout the tropics, and is an important infection to diagnose. It is transmitted when larvae penetrate the skin of humans walking barefoot. Non-specific gastrointestinal symptoms include diarrhoea and abdominal bloating, but it may also present with the pathognomonic larva currens, a transient, itchy, urticarial rash that typically moves by 1—10 cm/hour. It is profoundly itchy and usually seen in the perianal area and upper thighs (13). (Figure 2). In immunocompromised individuals (particularly those taking corticosteroids, undergoing chemotherapy, with leukaemia or T cell lymphoma, or with human T-lymphotropic virus type 1 (HTLV1)

Reference facilities[5]

Laboratories in the UK offering specialist parasitological diagnostic tests, and specialist tropical disease units in the UK providing telephone advice on clinical management.

Public Health England Fever Service.
Specialist service for the diagnosis of acute fevers due to travel-related infections.
Tel.: +44 (0) 844 778 8990.
http://www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1317133839448

Hospital for Tropical Diseases, London, UK.
Capper Street, off Tottenham Court Road, London WC1E 6JB, UK.
www.thehtd.org

Department of Clinical Parasitology (Public Health England (PHE) Parasitology Reference Laboratory).
Tel.: +44 (0) 020 3456 7890 ext 75413 (Serology) ext 75414 (Microscopy).
Fax: +44 (0) 20 7383 0041.

Clinical management.
Tel.: +44 (0) 845 155 5000 (24 h; ask for on call tropical/ID physician, bleep 5845).

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Diagnostic Parasitology Laboratory.
Tel.: +44 (0)151 705 3220.
http://www.liv.ac.uk/lstm/travel_health_services/diagnos_lab.htm

Clinical management.
Tel.: +44 (0) 151 705 3100 (0900—1700 h)
Tel.: +44 (0) 151 706 2000 (24 h; ask for tropical/ID physician on call).
Fax: +44 (0) 151 708 8733 or +44 (0) 151 705 3368.
http://www.liv.ac.uk/lstm/