

## Eosinophilia in asymptomatic returned travellers

J.S. Keystone MD TDU TG Hospital  
E C. Keystone MD RDU Mt.Sinai Hospital




---

---

---

---

---

---

---

---

---

---

## The Eosinophil Biology

- A tissue cell that hangs out in the blood:  
1 blood cell per 400 tissue cells
- Found at interface of body with environment: GIT, skin and lungs
- Diurnal variation: highest in am before endogenous steroids kick in
- Can vary by 100% from day to day
- Pyogenic infections → eosinopenia

---

---

---

---

---

---

---

---

---

---

## What do eosinophils do anyway?

Beneficial	Pathological
<p><b>Parasitic infection</b> (No direct evidence of their involvement on parasitic burden using <math>\alpha</math>dbl-GATA-1 and PHIL)</p> <p><b>Viral infection</b> (Ribonuclease effective on RNA virus such as RSV, PVM)</p> <p><b>Fungal infection</b> (Beta 2 integrin adhere to the fungal wall component <math>\beta</math>-glucan)</p> <p><b>Bacterial infection</b> (Mitochondrial DNA traps containing granule proteins in peritonitis have antimicrobial activity)</p>	<p><b>Allergy</b> Airway hyperactivity (PHIL and <math>\alpha</math>dbl-GATA-1 C57/Bu6) Mucus production (PHIL and <math>\alpha</math>dbl-GATA-1) Th2 cytokine production (PHIL and <math>\alpha</math>dbl-GATA-1) Collagen deposition (<math>\alpha</math>dbl-GATA-1 BALB/c)</p> <p><b>EGID</b> Possibly involved in tissue damage</p> <p><b>HES</b> Involved in tissue damage</p>

---

---

---

---

---

---

---

---

---

---

## Ask yourself 5 questions

1. Is there absolute eosinophilia?
2. Is the eosinophilia related to the symptoms?
3. Is the eosinophilia travel-related?
4. How do I investigate travel-related causes?
5. What if I can't find a cause?

4

---

---

---

---

---

---

---

## Non infectious causes of eosinophilia

- **Hereditary**
- **Vascular :** 1. CVD: Churg Strauss
  - 2. Hematologic:
  - HES ,Eos.gastroent.
- **Infammatory:** IBD, sarcoid
- **Metabolic:** Addisons

5

---

---

---

---

---

---

---

## Non infectious causes of eosinophilia con't

- **Neoplastic:** myelogenous leukemia,
  - lymphoma ,adenocarcinoma
- **Allergic:** drugs, asthma, atopy
- **Dermatologic:** pemphigoid,
  - pemphigus, Dermatitis herpetiformis
- **Miscellaneous:** cholesterol embolism
  - irradiation, Kimuras disease

6

---

---

---

---

---

---

---

## Infectious Causes of Eosinophilia

- **Parasitic:**
  - 1. Helminths:
    - a. roundworms, flukes, tapeworms
    - b. scabies, lice
  - 2. Protozoa: D. fragilis, isospora, toxoplasmosis
- **Non-parasitic:** coccidiomycosis, TB, HIV

7

---

---

---

---

---

---

---

---

## Helminth eosinophilia determinations

- Developmental stage
- Migration pattern
- Distribution in host
- Host immune response
- Highest in tissue migrators
- Lowest in lumen dwellers & cystic parasites

8

---

---

---

---

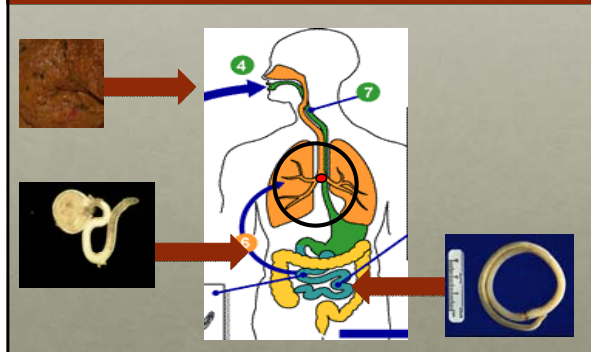
---

---

---

---

## Ascaris internal cycle



---

---

---

---

---

---

---

---

## Helminths and Eosinophilia ...or not!

<ul style="list-style-type: none"> <li>• <b>Tissue migrators</b></li> <li>• Filaria</li> <li>• Toxocariasis</li> <li>• Trichinosis</li> <li>• Strongyloides</li> <li>• Schistosomiasis</li> </ul>	<ul style="list-style-type: none"> <li><b>Non-migrators</b></li> <li>• Adult Ascariasis</li> <li>• Enterobiasis</li> <li>• Adult tapeworms</li> <li>• Clonorchiasis</li> </ul>
---	--

10

---

---

---

---

---

---

---

---

## Predictive value of eosinophilia for travel-related infections?

Diagnostic Significance of Blood Eosinophilia in Returning Travelers

C. Schulte, B. Krebs, T. Jelenc, H. D. Nethdardt, F. von Sonnenberg, and T. Löscher  
Department of Infectious Diseases and Tropical Medicine, University of Munich, Germany  
CID 2002;34:407

This study was conducted to investigate the predictive value of eosinophilia in returning travelers. The degree of eosinophilia in patients with helminthic infections may vary according to distribution, migration, maturation, and burden of the parasite. Various studies have showed different correlations between blood eosinophilia and multicellular pathogenic infections [6-8].

4.8% had eosinophilia

Patients with a blood eosinophil count of >500 eosinophils per mm<sup>3</sup> or blood or as a Vanc. count in which >7% of the WBCs were eosinophils. Examination of samples of fresh stool, urine, blood smear, wounds, and skin defects was performed for detection of any parasites.

---

---

---

---

---

---

---

---

## Etiology of Eosinophilia in screened ret.travelers N=14,298

Disease	N=248	No. of patients	Mean eosinophil count	
			Percentage of WBCs	Eosinophils/ μL of blood
Helminth infection		130	17.8	1545
Hookworm		18	22.9	3063
PPV for helminthiasis= 18.9%				
NPV = 98.7%				
Cutaneous larva		17	12.5	924
Echinococcosis		2	12.5	717
Trichuriasis		4	11.5	874
Enterobiasis		2	10.5	570

---

---

---

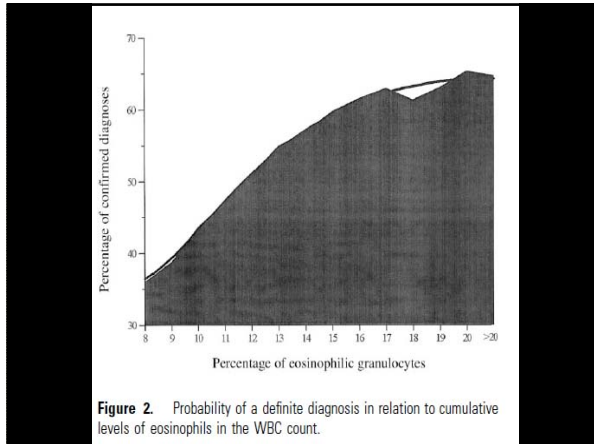
---

---

---

---

---




---

---

---

---

---

---

---

---

---

---

**Predictive value of eosinophilia for travel-related infections?**

**Screening for Schistosomiasis, Filariasis, and Strongyloidiasis Among Expatriates Returning from the Tropics**

Michael D. Libman, J. Dick MacLean, and Theresa W. Gyorkos

*From McGill University Centre for Tropical Diseases and the Division of Clinical Epidemiology, Montreal General Hospital, the Department of Microbiology, St. Mary's Hospital Centre, and the Department of Epidemiology and Biostatistics, McGill University, Montreal, Quebec, Canada*

**CID 1993;17:353**

*The clinical utility of eosinophil determinations, stool examinations, and serological studies*

---

**1981-87:1605 travellers screened**  
**Sensitivity of eosinophilia to Dx schistosomiasis, filariasis and strongyloidiasis = 38%**  
**PPV for any helminthic infection = 9%**

... would have picked up only 61% of our cases. In this population, eosinophil counts contribute little to the diagnostic accuracy obtained with stool examination and serological screening, and the low specificity of eosinophil counts generates high costs.

---

---

---

---

---

---

---

---

---

---

**Epidemiology is everything!**

- barefoot                hook, strongyloides
- fresh water            schistosomiasis
- prolonged stay        filariasis
- raw meat                trichinosis
- raw crayfish            paragonimiasis
- raw water cress        fascioliasis

15

---

---

---

---

---

---

---

---

---

---



## Diagnosing Tropical Eosinophilia

- History:** exposure, atopy, drugs
- Physical examination**
- Laboratory tests:**
  - Repeat CBC if borderline value
  - Stools ova & parasites x 3 alternate days
  - Serology prn: strongyloidiasis, filariasis, schistosomiasis etc.
  - Other: skin snips, urines O&P, agar plate

18



### Agar plate culture for strongyloidiasis




---

---

---

---

---

---

---

---

### Serologic diagnosis of selected helminthiases: "The Big 3"

Infection	Serology	
	sensitivity	specificity
Strongyloidiasis <small>(CDC)</small>	93	98
Schistosomiasis <small>(CDC)</small>	99 90	95
Filariasis (IgG4) <small>(NIH)</small>	96	100

---

---

---

---

---

---

---

---

### Eosinophilia diagnostic and therapeutic principles

- May occur in pre-patent period
- May increase with treatment
- May last for many weeks after treatment



Wait

---

---

---

---

---

---

---

---

## Oh Oh!...What to do if no cause is found? Do eosinophils kill?

- Repeat work up 3-6 months later
- Do nothing.
- Consider trial of therapy:
  - -albendazole 400 mg bid x 1 week
  - -ivermectin 200 ug/kg x 2 ds.

22

---

---

---

---

---

---

---

---

## What if we leave an untreated helminth infection behind?

- **Principles of helminth parasite pathogenesis**
  - 1. With one exception, parasites do *not* multiply in the human host
  - 2. Worm burden  $\alpha$  the degree of tissue damage which in turn is  $\alpha$  to severity of disease
- ↓
- Light worm burdens rarely cause human disease and often do not require treatment (unless they are in a bad location)

23

---

---

---

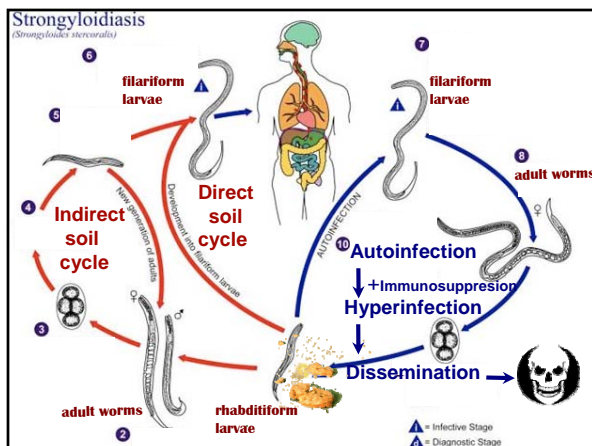
---

---

---

---

---




---

---

---

---

---

---

---

---



## Strongyloidiasis

- **Distribution:** global
- **Clinical:** asymptomatic mostly
  - symptomatic: epigastric pain, (cough), rash, urticaria
- **Diagnosis:** eosinophilia >70%
  - stools O&P : 30-50%
  - concentration techniques 60-70%
  - agar plate culture: 85%
  - serology: >90%
- **Treatment:** ivermectin  $\Rightarrow$ 95% ; albendazole: 85%

---

---

---

---

---

---

---

---

## What is the test of cure?

- Eosinophilia resolves within 2-3 months
- No larvae in the stool after 3 weeks
- Agar plate culture negative after 3 weeks
- Antibody levels reduce by 50 % in ~ 9-12 months

26

---

---

---

---

---

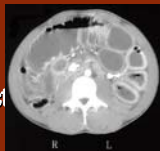
---

---

---



**Strongyloides hyperinfection  
dissemination**



# Immunosuppression HTLV-1

[No eosinophilia]

---

---

---

---

---

---

---

---

## Why HTLV1 & Disseminated strongyloidiasis?

- **High levels of gamma interferon:**
  - → decreased production levels of IL-4, IL-5, IL-13 and IgE
- **Increased levels of regulatory T-cells:**
  - → low eosinophil counts and ↓ antigen driven IL-5 production

• Parasite Immunol 2004; 26:487; PLoS Negl Trop Dis 2009; 3:e456.

---

---

---

---

---

---

---

---

## Whom to screen for strongyloidiasis?

- **Those from endemic areas and exposed travelers**
- Eosinophilia
- Compatible clinical history
- Immunosuppression (incl. HTLV1): prior to if possible and during if not .....even asymptomatic
- Unexplained Gram neg bacteremia

---

---

---

---

---

---

---

---

## Take home points

- Is the eosinophilia related to travel or symptoms?
- Consider tropical and non-tropical causes
- Travel-related eosinophilia low PPV/NPV but is helminthiasis until proven otherwise
- Eosinophilia is stage dependent in some and often resolves over time in others

---

---

---

---

---

---

---

---

## Take home points

- Investigations depend on travel and exposure history
- Early Dx not possible in some because of long-prepatent period
- Persistent eosinophilia may be due to strongyloidiasis : consider presumptive treatment

31

---

---

---

---

---

---

---

---

## Take home points

- Cryptic eosinophilia in a patient from an endemic area + imminent immunosuppression ~~strongyloides~~ serology & treat with ivermectin
- An immunocompromised patient from an endemic area with GI, pulmonary and gram neg. sepsis/meningitis disseminated ~~strongy.~~

32

---

---

---

---

---

---

---

---

## Da Bottom Line!

- Eosinophilia from the tropics is an helminth infection ...and strongyloidiasis until proven otherwise!

33

---

---

---

---

---

---

---

---

## References

- Nutman T. Eosinophilia in the returning traveller  
Infectious Disease Clinics of North America  
1998;2:504-21
- Meltzer, E. Eosinophilia Among Returning  
Travelers: A Practical Approach Am. J. Trop. Med.  
Hyg., 2008 78:702–709
- Seybolt LM ,Diagnostic Evaluation of Newly  
Arrived Asymptomatic Refugees with Eosinophilia  
Clinical Infectious Diseases 2006; 42:363–7

---

---

---

---

---

---

---

---