And eosinophilia after a stay in the tropics?

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Should we investigate?

- Diagnosis of tropical conditions causing eosinophilia is important:
  - Almost all helminths can occasionally cause serious pathology
  - Almost all helminths are easily treated

- Untargeted investigation can be
  - Time consuming
  - Frustrating for physician & patient
  - Expensive

Should we investigate?

- Wide variety of causes:
  - Allergic illness
  - Skin diseases
  - Malignant conditions
  - Hematological disorders
  - Medication use
  - Parasitic infection
  - …
How to investigate?

- Identifying / ruling out as many important diagnoses on the 1st occasion
- Taking account of the prevalence of helminth infections in area of travel

How to define eosinophilia

- Normal subjects < 350/mL (1-3%)
- Daytime fluctuation (cortisol) up to 40%
- Absolute more reliable than percentage
- Degree of eosinophilia:
  - Mild: up to 1500/mL
  - Moderate: 1500-5000/mL
  - Severe > 5000/mL

Common finding?

- 5% of travellers returning from tropics?
- 8%-10% in asymptomatic returning travellers
- Related to destination:
  - 48% from Africa vs 31% of all destinations
  - highest RR 2.95 for West- and central-Africa
  - Lowest RR for Indian subcontinent and Latin America
Eosinophilia ≠ helminth

- 36% definite diagnosis (19% helminth)
- PPV 14% for helminth infection
- Up to 39% ?
- Diagnostic value of eosinophilia alone is limited

Symptoms

- Asymptomatic 21-30%
- Gastro-intestinal symptoms 27%
- Skin related symptoms 15%
- Fatigue, non-specific symptoms 37%
- Difference between traveller & immigrant:
  - Up to 80% have asymptomatic intestinal helminths

Travel history

- "Unde venis?"
- When did you travel, how long, when did you return?
- What did you do?
- Exposure:
  - Drinking untreated water / unpasteurised milk
  - Undercooked fish or meat
  - 'Fresh water' swimming
  - Bare foot walking
  - Contact with locals?
- Symptoms in other travellers?
Timing

- Eosinophilia may be transient
  - Tissue migration phase
  - Prepatent period: no ova detectable
- Serological tests: 4-12 weeks after infection
  - Sometimes cross-reaction between tests

Investigating asymptomatic eosinophilia

- Common causes: intestinal helminths, schistosomiasis, strongyloides and filaria
- All travellers: (concentrated) stool examination, strongyloides serology
- Returning from Africa: + serology schisto and filaria, and urine analysis for ova Schistosoma haematobium
- Returning from West Africa: + serology filaria, (day-night) blood exam for filaria, skin snips (sero+)

Investigating asymptomatic eosinophilia

- Checkley A. et al. Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management. J Infect 2010;60,1-20

Eosinophilia with symptoms

- Fever
  - Katayama
  - Loeffler's
  - Visceral larva migrans
  - Tropical pulmonary eosinophilia

- GI symptoms
  - Ascariasis
  - Strongyloides
  - Bilharzia
  - Trichuris T.
  - Trichinella sp.
  - Anisakiasis
  - Fascioliasis
  - ... 

- Skin
  - Filariasis
  - Gnatostomiasis
  - Larva migrans
  - Larva currens

- Other
  - Paragonimiasis
  - S. Haematobium

Eosinophilia with fever

- Katayama fever – Schistosoma sp.
  - Incubation 2-9 weeks
  - Africa
  - Fresh water exposure: cercaria penetrate skin
  - Severe eosinophilia, fever, dry cough, urticarial rash
  - Low sensitivity of stool/urine exam and serology
  - Corticosteroids + praziquantel 40 mg/kg (repeat)

- Loeffler's syndrome:
  - Migration of larval stadia of nematodes
  - Ascaris L., strongyloides, hookworms
  - Incubation 1-2 weeks
  - Fever, urticaria, wheezes, dry cough
  - Clinical diagnosis, migratory infiltrates on XR
  - Charcot-Leyden crystal
  - Albendazole 400 mg bd 3 days


Checkley A. et al. Eosinophilia in returning travellers and migrants from the tropics: UK recommendations for investigation and initial management. [Infect 2010;60,1-20](https://www.ncbi.nlm.nih.gov/pubmed/20206525)
**Eosinophilia with fever**

- **Visceral larva migrans – acute toxocariasis**
  - Worldwide
  - Ingestion soil contaminated eggs *T. Canis T. catis*
  - Mostly children
  - Often asymptomatic, fever, wheezes, cough
  - Abdominal pain, HSM, urticarial rash
  - Serology
  - Albendazole 400 mg, steroids, antihistamine

- **Tropical pulmonary eosinophilia – *W. Bancrofti / B. Malayi***
  - Hypersensitivity reaction < lymphatic filarial worms
  - Fever, dry cough, dyspnea, wheezes
  - Severe eosinophilia, IgE, chest XR, PFT
  - Serology +, blood microscopy –
  - DiEthylCarbamazine ± steroids
  - Delayed or incomplete treatment : lymphatic damage and fibrosis

**Eosinophilia with GI-symptoms**

- **Ascariasis – *Ascaris lumbricoides***
  - World-wide, faeco-oral transmission
  - Pre-patent period 2-3 months
  - May present acutely: Loeffler’s syndrome
  - Asymptomatic, vague abdominal pain, diarrhea
  - Obstruction (children), biliary obstruction
  - Concentrated stool exam
  - Albendazole 400 mg once (or mebendazole 100mg bd 3days)
Eosinophilia with GI-symptoms

- Strongyloides - *Strongyloides stercoralis*
  - Incubation period: days to weeks for larva currens (or Loeffler’s syndrome), 2 weeks later vague abdominal symptoms (diarrhea, bloating)
  - Serology! Low sensitivity of stool samples
  - Ivermectin 200μg/kg once

- Hyperinfection syndrome:
  - Paralytic ileus, G-sepsis (<translocation across bowel wall)
  - Often pulmonary involvement (larva ++ sputum and stools)
  - Low or absence of eosinophilia!
  - Associated with steroids, chemo/malignancy, HTLV-I
  - Broad-spectrum AB, ivermectin IV (duration?)

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Eosinophilia with GI-symptoms

- Bilharzia – *Schistosoma mansoni (japonicum)*
  - *S.Mansoni*: Africa, Arabian peninsula, S-America
  - *S.Japonicum*: China, Indonesia, Phillippines
  - Swimmer’s itch, Katayama fever
  - Abdominal pain, diarrhea (heavy infection, dysentery)
  - Serology (4-8 wks), stool exam (low sensitivity)
  - Praziquantel 40mg/kg single dose

- Chronic infection: HSM, fibrosis, portal HT, esophageal varices (endoscopy, ultrasound)

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Eosinophilia with GI-symptoms

- Whipworm - *Trichuris trichiura*
  - Worldwide, faeco-oral transmission
  - Prepatent period: 4-12 weeks
  - Usually asymptomatic
  - Heavy infestation in children: anemia, dysentery or rectal prolapse
  - Mebendazole 100mg bd (albendazole 400-800 mg bd) 3days

- Pin worm – *Enterobius vermicularis*
  - Worldwide, faeco-oral transmission
  - Pruritis ani, occasionally colitis with eosinophilia
  - "sellotape test"
  - Albendazole 400 mg (mebendazole 100 mg) single dose
**Eosinophilia with GI-symptoms**

- **Trichinellosis – *Trichinella sp.***
  - Consumption of raw (undercooked) meat; outbreaks
  - Worldwide (Eastern Europe, Russia, Argentina, China)
  - Incubation: 7-10 days (enteral phase), 2-6 weeks (parenteral)
  - Enteral phase: abdominal pain, N+V+D+, fever
  - Parenteral phase: myalgia, weakness.
  - Respiratory failure, facial/periorbital edema, conjunctivitis, rash
  - Severe presentation: meningo-encephalitis, myocarditis
  - Creatinine kinase levels ↑, severe eosinophilia
  - Serology, muscle biopsy
  - Albendazole 400 mg 3 days
  - 14 days severe disease (with prednisolone)

- **Anisakiasis – *Anisakis* spp.**
  - Worldwide (consumption raw/pickled seafood)
  - Incubation 2-5 hours
  - Acute severe abdominal pain, N+V+
  - Rarely anaphylaxis
  - Diagnosis usually at endoscopy, serology
  - Endoscopic (surgical) removal (or albendazole 400 mg)

- **Fasciola hepatica / *F. gigantica***
  - Worldwide (Middle East, SE Asia, Eastern Europe)
  - Consumption of contaminated vegetation (intermediate encysted metacercaria) e.g. watercress
  - Incubation 3-12 weeks, prepatent period 3-4 months
  - Acute phase: (month 3-5) fever, hepatomegaly with pain
  - Chronic phase: biliary obstruction, cholecystitis, abscess (50% asymptomatic)
  - Diagnosis:
    - Acute phase: clinical, serology confirms later.
    - Chronic phase: serology, (stool microscopy), imaging (US or CT)
  - Triclabendazole 10 mg/kg single dose
Eosinophilia with GI-symptoms

- Other causes:
  - Protozoa: Isospora bella, Dientamoeba fragilis, Toxoplasmosis
  - Tapeworm: Taenia saginata / T. Solium (cysticercosis)
  - Dwarf tapeworm: Hymenolepis nana
  - Hookworms: Ankylostoma braziliensis, Necator americanus
  - Hydatid disease: Echinococcus granulosis, E. multilocularis
  - Angiostrongylus costaricensis
  - Liver flukes: clonorchis sinensis, Opisthorchis sp.

Eosinophilia with skin/musculoskeletal symptoms

- Cutaneous larva migrans
  - Characteristic migratory rash
  - Ivermectin 200 μg/kg (or albendazole 400 mg od 3 days)
- Larva currens – Strongyloides stercoralis
  - Itchy, linear, urticarial rash
  - Usually trunk, upper legs, and buttocks
- Trichinellosis – Trichinella spiralis
  - 2nd 'parenteral' phase: facial, periorbital edema, urticarial rash, myalgia
- Schistosomiasis: 'swimmer’s itch
  - Itchy maculo-papular rash
  - Often caused by schistosoma spp. of birds

Eosinophilia with skin/musculoskeletal symptoms

- Onchocerciasis – *onchocerca volvulus*
  - Near rivers, predominantly Africa
  - Incubation 8-20 months
  - Diffuse pruritic dermatitis (legs and buttocks)
  - 'leopard skin' in chronic cases
  - Anterior chamber eye: keratitis, uveitis, choroidoretinitis
  - Serology: skin snips, slip lamp exam
  - Ivermectin 200 μg/kg repeated for months
Eosinophilia with skin/musculoskeletal symptoms

- **Lymphatic filariasis –** *W. bancrofti, B. malayi*
  - Incubation period: 1 to 16 months
  - *W. bancrofti*: worldwide tropical, *B. malayi*: mainly Asia
  - Fever, lymphadenitis, lymphoedema
  - Non-immune travellers: fever, respiratory symptoms
  - Serology, microscopy ‘night’ blood (midnight)
  - DiEthylCarbamazine, limb care

- **Eosinophilia with skin/musculoskeletal symptoms**

- **Loiasis –** *Loa Loa*
  - Incubation 6 months to 6 years
  - West and Central Africa
  - Migratory ‘calabar’ soft tissue swelling of limbs
  - 10-20% cases: migrating worm across conjunctiva
  - Serology, ‘day’ blood microscopy
  - DiEthylCarbamazine

- **Gnathostomiasis –** *Gnathostoma spinigerum*
  - Incubation only 3-7 days
  - SE Asia, usually outbreaks
  - Eating undercooked fish, chicken (frog, snake)
  - Intermittent subcutaneous swelling, pruritus
  - Occasionally eosinophilic meningitis, myelitis
  - Clinical diagnosis, serology
  - Albendazole 400 mg bd 3 weeks

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Ottesen EA Lymphatic filariasis: treatment, control and elimination; *Adv Parasitol* 2006;61:395-441


Eosinophilia with urinary symptoms

- **Bilharzia – Schistosoma haematobium**
  - Africa (great lakes, Malawi, Victoria, Okavango)
  - Hematuria (micro/macro), dysuria, hematospermia
  - Serology, urine analysis
  - Praziquantel 40 mg/kg once
  - Long term complications: squamous cell bladder Ca, obstructive uropathy

Eosinophilia with pulmonary symptoms

- **Paragonimiasis – Paragonimus sp.**
  - Most cases SE Asia
  - Ingestion raw crab or crayfish
  - Abdominal pain, diarrhea, urticaria
  - Pleuritic chest pain, pleural effusions, chronic cough, hemoptysis
  - Chest XR, Sputum analysis, serology
  - Praziquantel 25 mg tds (2 days)

Take home messages

- Eosinophilia is common in returning travellers
- Always investigate eosinophilia in a returning traveller
- Wide variety of causes
- Diagnostic value of eosinophilia alone has limited value
Take home messages

- About 1/3 asymptomatic
- Degree of eosinophilia
- Travel history!

In all travellers stool exam,

strongyloides serology

Africa: include schisto/filarial serology

West & Central Africa
- Also include blood exam for microfilaria

Investigate
- Symptoms
- Region of travel and prevalence of helminths