Eosinophilia in asymptomatic returned travellers
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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?

<table>
<thead>
<tr>
<th>Beneficial</th>
<th>Pathological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parasitic infection</td>
<td>Allergy</td>
</tr>
<tr>
<td>Viral infection</td>
<td></td>
</tr>
<tr>
<td>Fungal infection</td>
<td></td>
</tr>
<tr>
<td>Bacterial Infection</td>
<td></td>
</tr>
<tr>
<td>(Mitochondrial DNA)</td>
<td></td>
</tr>
</tbody>
</table>
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?

Non infectious causes of eosinophilia

- Hereditary
- Vascular: 1. CVD: Churg Strauss
- Inflammatory: IBD, sarcoid
- Metabolic: Addisons

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, Kimura’s disease
Infectious Causes of Eosinophilia

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

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**Helminth eosinophilia determinations**

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

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**Ascaris internal cycle**
Helminths and Eosinophilia
...or not!

- **Tissue migrators**
  - Filaria
  - Toxocariasis
  - Trichinosis
  - Strongyloides
  - Schistosomiasis

- **Non-migrators**
  - Adult Ascarisis
  - Enterobiasis
  - Adult tapeworms
  - Clonorchiasis

Predictive value of eosinophilia for travel-related infections?

**Diagnostic Significance of Blood Eosinophilia in Returning Travelers**

CID 2002;34:407

4.8% had eosinophilia

<table>
<thead>
<tr>
<th>Disease</th>
<th>N=248</th>
<th>Mean eosinophil count</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td></td>
<td>Percentage WBCs</td>
</tr>
<tr>
<td>Helminth infection</td>
<td>130</td>
<td>17.8</td>
</tr>
<tr>
<td>Hookworm</td>
<td>18</td>
<td>22.9</td>
</tr>
</tbody>
</table>

**PPV for helminthiasis= 18.9%**

<table>
<thead>
<tr>
<th>Disease</th>
<th>No. of patients</th>
<th>Percentage WBCs</th>
<th>Eosinophils/µL of blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous larva</td>
<td>17</td>
<td>12.5</td>
<td>924</td>
</tr>
<tr>
<td>Echinococcosis</td>
<td>2</td>
<td>12.5</td>
<td>717</td>
</tr>
<tr>
<td>Trichinosis</td>
<td>4</td>
<td>11.5</td>
<td>874</td>
</tr>
<tr>
<td>Enterobiasis</td>
<td>2</td>
<td>10.6</td>
<td>570</td>
</tr>
</tbody>
</table>

NPV = 98.7%
Predictive value of eosinophilia for travel-related infections?

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

Michael D. Lehman, J. Dick Moolman, and Theresa W. Gyorkos

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%

Epidemiology is everything!

- barefoot
- hook, strongyloides
- fresh water
- schistosomiasis
- prolonged stay
- filariasis
- raw meat
- trichinosis
- raw crayfish
- paragonimiasis
- raw water cress
- fascioliasis
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
Agar plate culture for strongyloidiasis

Serologic diagnosis of selected helminthiases: “The Big 3”

<table>
<thead>
<tr>
<th>Infection</th>
<th>Serology sensitivity specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongyloidiasis</td>
<td>93 98</td>
</tr>
<tr>
<td>(CDC)</td>
<td></td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>99 95</td>
</tr>
<tr>
<td>(CDC)</td>
<td></td>
</tr>
<tr>
<td>Filariasis (IgG4)</td>
<td>96 100</td>
</tr>
<tr>
<td>(NIH)</td>
<td></td>
</tr>
</tbody>
</table>

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.

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 = the degree of tissue damage which in turn is α to severity of disease
  - Light worm burdens rarely cause human disease and often do not require treatment (unless they are in a bad location)

Strongyloidiasis

- Autoinfection
- Direct soil cycle
- Indirect soil cycle
- Hyperinfection
- Dissemination
- Immunosuppression

- Filariform larvae
- Rhabditiform larvae
- Adult worms
**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: >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

**Strongyloides hyperinfection**

- Enteritis
- Pneumonitis
- Gram negative bacteremia/meningitis

**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

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

- 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.

Da Bottom Line!

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

• Nutman T. Eosinophilia in the returning traveller. Infectious Disease Clinics of North America 1998;2:504-21
