# The investigation of eosinophilia

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## 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 can differ between individuals 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 can 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; MRCP; schistosomiasis; *Strongyloides*; traveller

## Key points

- Helminth infection is the most common cause of eosinophilia worldwide
- Up to 33% of travellers and migrants with eosinophilia are asymptomatic. Investigations should be based upon the geographical areas the patient has visited
- Investigation of eosinophilic patients should be carried out or repeated at 3 months to increase serological diagnosis and detection of ova
- It is strongly advised to seek specialist advice on appropriate diagnostic tests and medications that are often not available in routine healthcare settings
- If a tropical cause for the eosinophilia cannot be found despite thorough testing, ensure that non-helminth causes are explored

## Introduction

Eosinophilia is defined as an eosinophil count $>0.45 \times 10^9$/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 commonly signifies an underlying helminth infection.[1] This article focuses on the investigation of eosinophilia in this population; UK guidelines provide more detail.[2]

## Which infectious agents cause eosinophilia?

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

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

Investigations should be based on the geographical area visited.[2] All patients returning from the tropics should have concentrated stool microscopy and *Strongyloides* serology, *Strongyloides* stool culture and an HIV test. Concentrated stool microscopy, available in all hospital microbiology departments, identifies most soil-transmitted helminths (*Ascaris lumbricoides*, *Trichuris trichiura*, hookworm spp.) but has low sensitivity in detecting *Strongyloides*.

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## Reference facilities

### 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, Imported Fever Service** (specialist service for the diagnosis of acute fevers caused by travel-related infections)
  Tel: +44 (0) 844 778 8990
  www.gov.uk/guidance/imported-fever-service-ifs
- **Hospital for Tropical Diseases,** Mortimer Market, Capper Street, London WC1E 6JB, UK
  www.thehtd.org

  *Department of Clinical Parasitology (Public Health England (PHE) Parasitology Reference Laboratory):*
  Tel: +44 (0) 20 3447 5418
  Fax: +44 (0) 20 7383 0041

  *Clinical management:*
  Tel: +44 (0) 203 456 7890 (24 hours; ask for on call tropical/infectious diseases physician)
- **Liverpool School of Tropical Medicine,** Pembroke Place, Liverpool L3 5QA, UK

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

  *Clinical management:*
  Tel: +44 (0) 151 705 3100 (09:00–17:00 hours)
  Tel: +44 (0) 151 706 2000 (24 hours; ask for on-call tropical/infectious diseases physician)
  Fax: +44 (0) 151 708 8733 or +44 (0) 151 705 3368
  www.lstmed.ac.uk/services/tropical-medicine-services-forhealth-professionals
- **Scottish Parasite Diagnostic & Reference Laboratory (SPDL),** Level 5, New Lister Building, 10–16 Alexandra Parade, Royal Infirmary, Glasgow G4 0SF, UK
  Tel: +44 (0) 141 201 8667
  www.nhsggc.org.uk/about-us/professional-support-sites/microbiology/scottish-microbiology-reference-laboratories/scottishparasite-diagnostic-reference-laboratory/
- **Mycology Reference Laboratory,** Southwest HPA Laboratory, Myrtle Road, Kingsdown, Bristol BS2 8EL, UK
  Tel: +44 (0) 117 342 5028
  Fax: +44 (0) 117 922 6611
  www.gov.uk/government/collections/mycology-referencelaboratory-mrl

### Other information sources:

- **Public Health England (PHE)** (previously Health Protection Agency)
  www.hpa.org.uk
- **Centers for Disease Control and Prevention (CDC)**
  www.cdc.gov
- **National Travel Health Network and Centre (NaTHNaC)**
  nathnac.net/
- **ProMED, International Society for Infectious Diseases (ISID)**
  www.promedmail.org/pls/otn/f?pZ2400:1000
- **Fever Travel** (comprehensive information on disease distribution by individual country)
  www.fevertravel.ch
- **Geosentinel** (worldwide and European surveillance data on imported infections)
  www.istm.org/geosentinel
- **TropNet Europe** (worldwide and European surveillance data on imported infections)
  www.tropnet.net/

Adapted from Checkley AM et al. Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management. *J Infect* 2010; **60**: 1–20.

**Box 1**

Other screening investigations vary depending on the region visited. Terminal urine microscopy (for ova) and serology for schistosomiasis should be performed in individuals returning from Africa. The filarial parasites *Loa loa*, *Onchocerca volvulus* and *Wuchereria bancrofti* are relatively common in West Africa, so filarial serology should additionally be requested. Day and night blood samples have previously been recommended as a first-line investigation in individuals returning from West Africa.[2] Given the global decrease in cases of filariasis and resultant decrease in imported cases to the UK, we recommend that these tests are reserved for individuals with suggestive symptoms or continuing eosinophilia only.

Figure 1 outlines 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, and 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 × $10^9$/litre), dry cough, urticarial rash and sometimes hepatosplenomegaly or pulmonary infiltrates on chest radiography. Serology and stool and terminal urine microscopy are often negative during this early stage. When this presentation is accompanied by a history of freshwater 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 eruption can also occur immediately following cercarial penetration of the skin.




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