

# Fever in returning traveler: Survey of select tropical diseases



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# Discussion outline

1. Background: illness in travelers
2. Approach to traveler illness
3. 5 Cases of common tropical diseases



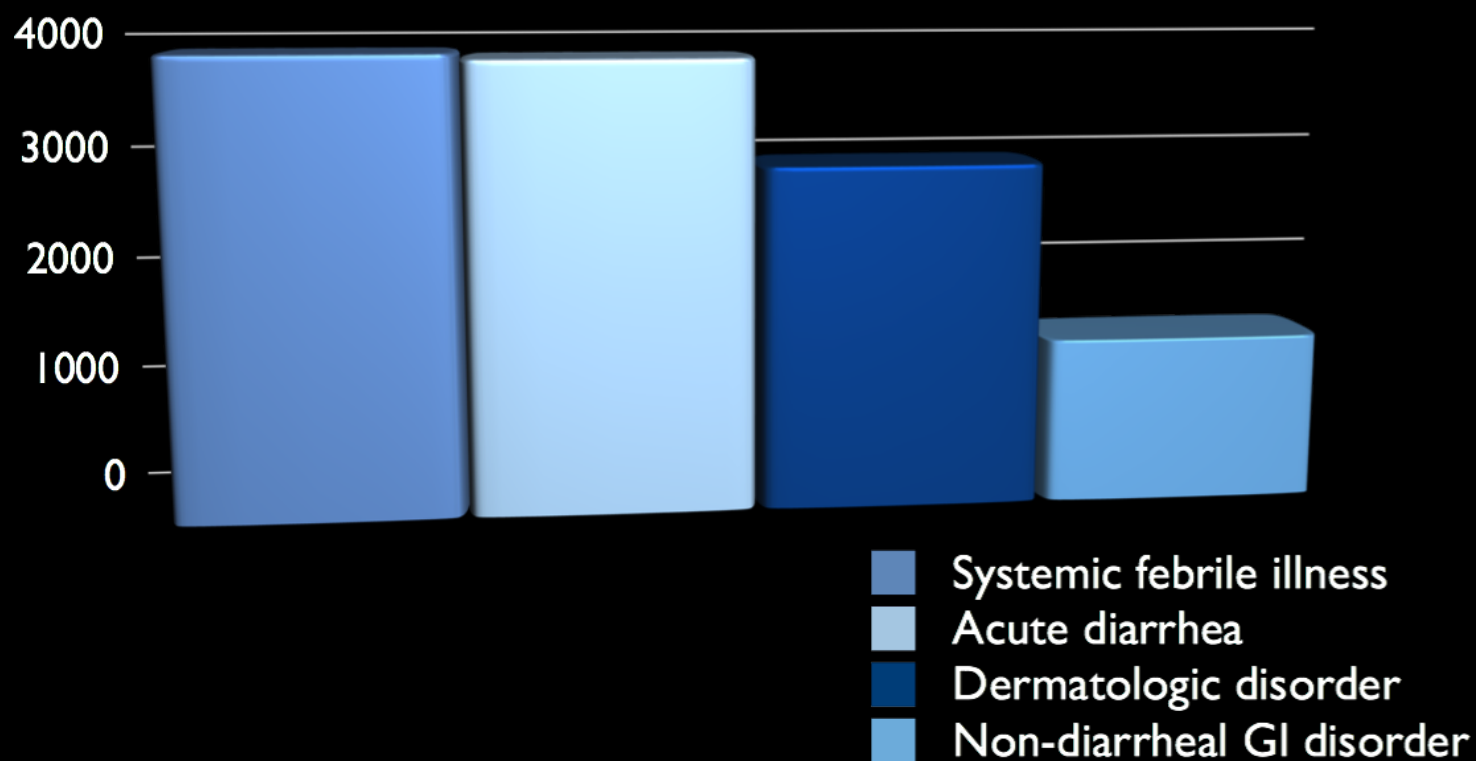
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# Illness in returning travellers

- Post-travel illness is common
  - 22-64% of returning travelers
- Majority fall into 4 general categories:
  - systemic febrile illness
  - acute diarrhea
  - dermatologic disorder
  - non-diarrheal GI disorder

# Relative frequency of diagnostic categories

Among 17,353 patients in GeoSentinel network (CDC, ISTM)



Systemic febrile illness (n= 3907)	
Malaria	35%
Dengue	10
Mononucleosis	3
Rickettsial infection	3
Salmonella typhi or S. paratyphi infection	3
No specific cause reported	41

Acute diarrhea (n = 3859)	
Parasitic diarrhea (e.g. giardiasis, amebiasis)	35%
Bacterial diarrhea (e.g. SSYCE)	27
Unspecified and viral diarrhea	40

Dermatologic disorder (n= 2947)	
Insect bite	19%
Cutaneous larva migrans	13
Allergic rash or reaction	11
Skin abscess	10
Mycosis	6
Animal bite	5
Leishmaniasis	4
Myiasis	4
Mite infestation (e.g. scabies)	2

Non-diarrheal GI disorder (n = 1421)	
Intestinal nematodes (e.g. strongyloides, ascaris)	24%
Gastritis or peptic ulcer disease	13
Acute hepatitis	12

# Travel history

- Countries visited -- urban or rural
- Duration of stay in each place
- Accommodations
- Vaccines and chemoprophylaxis
- Sex or other intimate contact
- Animal and arthropod exposures
- Needle and blood exposures
- Food, water, and soil exposures

# Incubation periods

Short (<10 days)	Intermediate (10-12 days)	Long (>21 days)
Malaria	Malaria	Malaria
Influenza	Viral hemorrhagic fevers	Hepatitis A, B, C, E
Arboviral infections including dengue, yellow fever	Typhoid fever	Schistosomiasis (Katayama fever)
Plague	Scrub typhus	Leishmaniasis
Enteric bacterial infections including paratyphoid fever	Q fever	Amoebic liver abscess
African tick bite fever	Relapsing fever ( <i>Borrelia</i> spp)	Tuberculosis
Spotted fever group (including Rocky Mountain spotted fever)	African trypanosomiasis	Filariasis
	Brucellosis	HIV
	Leptospirosis	

Source: Leggat P. Assessment of febrile illness in the returning traveller. *Australian Family Physician*. 2007;36(5).



# Laboratory tests

- Common initial labs:
  - CBC with differential
  - Thick/thin blood malaria films
  - LFTs
  - Cultures of blood and stool
  - UA and urine culture
- Other tests based on history and initial findings:
  - E.g. serological tests, string test, splenic bx, etc.



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Cases:  
common tropical diseases  
in returning travellers

# Clinical case

- 18yo M student returns from 1-month trip to SE Asia 4 days ago
- P/w:
  - high-grade fever
  - headache / pain behind eyes
  - bone and muscle aches
  - blanching rash



Image by U.S. Government, retrieved from <http://en.wikipedia.org/wiki/File:Denguerash.JPG>. Image in public domain and used under a Creative Commons license.

# Dengue

- Most prevalent mosquito-borne viral disease
- Ranges from mild febrile illness to life-threatening shock
- >50 million infections each year
- >2.5 billion at risk in ~100 countries

[WHO map of dengue incidence.  
Available at: [http://www.who.int/csr/resources/publications/dengue/CSR\\_ISR\\_2000\\_1/en/index5.html](http://www.who.int/csr/resources/publications/dengue/CSR_ISR_2000_1/en/index5.html) ]

# Dengue transmission

- Transmitted by female *Aedes* mosquito
- Dengue viruses 1-4
- Infection with one serotype doesn't protect against others
- Sequential infections risk dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS)



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=9534>. Image in public domain.

# Classic dengue presentation

- Incubation period 3-14 days
- Acute febrile illness
- Retro-orbital pain
- Marked muscle and bone pain (“break-bone fever”)
- Rash....



# DHF and DSS

- Dengue hemorrhagic fever:
  1. fever 2-7 days
  2. increased vascular permeability
  3. thrombocytopenia (<100k)
  4. hemorrhagic tendency
- Dengue shock syndrome:
  - above, plus shock

[ Image of dengue-related hemorrhage on arm. Available at: <http://www.niaid.nih.gov/SiteCollectionImages/topics/denguefever/michaelRossmannStory.JPG> ]



# Dengue diagnosis

- Mostly a clinical diagnosis
- Lab: elevated HCT, low platelet, elevated LFTs
- In resource-rich settings....
  - serology testing
  - virus detection (culture, RT-PCR)

# Dengue treatment

- Classic dengue fever:
  - supportive care (fluids, antipyretics, etc.)
- DHF/DSS:
  - plus, prn PRBCs, platelets, IVFs

# Dengue prevention

- Reduce mosquito exposure
  - Day-biter, so long clothing and DEET vs bednets
- Tetravalent vaccines in development
- Public health control of mosquitoes and mosquito-breeding sites

# Clinical case

- 22yo M U.S. soldier returns from Afghanistan
- P/w:
  - several-month h/o intermittent low-grade fever
  - growing, non-painful ulceration on left hand
  - not responding to any topical treatment



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# Leishmaniasis

- Parasitic disease spread by bite of female sandfly
- Two forms:
  - Cutaneous leishmaniasis
  - Visceral leishmaniasis (Kalazar)
- Leish & HIV worsen one another



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=10275>.  
Image in public domain.

# Leishmaniasis life cycle

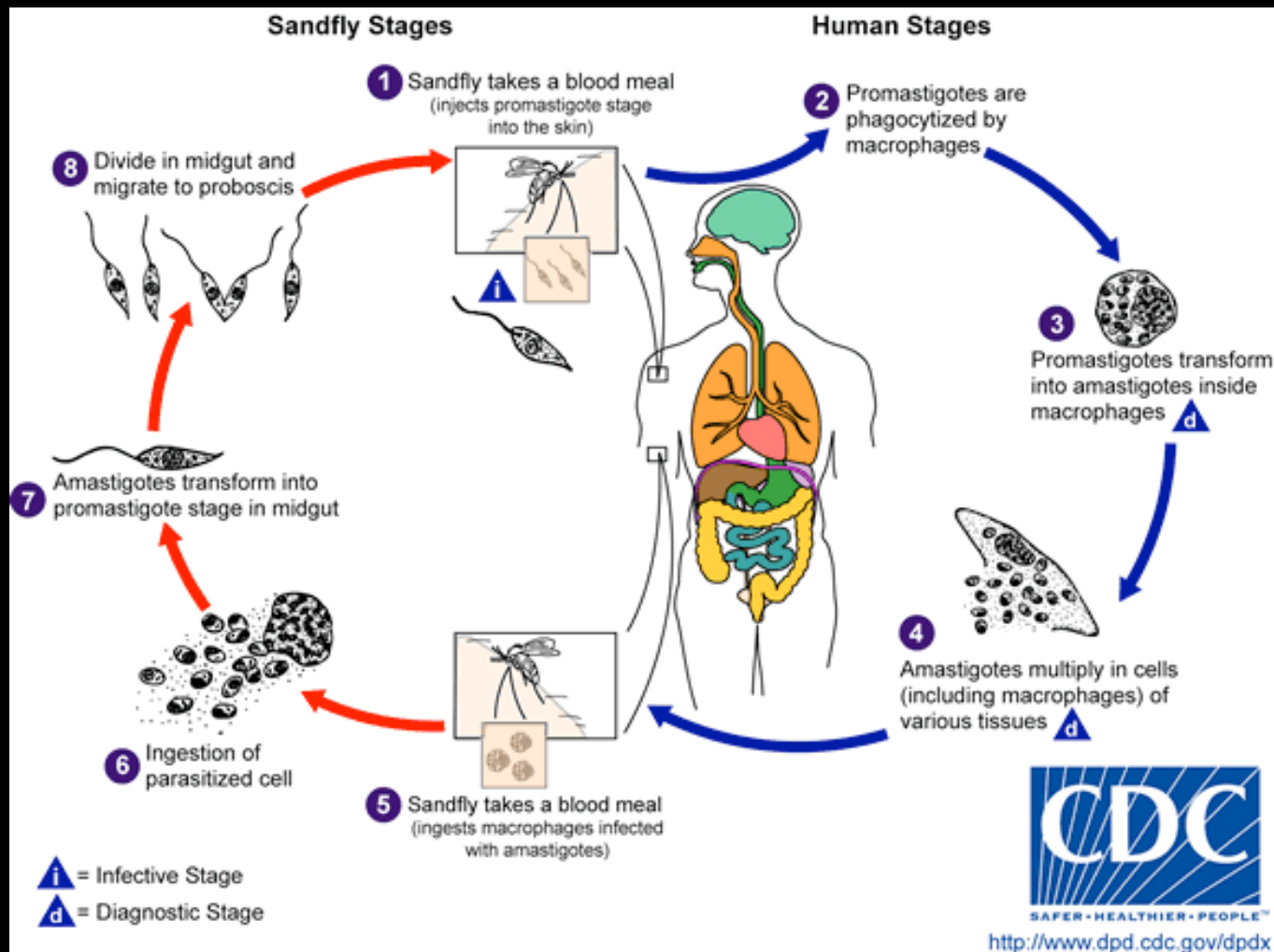


Image retrieved from [http://www.dpd.cdc.gov/dpdx/images/ParasitelImages/G-L/Leishmaniasis/Leishmania\\_LifeCycle.gif](http://www.dpd.cdc.gov/dpdx/images/ParasitelImages/G-L/Leishmaniasis/Leishmania_LifeCycle.gif). Image in public domain.

# Cutaneous leish. presentation

- Several cutaneous forms
- Ranging from lesion at site of bite to destruction of mucosal areas
- Lesions develop over weeks-years
- Recurrences possible



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=12161>. Image in public domain.

# Visceral leish. presentation

- Fever (for weeks)
- Vomiting and diarrhea
- Cough
- Fatigue
- HSM
- Anemia, thrombocytopenia



Image retrieved from [http://www.who.int/leishmaniasis/surveillance/slides\\_manual/en/index.html](http://www.who.int/leishmaniasis/surveillance/slides_manual/en/index.html). Image in public domain.



# Leishmaniasis diagnosis

- Identify amastigotes within affected tissue
  - Biopsy of skin or spleen (or marrow, lymph node)
  - Montenegro test
  - Serology

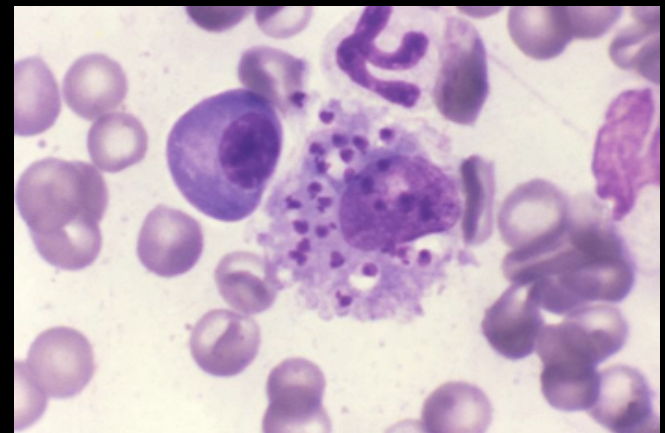


Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=30>. Image in public domain.

# Leishmaniasis treatment

- First line:
  - Sodium stibogluconate (SbV) OR meglumine antimonate x3-4 weeks IV/IM
- Others:
  - Amphotericin B, pentamidine, miltefosine

*Rx of cutaneous leish reduces risk of mucosal leish*

# Leishmaniasis prevention

- No vaccine available :(
- Limit exposure
  - avoid dusk/dawn biting, long sleeves, window screens, fine-mesh/insecticide-treated bednets
- Insecticide spraying of sandflies (particularly in epidemics)
- Control animal reservoirs

# Clinical case

- 17yo F returns after a 1-month trip to Malawi with schoolmates. 6 weeks later...
- P/w:
  - mild fever with flu-like symptoms
  - generalized urticarial rash
- Recalls h/o resolved rash after swimming
- Labs show eosinophilia



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=5249>. Image in public domain.

# Schistosomiasis

- Infection by 3 related parasitic blood flukes, often chronic
  - *S. hematobium* (bladder)
  - *S. mansoni* (GI, liver)
  - *S. japonicum* (GI, liver)
- Second most socioeconomically devastating parasitic disease after malaria



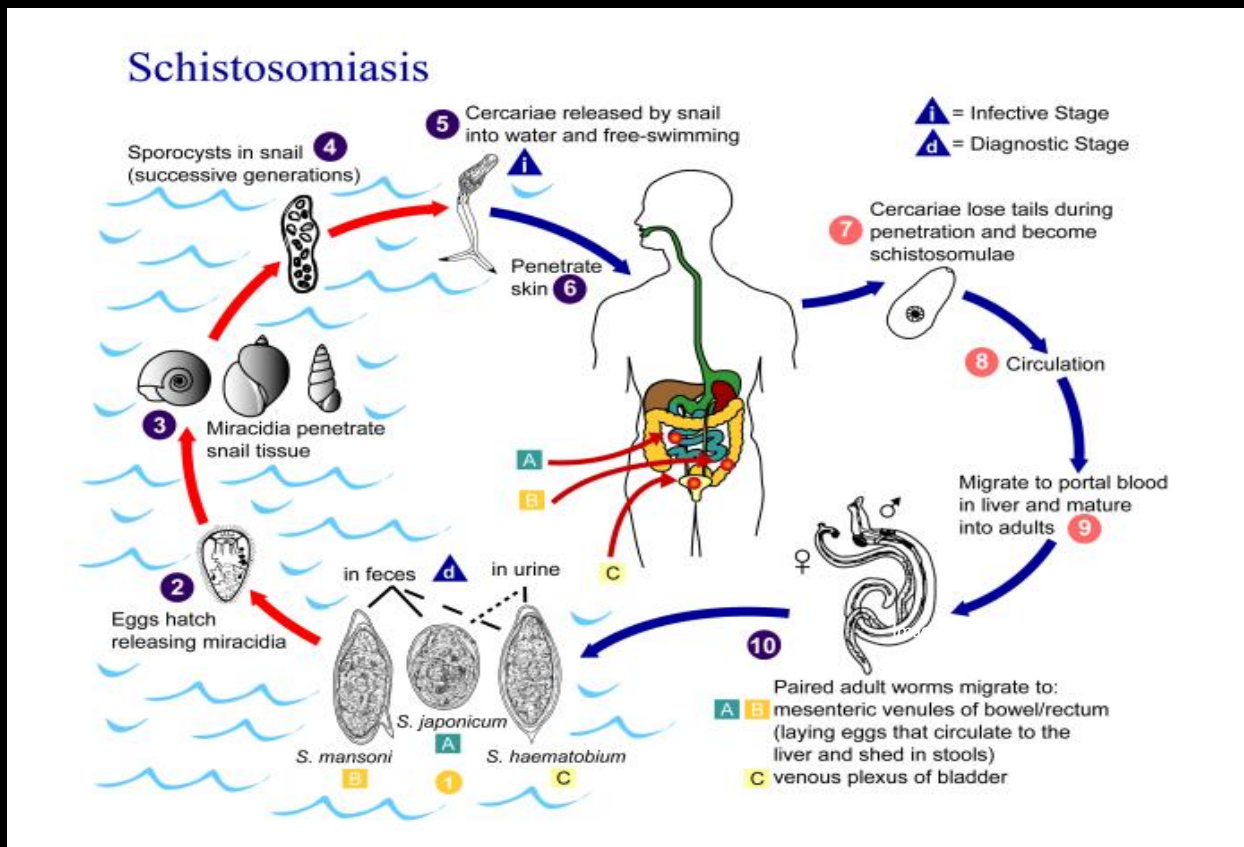
Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=8556>. Image in public domain.

# Schistosomiasis distribution

- >200 million currently infected (1 in 30)
- >200,000 deaths annually

[ Map of global distribution of schistosomiasis. Available at: <http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-3-infectious-diseases-related-to-travel/schistosomiasis.htm> ]

# Schistosomiasis life cycle



details.asp?pid=10275.

# Schistosomiasis presentation

- Acute:
  - Swimmer's itch / rash
  - Katayama fever (fever, urticaria, eosinophilia, cough, HSM)
- Chronic:
  - terminal hematuria
  - bloody diarrhea



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=5249>.  
Image in public domain.



# Schistosomiasis complications

- Ectopic eggs and worms:
  - Papillomas in GU system
  - Calcification of bladder
  - Cor pulmonale
  - Liver fibrosis
  - Neuroschistosomiasis

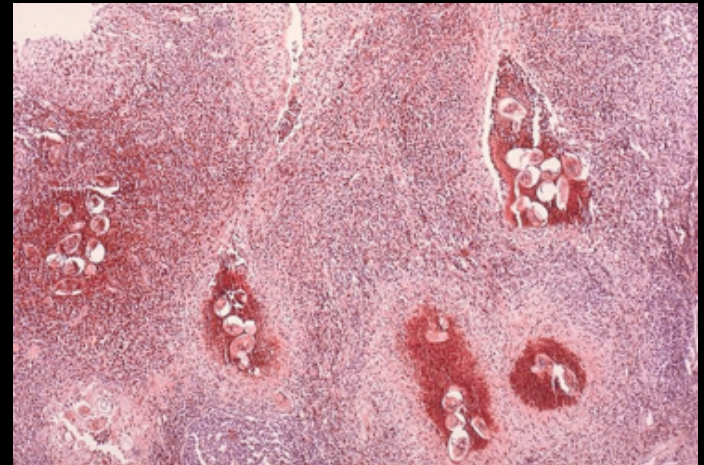


Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=3417>. Image in public domain.

# Schistosomiasis diagnosis

- Adult worms inaccessible; look for eggs
  - mid-day urine
  - concentrated fecal smear
- Occasionally useful:
  - serology, rectal bx, radiological changes, eosinophilia

# Schistosomiasis treatment

- Praziquantal
  - 40-60mg/kg x 1-3 doses, depending on spp.
  - Repeat treatment in 3 months to kill previously maturing worms
- +/- steroids to reduce immune response

# Schistosomiasis prevention

- Limit exposure to endemic fresh water
- Chlorinate or filter water of cercariae
- Eliminate snail habitat
- Mass treatments of school children where prevalence >40%
  - may treat only those w/dipstick hematuria

# Clinical case

- 19yo M presents after living with family in East Africa for several years
- P/w:
  - Several-year h/o episodes (lasting several hours) of migrating, pruritic, raised, linear rashes
  - Lesions have been peri-anal, trunk, etc.



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=5224>. Image in public domain.

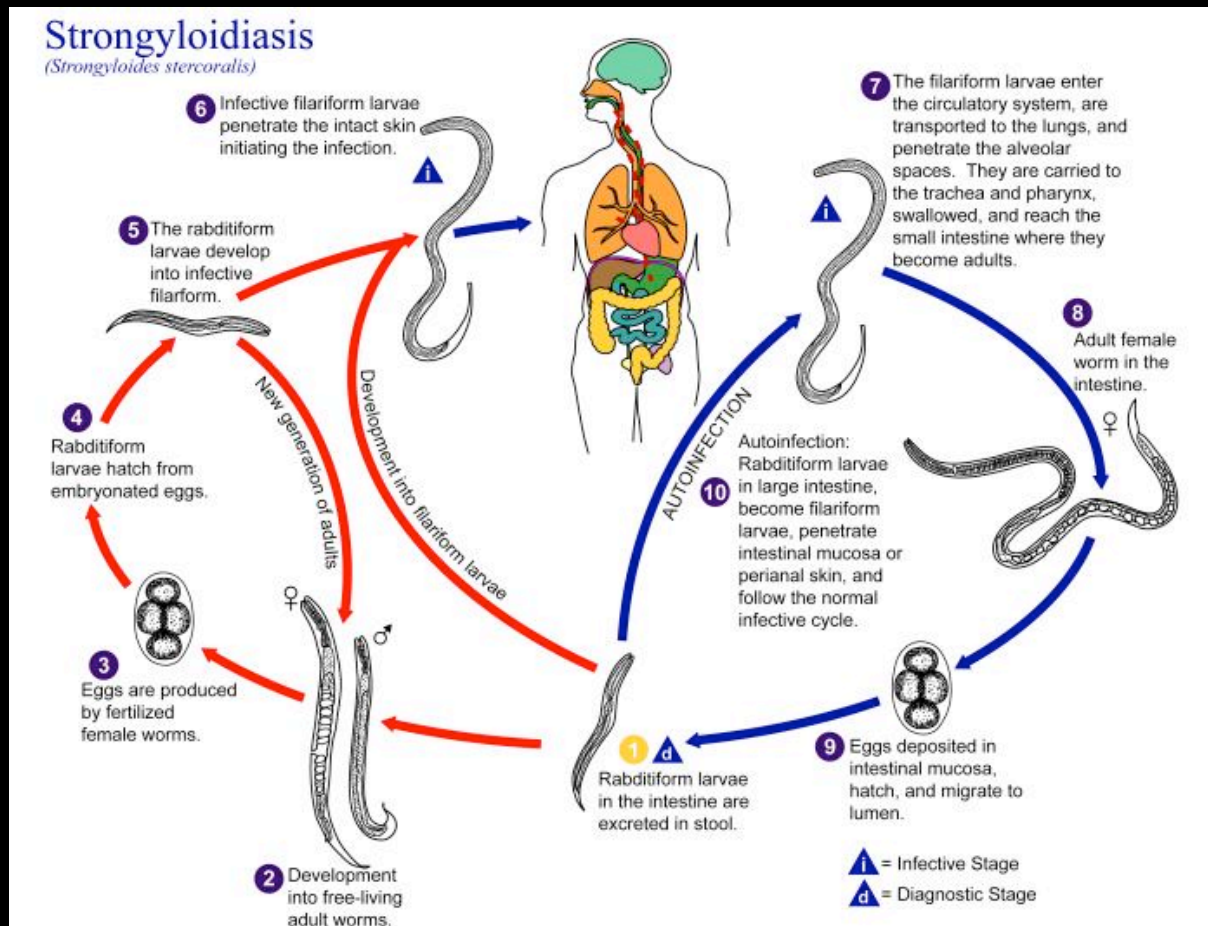
# Strongyloidiasis

- Small bowel infection with the barely-visible roundworm, *Strongyloides stercoralis*
- Individuals become infected through contact with contaminated soil



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=1448>.  
Image in public domain.

# Strongyloidiasis life cycle



# Strongyloidiasis presentation

- Acute s/sx (although usually asymptomatic):
  - itchy eruption where larvae entered
  - cough, wheeze, abdominal pain, diarrhea
- Chronic s/sx:
  - larva currens, GI sx
- Hyperinfection syndrome in immunosuppressed



# Strongyloidiasis diagnosis

- Clinical diagnosis
  - eosinophilia, diarrhea, larva currens
- Stool microscopy
- Duodenal string test
- Serology

# Strongyloidiasis treatment

- Options:
  - Ivermectin (most effective)
  - Albendazole
  - Thiabendazole (least effective)
- Second course after 2 weeks for chronic/  
severe infections

# Strongyloidiasis prevention

- Footwear
- Screen at-risk individuals before giving steroids or immunosuppressive therapy
- Also consider screening for amebiasis and TB

# Clinical case

- 12yo F returns from recent 1-month trip to west Africa after accompanying parents on a medical service trip
- P/w:
  - 1-week persistent high-grade fevers
  - abdominal pain, diarrhea
  - PE: febrile, unwell, abdominal distention and tenderness
  - New-onset rash...



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=2215>. Image in public domain.

# Typhoid

- Life-threatening infection caused by bacteria *Salmonella typhi* and *S. paratyphi*
- Fecal-oral transmission
- 21.5 million/yr
- 400 cases in U.S.,  
75% acquired internationally

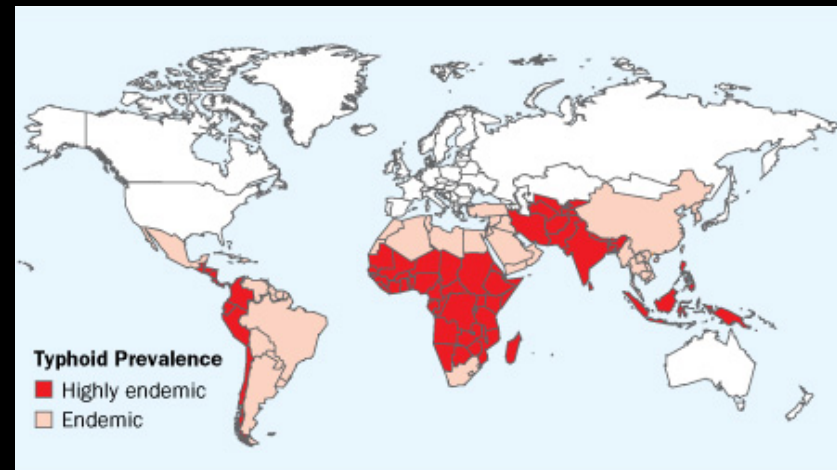


Image retrieved from [http://www.sciencenews.org/view/access/id/45826/title/Typhoids\\_reach](http://www.sciencenews.org/view/access/id/45826/title/Typhoids_reach).  
Image by CDC/WHO and in public domain.

# Typhoid life cycle

[ Image of "Typhoid Mary." Available at:  
[http://  
history1900s.about.co  
m/od/1900s/a/  
typhoidmary.htm](http://history1900s.about.com/od/1900s/a/typhoidmary.htm) ]

- Asymptomatic carriers most important reservoirs
- Ingestion of contaminated water/food
- Bacteria attach and penetrate GI
- Spread through body via macrophages

# Typhoid presentation

- Fever
- Quite unwell, malaise, abdominal pain, diarrhea
- Rose spots
- Complications:
  - intestinal perforation/hemorrhage
  - shock, organ failures



Image retrieved from <http://phil.cdc.gov/phil/details.asp?pid=2215>. Image in public domain.

# Typhoid diagnosis

- Blood culture (best)
- Other:
  - string capsule
  - aspirate of rose spots, CSF, abscess, marrow
- Widal test (low sensitivity/specificity)



# Typhoid treatment

- Chloramphenicol (or amox, cotrimoxazole) was first line
- Flouroquinolones (cipro), CTX, azithro now used due to increasing resistance
- Steroids if severe sx (delirium, coma, shock)
- Surgical resection (not just suturing) of perforations

# Typhoid prevention

- Treatment of chronic carriers
  - “Typhoid Mary”
  - Carriers have nidus in gallbladder (fecal carriers) or urinary tract (urinary carriers)
- Two vaccines:
  - Killed IM vaccine (booster after 2yrs)
  - Live oral Ty21a (3-4 doses over 5 days, booster after 5yrs)

# Conclusion (I)

- Illness is relatively common amongst travellers
- Diagnosis assisted by history, incubation period, exam, simple labs
- Today, we discussed....

# Conclusion (2)

## Dengue

*virus via Aedes, fever/pain/rash, DHF/DSS, clinical dx, supportive care*

## Leishmaniasis

*sandfly, cutaneous/visceral forms, dx find amastigotes, rx sodium stibogluconate*

## Schistosomiasis

*blood fluke, chronic tissue disruption, look for eggs in urine/stool, rx praziquantal*

## Strongyloidiasis

*soil worm infects GI, usually no sx, larva currens, hyperinfection, rx ivermectin*

## Typhoid

*fecal-oral, fever/unwell/GI/rosecspots, dx culture/string/Widal, rx cipro +/- steroids*