



Brigham and Women's Hospital
Founding Member, Mass General Brigham

Tropical Medicine and Parasitology

Carolina Geadas, MD, MSc, DTM&H

Associate Physician, Division of Infectious Diseases

Brigham and Women's Hospital

Instructor in Medicine, Harvard Medical School



Carolina Geadas, MD, MSc, DTM&H



- Internal Medicine Residency @ Boston University Medical Center
- Infectious Disease Fellowship @ Brigham and Women's Hospital / Massachusetts General Hospital
- MSc in Population Health Research @ Boston University School of Public Health
- Diploma in Tropical Medicine & Hygiene (DTM&H) @ Gorgas Course
- Certified in Clinical Tropical Medicine and Travelers' Health (CTropMed®) by the American Society of Tropical Medicine and Hygiene (ASTMH)
- Instructor of Medicine @ Harvard Medical School
- Clinical focus: Tropical and Travel Medicine, Parasitology, Mycobacterial Infections



DISCLOSURES

- Sanofi - Moderator of rabies discussion group



LEARNING OBJECTIVES

Upon completion of this activity, participants will be able to:

- Identify common tropical conditions in returning travelers and migrant populations
- Apply a framework to febrile travelers considering timeline, syndrome, geography, and specific exposures
- Summarize the presentation, diagnosis, and management of common tropical conditions
- Case-based lecture



✓ Look for these for quick pearls for your review



Travel-related Illness



Travel-related Illness

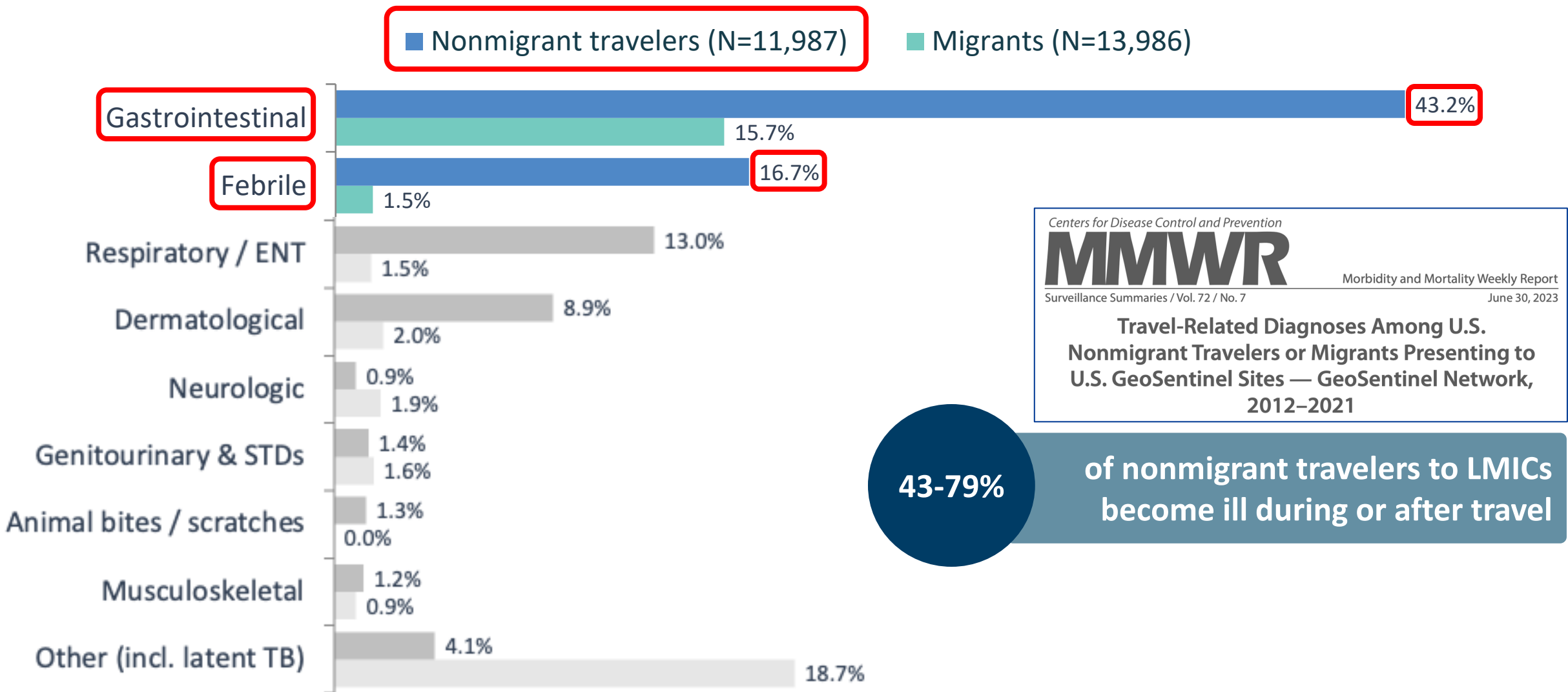


Visits to 20 GeoSentinel Sites over 10 years

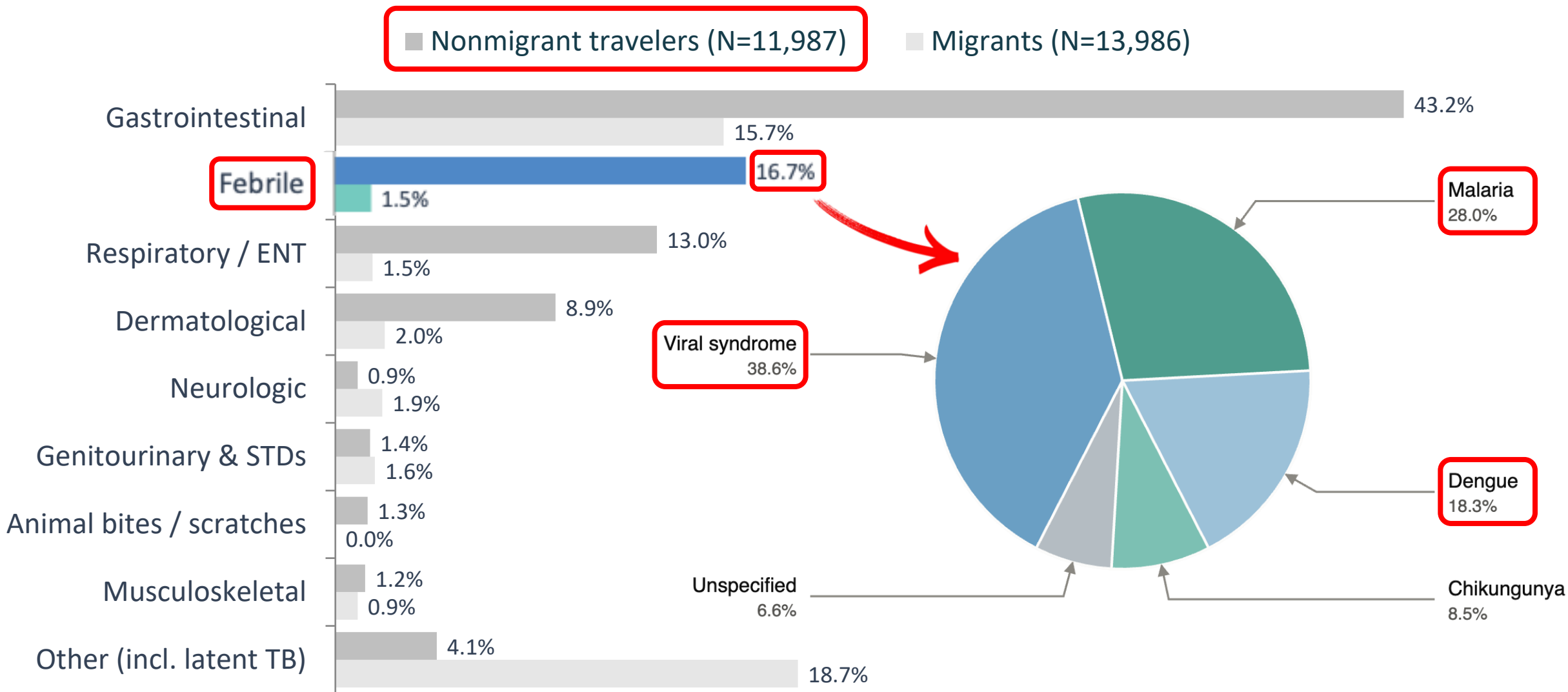
GeoSentinel – Network of 71+ specialized travel/tropical-medicine clinics across 29 countries (run by the ISTM and CDC since 1995) that systematically report on illness in returned travelers, visitors, and migrants



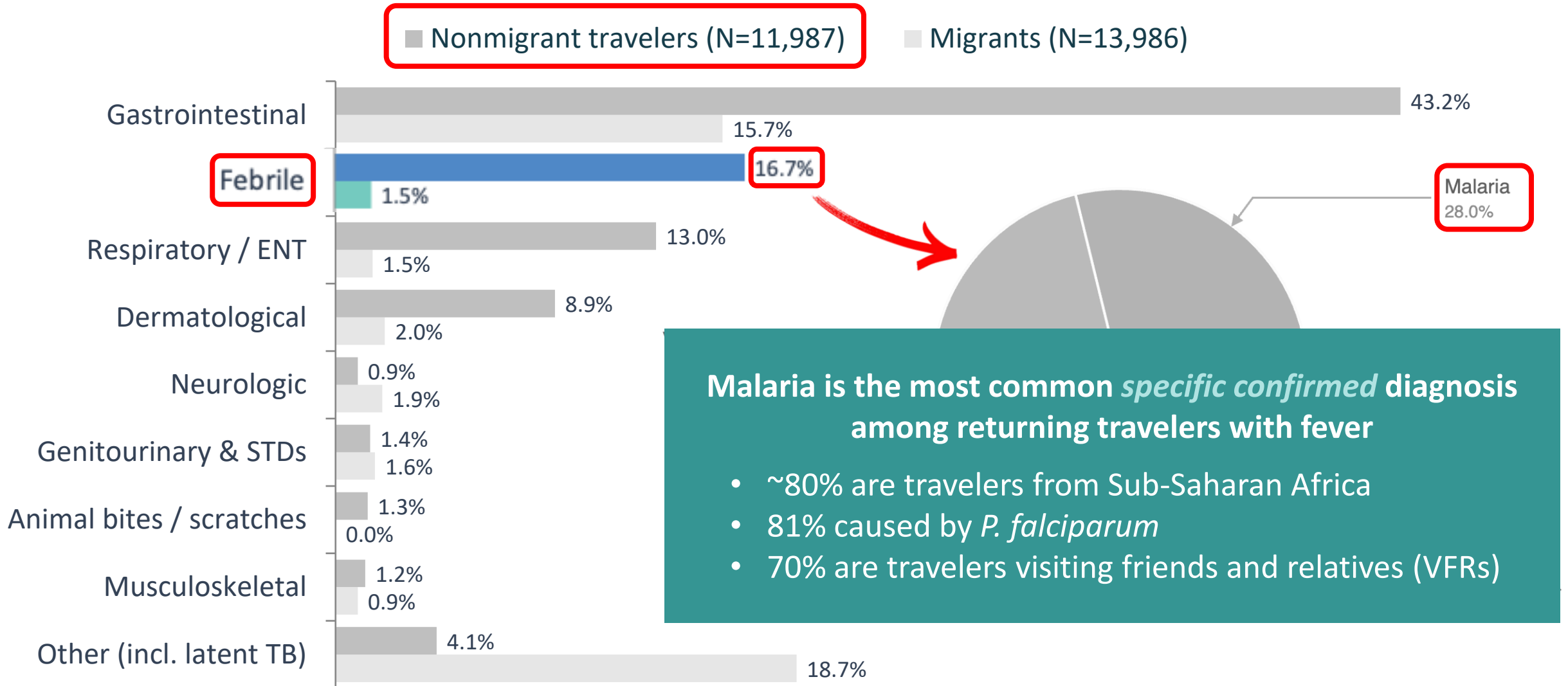
Travel-related Illness – Nonmigrant Travelers



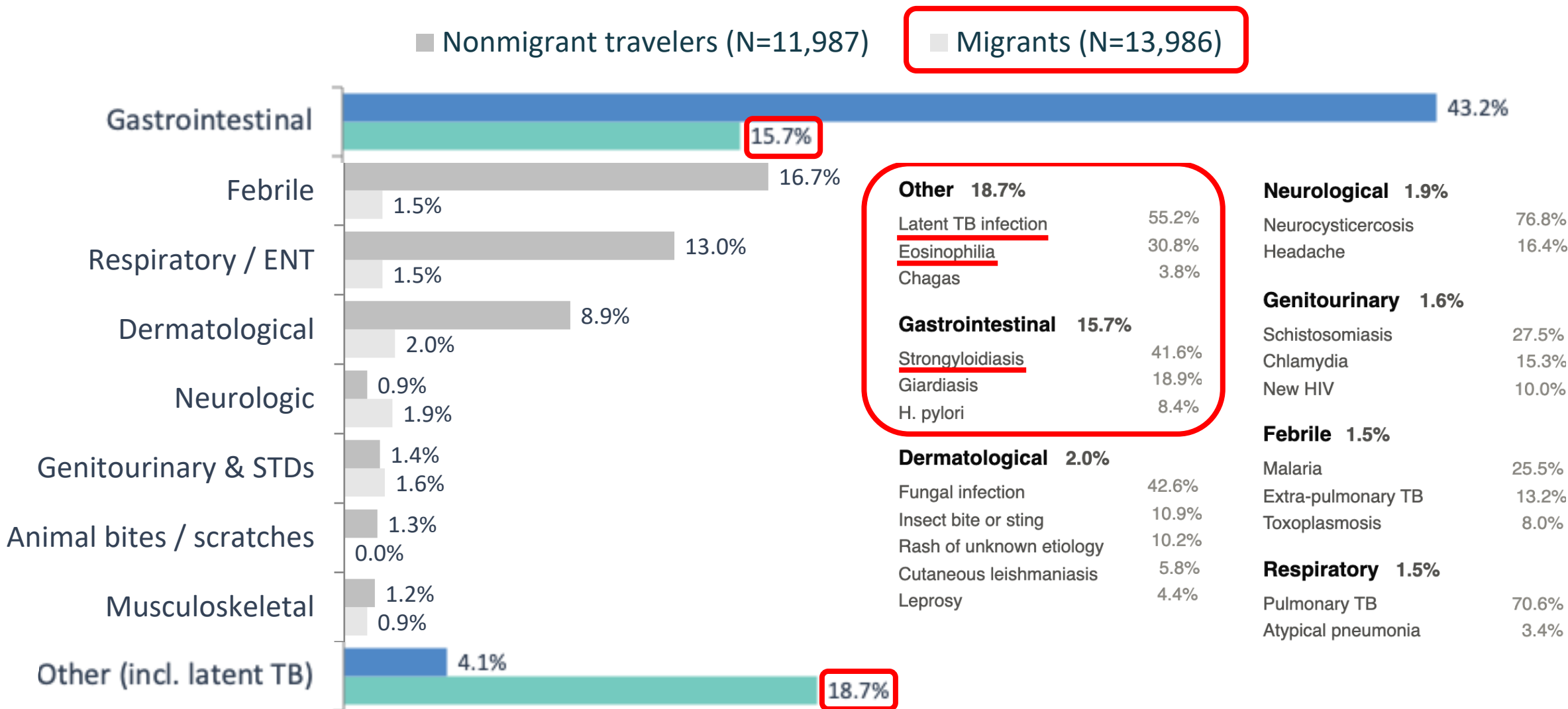
Travel-related Illness – Nonmigrant Travelers



Travel-related Illness – Nonmigrant Travelers



Travel-related Illness – Migrants



Travel-related Fever

Etiology of fever in **returning travelers + migrants**

Not all travel-related illness is *tropical*

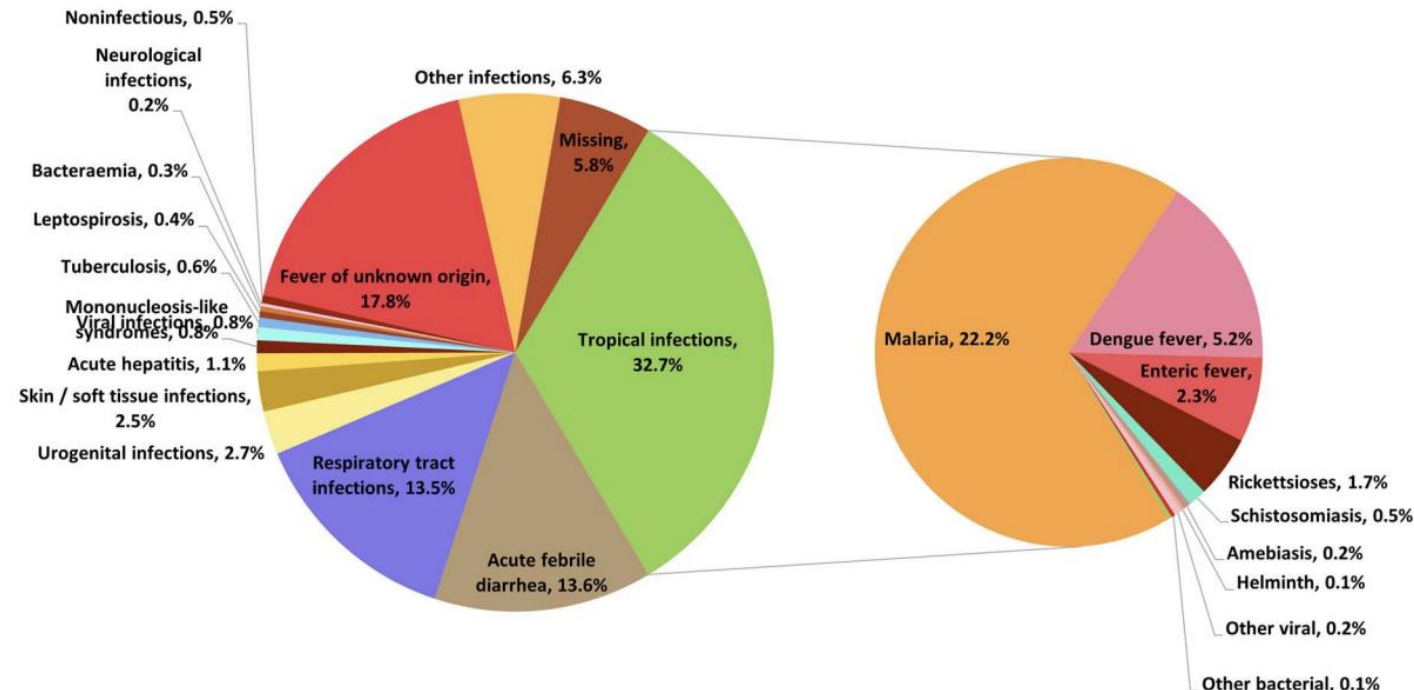
- **39% Non-tropical infections**

- Acute gastroenteritis 14%
- Respiratory infections 13%

- **33% Tropical infections**

- **Malaria** 22%
- **Dengue** 5.0%
- Enteric fever 2.3%
- Rickettsioses 1.7%

- **24% Unknown**





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Original Article

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**Aetiology of fever in returning travellers and migrants:
a systematic review and meta-analysis**

**Imogen Buss MBChB, MScGH, EADTMH¹, Blaise Genton MD, PhD^{1,2,*} and
Valérie D'Acremont MD, PhD^{1,2}**

Travel-related Fever

Original Article

Aetiology of fever in returning travellers and migrants: a systematic review and meta-analysis

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Etiology of fever in **returning travelers + migrants**

• Africa

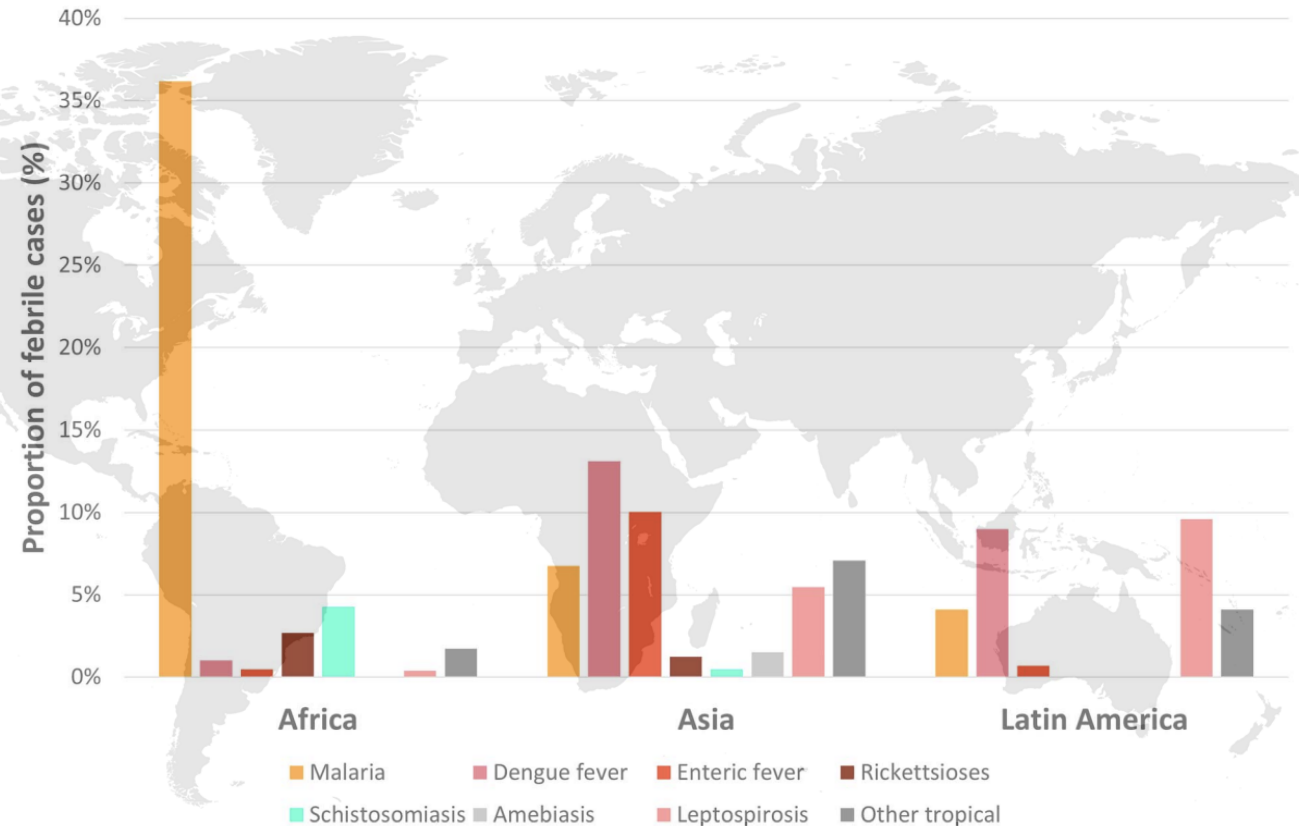
- **Malaria** 28-47%
- Schistosomiasis 3-6%
- Rickettsioses 1-5%

• Asia

- **Dengue** 13-18%
- Enteric fever 3-17%
- Other ~7%
- Malaria 4-11%

• Latin America

- Dengue 8-13%
- Malaria ~4%
- Leptospirosis 10% (single study)



Post-Travel Illness - Framework



By incubation period

< 14 days: Arboviruses (dengue, chikungunya, zika), malaria, typhoid, rickettsioses, leptospirosis, traveler's diarrhea

2–6 weeks: Malaria, typhoid, hepatitis A/E, acute schistosomiasis (Katayama), amebic liver abscess, acute HIV

> 6 weeks: Malaria (P. vivax/ovale relapse), TB, hepatitis B, visceral leishmaniasis, chronic schistosomiasis, filariasis



By syndrome

Undifferentiated fever: Malaria, typhoid, dengue, rickettsioses, leptospirosis

Fever + rash: Dengue, chikungunya, rickettsia (eschar), acute HIV, typhoid fever

Diarrhea: ETEC, Campylobacter, Shigella, Salmonella, Giardia, Entamoeba

Eosinophilia: Strongyloides, schistosomiasis, filariasis, hookworm

Jaundice / hepatitis: Hepatitis A/E, leptospirosis, malaria, amebic liver abscess

CNS / ↓mental status: Cerebral malaria, neurocysticercosis, Japanese encephalitis, rabies



By geography & exposure

REGION

Sub-Saharan Africa: Malaria, rickettsioses, schistosomiasis, VHF

S/SE Asia: Dengue, typhoid, malaria, chikungunya

Latin America: Dengue, malaria, Chagas, leishmaniasis, Zika

EXPOSURE

Freshwater swim: Schistosomiasis, leptospirosis

Unpasteurized dairy: Brucellosis

Undercooked food/water: Typhoid, hepatitis A/E

Animal/tick bite: Rabies, rickettsioses



Exclude malaria in every febrile returning traveler, even if they took prophylaxis

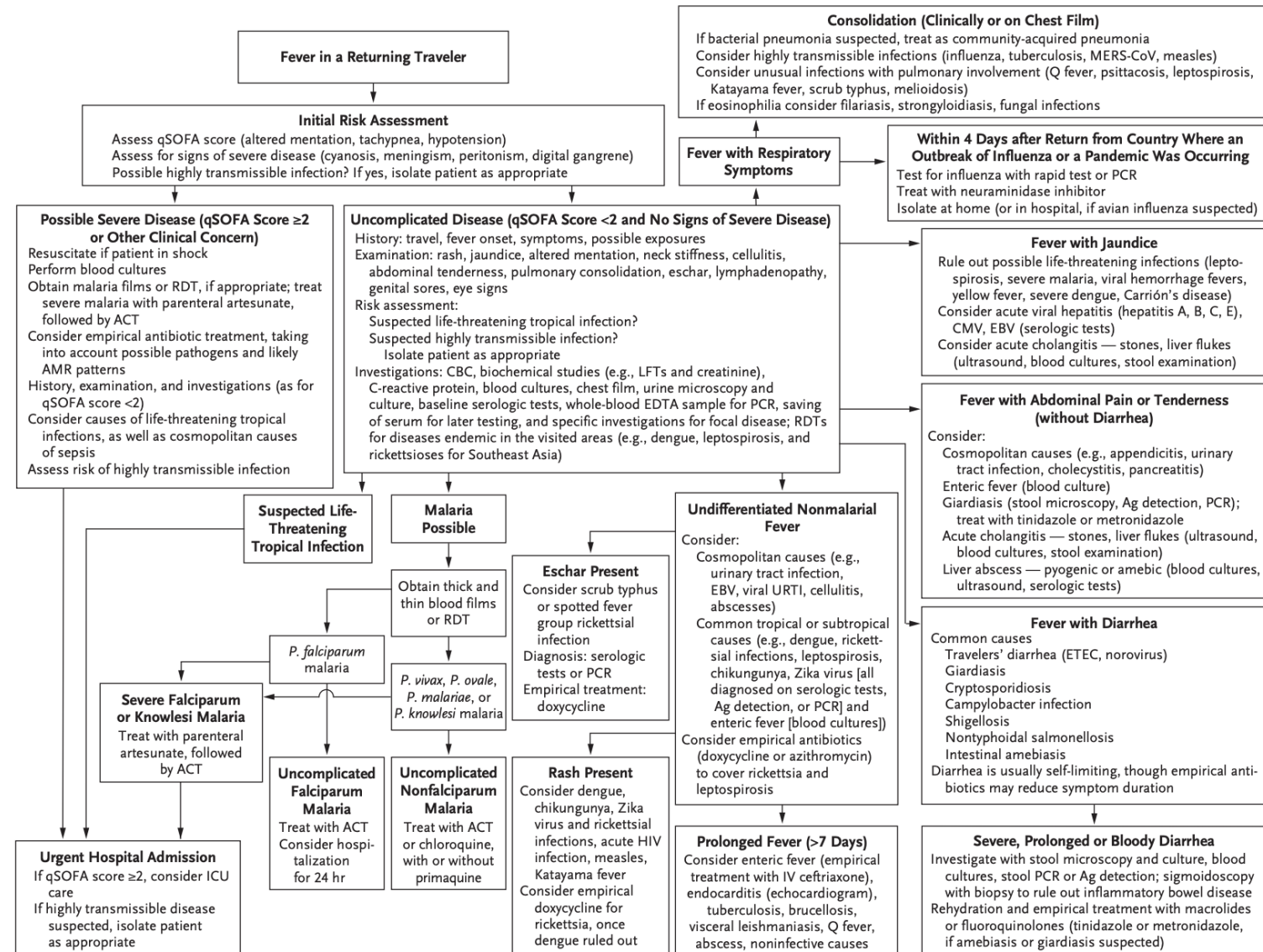
Approach to the Ill Traveler

Initial Investigation:

- Complete blood cell count
- Liver and renal function
- Blood smear
- Blood cultures
- Rapid diagnostic tests for malaria and dengue
- Respiratory viral panel
- HIV Ab/Ag screening
- Hepatitis panel
- Chest X-ray
- Urinalysis, culture, and microscopy

Guided by clinical syndrome/suspicion:

- Targeted PCR and serologies
- Stool O&P
- Advanced imaging (chest, abdomen/pelvis, brain)
- Lumbar puncture



Cases

Seven patients an internist might actually see



Case 1



A 50-year-old woman presents with 1 day of fever, headache, and myalgias. She returned 6 days ago from a 2-week trip to the Brazilian Amazon with numerous mosquito bites. She is from Brazil and had prior chikungunya infection and received the yellow fever vaccine. She took atovaquone–proguanil prophylaxis, stopping 3 days after return. Exam shows T 39.1°C, no hemodynamic instability, and a petechial rash on the lower extremities. Labs: WBC 3,400/ μ L, Hgb 9 g/dL, platelets 33,000/ μ L, AST 198 U/L, ALT 145 U/L, normal bilirubin. What is the **most likely diagnosis**?

- A. Malaria
- B. Dengue
- C. Zika
- D. Chikungunya
- E. Yellow Fever



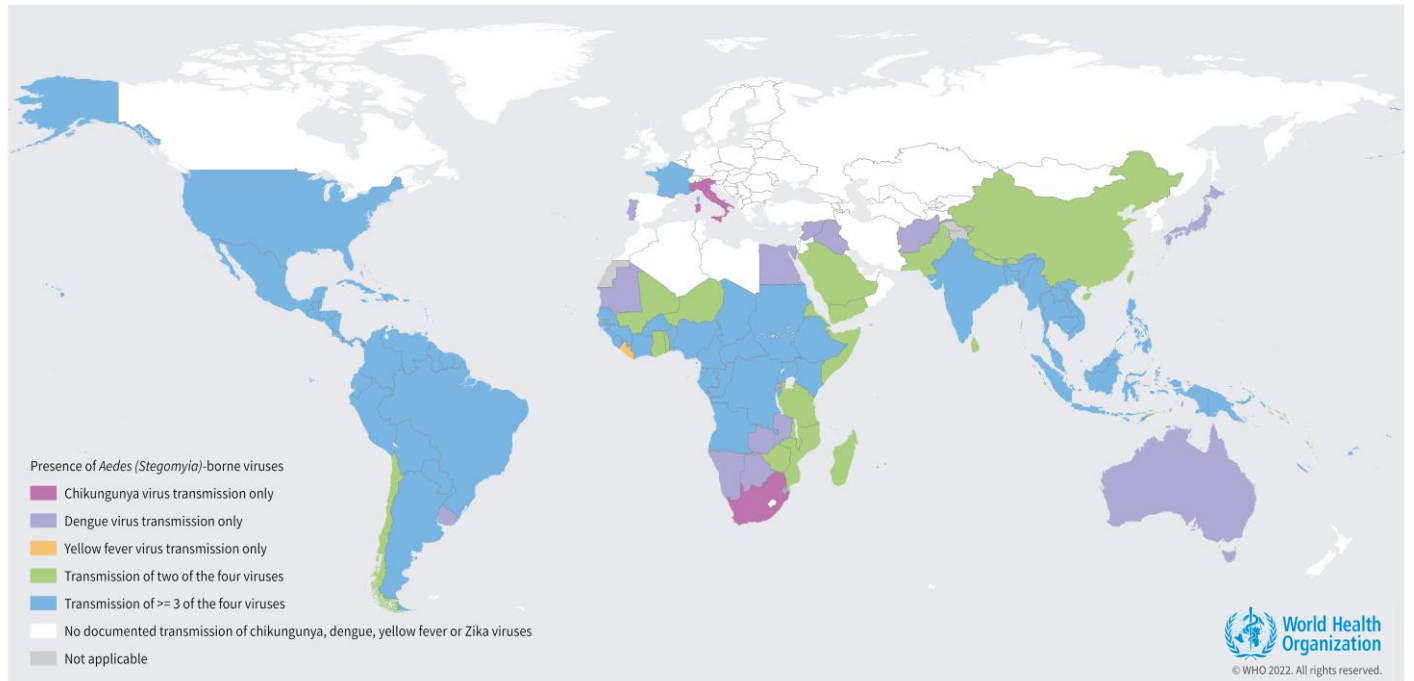
Dengue



Dengue

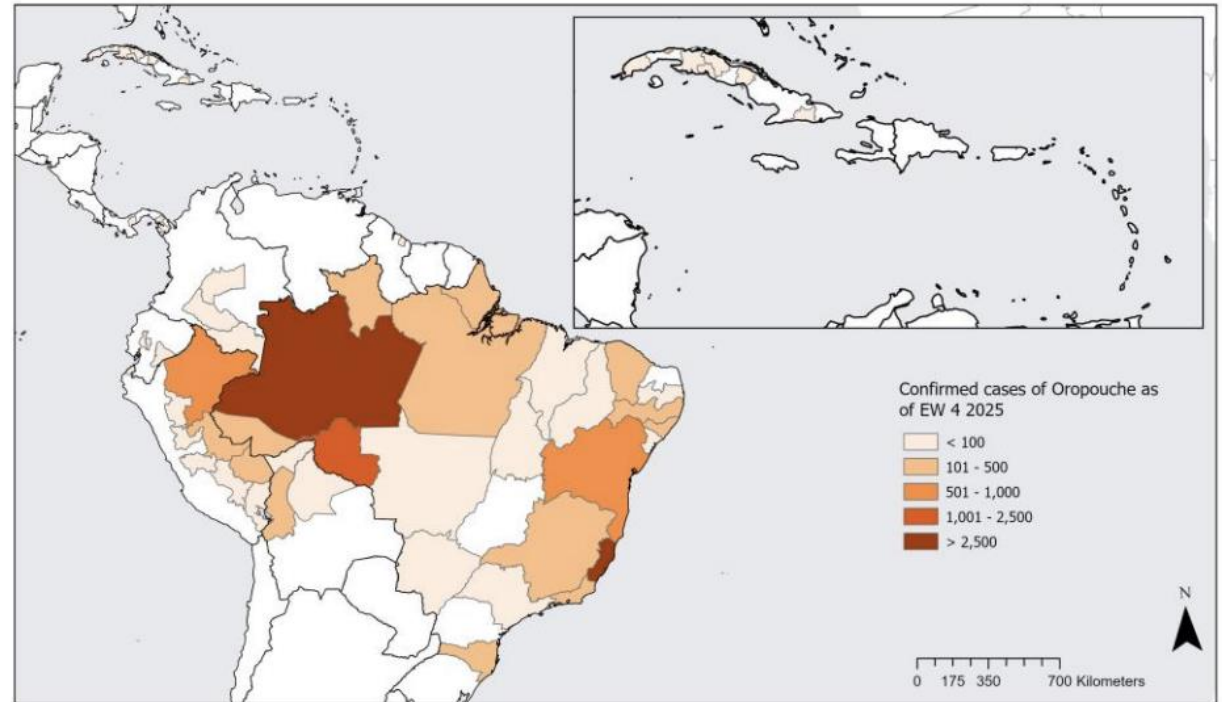
- Arboviruses are a common cause of fever <2 weeks after return
- **Dengue is the most common tropical infection in febrile travelers from Latin America**
- Dengue, Zika, Chikungunya, Yellow Fever, and Oropouche can overlap
- Zika, Chikungunya, Yellow Fever
 - Latin America, Sub-Saharan Africa, Southeast Asia
 - Same vector (*Aedes mosquito*) – city dweller, urban outbreaks
 - Incubation <2 weeks
- Oropouche
 - More limited: Central and South America (Brazil, Peru, Panama)
 - Different vector: Biting midge (*Culicoides paraensis*) and *Culex* mosquitos

Countries and territories with current or previous transmission of chikungunya, dengue, yellow fever or Zika viruses



Dengue

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Dengue



- **Cause:** Dengue virus (4 serotypes)
- **Transmission:** Aedes aegypti and A albopictus mosquitos (city dwellers, day biters)
- **Epidemiology:** Widespread in tropical/sub-tropical areas
- **Pathophysiology:** Capillary leak, thrombocytopenia → shock, hemorrhage
 - Secondary infection with different serotype ↑ risk of severe disease
- **Clinical Manifestations:**
 - **Dengue without warning signs** (“breakbone fever”):
Travel history + fever + 2 of these: rash, headache/myalgias/ocular pain, nausea/vomiting, leukopenia, positive tourniquet test
 - **Dengue with warning signs:**
As above + any of these: lethargy/restlessness, persistent vomiting, abdominal pain, fluid accumulation (ascites, pleural effusion), bleeding, hepatomegaly, ↑ Hct ↓ PLT
 - **Severe Dengue:** Plasma leakage → shock, severe bleeding, end-organ failure



Dengue

- **Clinical Phases:**

- **Febrile phase:** Lasts 2–7 days; fever, headache, myalgia, arthralgia, retro-orbital pain, rash, petechiae, + tourniquet test; most recover
- **Critical phase:** Days 4–6, lasts 24–48h; clinically defervesce, but can have warning signs; ↑capillary permeability → plasma leakage, bleeding, shock
- **Recovery phase:** Plasma leakage resolves, rapid improvement; convalescent, pruritic, desquamating rash (“islands in a sea of red”)

- **Diagnosis:**

- Clinical + travel history (<2 weeks)
- Labs: ↓WBC, ↓PLT, ↑Hct, ↑AST/ALT
- Viral PCR or antigen (NS1): 1st week
- Serologies:
 - IgM: ~4 days, convalescent tiers in 2 weeks (↑ 4-fold)
 - IgG: in primary infection, ~1 week; more useful in secondary infection (rapid ↑)



Dengue

- **Management:**

- No specific antiviral - supportive, fluid replacement
- Avoid NSAID/ASA
- RBC transfusion in severe cases
- No role for platelet transfusions

- **Prevention:**

- Vector control: Eliminate standing water
- Vaccine: Previously available for ages 9-16 in endemic areas of U.S. (Puerto Rico, American Samoa, Virgin Islands, etc) with prior dengue – not for travelers → Discontinuation announced in 2024
- Insect repellents (DEET $\geq 30\%$, picaridin $\geq 20\%$, permethrin)
- Air conditioning, mosquito nets, long sleeves and pants



Dengue Differential Diagnosis - Arboviruses

Feature	Dengue	Zika	Chikungunya	Oropouche	Yellow Fever
Vector	<i>Aedes aegypti/albopictus</i>	<i>Aedes aegypti/albopictus</i>	<i>Aedes aegypti/albopictus</i>	Biting midge (<i>Culicoides paraensis</i>), Culex mosquitos	<i>Aedes aegypti</i> , Haemagogus spp
Distribution	Tropics/subtropics globally; ↑↑ in Americas, Asia	Tropics globally	Tropics globally	Amazon basin, Central/South America; ↑ outbreak	Sub-Saharan Africa, South America; urban and sylvatic
Incubation	4–7 days	2–14 days	1–14 days	3–10 days	3–6 days
Fever pattern	Sudden high fever, biphasic possible	Low-grade or absent	Sudden high fever	Sudden high fever, biphasic possible	Biphasic: initial high fever, remission, then severe
Rash	Maculopapular, petechiae , islands of sparing in recovery	Maculopapular , pruritic	Maculopapular	Maculopapular	Rare, maybe transient maculopapular or petechial
Arthralgia/myalgia	↑↑ Myalgia , arthralgia less	Mild myalgia/arthralgia	↑↑ Polyarthralgia and myalgia, often severe/chronic	Mild myalgia/arthralgia	Mild myalgia/arthralgia
Neurological complications	Rare	Guillain-Barré	Rare	Aseptic meningitis/encephalitis , Guillain-Barré	Rare
Hemorrhagic complications	Common in severe cases	Rare	Rare	Rare	Common in severe cases
Lab features	↓ WBC, ↑ Hct , ↓↓ PLT , ↑ LFTs	Mild leukopenia, normal PLT, mild transaminitis	Mild leukopenia, normal PLT, mild transaminitis	Mild leukopenia, normal PLT, Mild transaminitis	↓ WBC, ↓ PLT , ↑↑ LFTs
Vaccine	No (Dengvaxia limited)	No	No	No	Yes (live attenuated)
Pregnancy risk	Increased risk of severe disease; fetal loss if severe	Congenital microcephaly , other congenital defects	Rare	Fetal loss, congenital defects (emerging data)	Increased risk of severe disease; fetal loss if severe

Dengue Differential Diagnosis - Malaria

- Malaria always on the differential – can't miss!; overlapping features

Feature	Dengue	Malaria
Pathogen	Flavivirus (RNA virus); 4 serotypes	Plasmodium protozoan parasite
Vector	<i>Aedes aegypti</i> mosquito	<i>Anopheles</i> mosquito
Biting setting	Daytime / dusk biter; more urban	Night biter (dusk to dawn); more rural
Incubation	4-7 days (up to 14)	Usually >7 days ; <i>P. falciparum</i> usually ≤ 1 month; <i>P. vivax/ovale</i> can relapse months–years later
Classic symptoms	Abrupt high fever, "breakbone" myalgia , arthralgia , retro-orbital headache, rash (maculopapular/petechial → erythematous)	Fever $\pm$ paroxysms/chills, headache, malaise; often nonspecific; no rash
Key labs	Leukopenia , thrombocytopenia , transaminitis, hemoconcentration	Thrombocytopenia, hemolytic anemia , hyperbilirubinemia /↑LDH; parasites on smear
Severe disease	Plasma leakage, shock, bleeding – during defervescence (critical phase, days ~4–7); risk ↑ with 2nd heterologous serotype	Severe <i>P. falciparum</i> : cerebral malaria, ARDS, AKI, severe anemia, hypoglycemia, acidosis
Diagnosis	NS1 antigen (early), IgM/IgG serology, PCR	Blood smear (thick + thin) is gold standard; rapid antigen test

Case 1



A 50-year-old woman presents with 1 day of fever, headache, and myalgias. She returned 6 days ago from a 2-week trip to the Brazilian Amazon with numerous mosquito bites. She is from Brazil and had prior chikungunya infection and received the yellow fever vaccine. She took atovaquone–proguanil prophylaxis, stopping 3 days after return. Exam shows T 39.1°C, no hemodynamic instability, and a petechial rash on the lower extremities. Labs: WBC 3,400/ μ L, Hgb 9 g/dL, platelets 33,000/ μ L, AST 198 U/L, ALT 145 U/L, normal bilirubin. Which is true about the **most likely** diagnosis?

- A. Malaria
- B. Dengue**
- C. Zika
- D. Chikungunya
- E. Yellow Fever



Dengue

- 
- ✓ Diagnosis from clinical suspicion (history, exam, labs) + travel <2 wks
 - ✓ Confirmatory tests take long
 - ✓ Learn warning signs
 - ✓ Dengue, Zika, Chikungunya, Oropouche overlap in many ways
 - ✓ It can get better before it gets worse
 - ✓ Treatment supportive, fluids most important, avoid NSAID/ASA

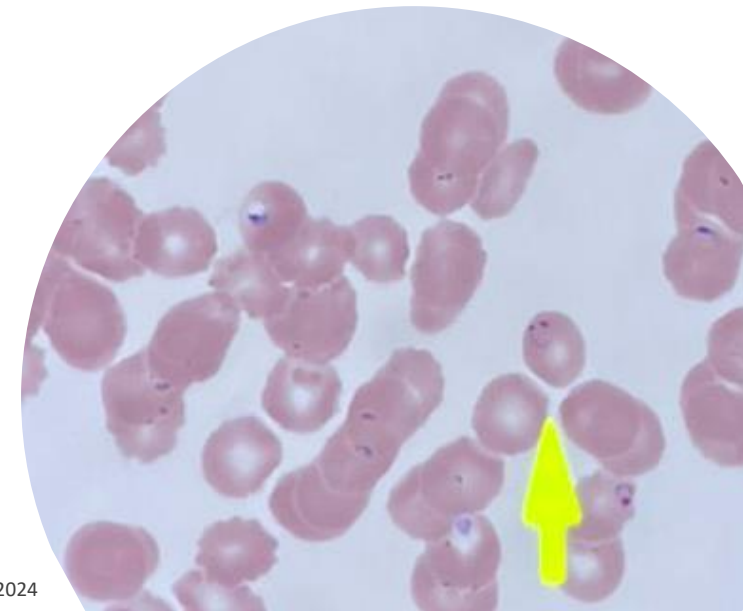


Case 2



A 32-year-old female with no significant medical history presents with 2 days of fevers, headaches, nausea, abdominal pain, and diarrhea. She returned 1 week ago from a month in Nigeria to visit friends and relatives. She moved from Nigeria to the US around 20 years ago. She took atovaquone-proguanil as prescribed. She is febrile to 38.4°C, but hemodynamically stable. On exam she is diaphoretic, with mild icterus, and abdominal palpation is uncomfortable. Laboratory results show WBC 9,000 μ L, Hgb 6.3 g/dL, platelets 85,000/ μ L, AST 51 U/L, ALT 62 U/L, total bilirubin 2.9 mg/dL, and direct bilirubin 1.2 mg/dL. Blood smear is shown. What is the **first-line initial treatment**?

- A. Oral artemether-lumefantrine or atovaquone-proguanil
- B. Quinine + doxycycline/tetracycline/clindamycin
- C. Oral doxycycline
- D. Intravenous artesunate + artemisinin combination therapy
- E. Exchange transfusion



Malaria



Malaria

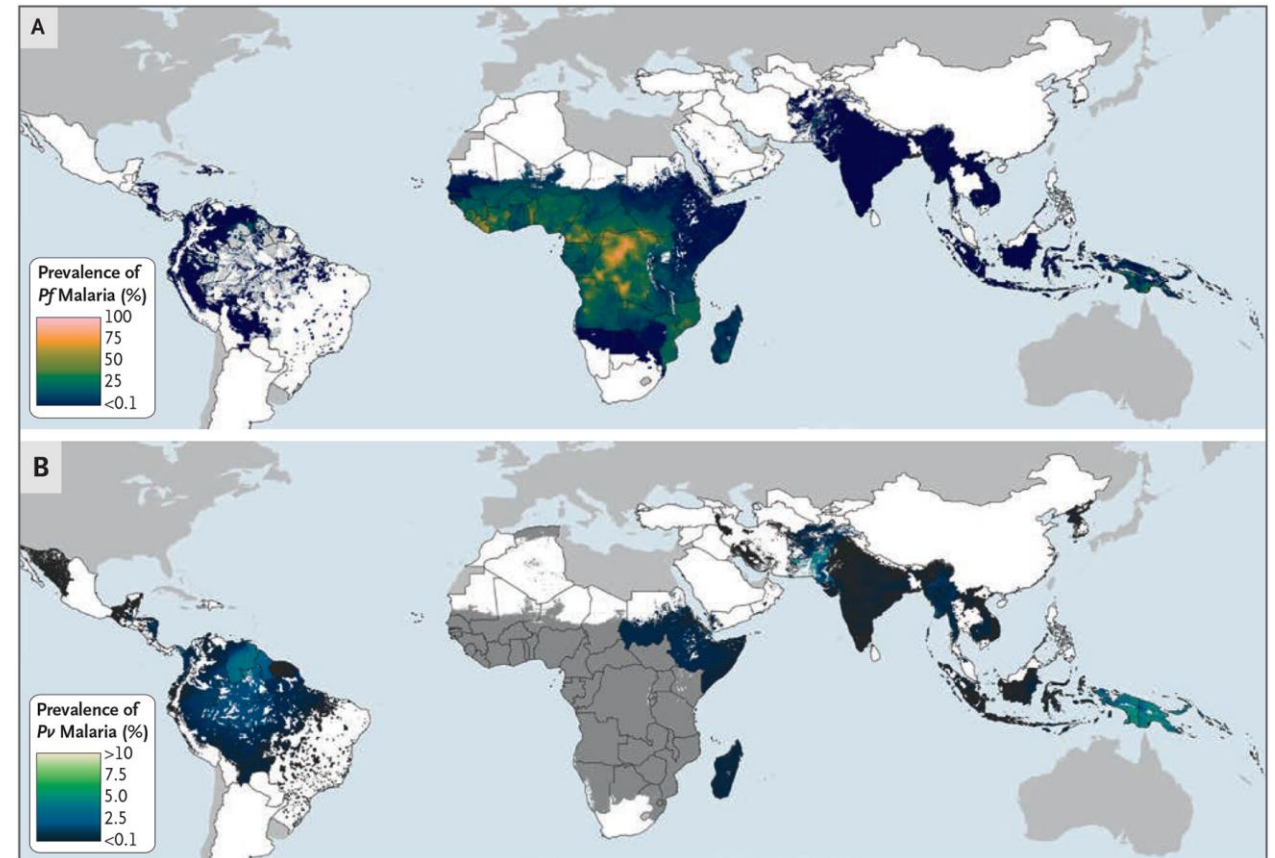
- **Cause:** Parasite *Plasmodium* spp (*P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, *P. knowlesi*)
- **Transmission:** Anopheles mosquito; rarely blood transfusion, transplant, congenital
- **Epidemiology:** Endemic in Latin America, Sub-Saharan Africa, South Asia
- Malaria is the most common tropical infection diagnosed in febrile travelers from Africa (especially *P. falciparum* in Sub-Saharan)



Distribution of
P. falciparum

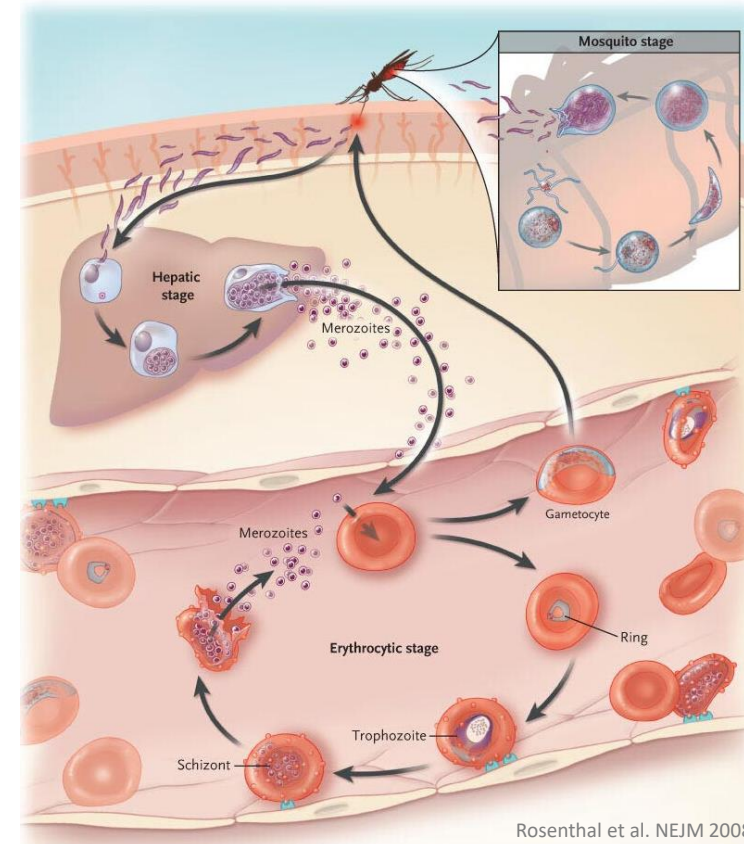
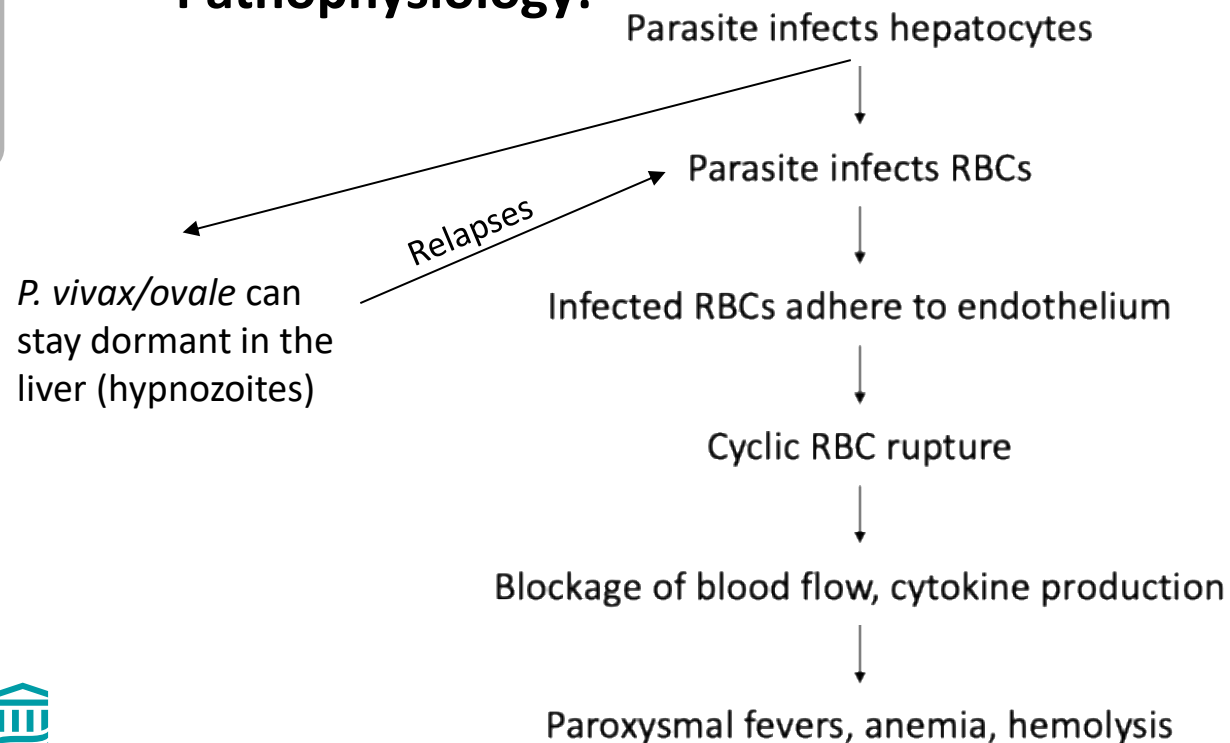
Distribution of
P. ovale

Distribution of
P. vivax



Malaria

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- Malaria is the most common tropical infection diagnosed in febrile travelers from Africa (especially *P. falciparum* in Sub-Saharan)
- **Pathophysiology:**



Malaria

- **Clinical Manifestations:**

- Fevers (cyclical), myalgias, headache, abdominal pain, diarrhea, cough
- Physical exam: diaphoresis, pallor, jaundice, splenomegaly
- Labs: hemolytic anemia, hyperbilirubinemia, WBC ↓/normal, thrombocytopenia, transaminitis

- ⚠️ Think malaria in anyone with fever + travel to endemic area (≤ 1 year, especially ≤ 1 month)
- ⚠️ *P. falciparum* is a medical emergency (rapid progression, ↑parasitemia) → hospital referral

⚠️ **Severe *P. falciparum* Malaria** (parasitemia + one of the following)

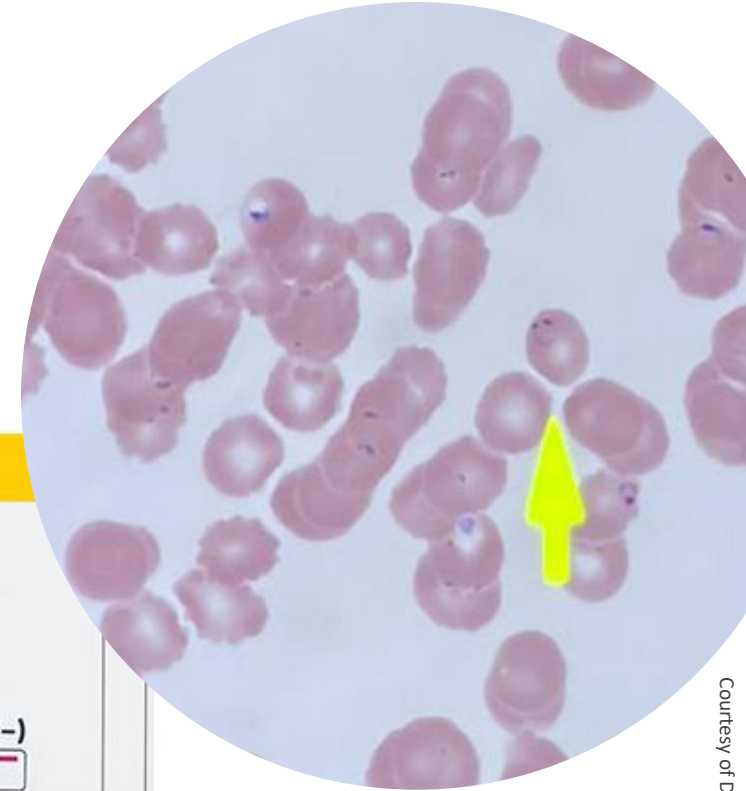
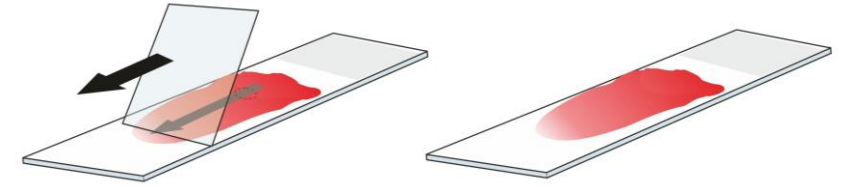
Impaired consciousness	Hyperparasitemia ($>10\%$, or $\geq 5\%$ if non-immune)
Prostration	Severe anemia (Hgb <7 g/dL or Hct $<20\%$)
Multiple convulsions	Renal impairment (Cr >3 mg/dL or BUN >20 mmol/L)
Significant bleeding	Pulmonary edema
Shock	Acidosis
Jaundice	Hypoglycemia



Malaria

- **Diagnosis:**

- Microscopy: Thick and thin peripheral blood smears; gold standard
 - Speciation, parasitemia, monitoring treatment response
- Rapid diagnostic tests (RDTs):
 - If microscopy unavailable
 - One antigen for *P. falciparum* and another pan-species
 - False-negatives from low parasitemia, gene deletions
 - Can't measure parasitemia; stays positive while; so not for treatment monitoring
- If high suspicion but tests are repeat



Malaria Treatment



	Scenario	First-line	Alternatives / key notes
Uncomplicated	<i>P. falciparum</i> (or species unknown), chloroquine-resistant area	Artemisinin combination therapy (ACT) Eg. artemether-lumefantrine	- Atovaquone-proguanil - Quinine + doxycycline/tetracycline/clindamycin - Mefloquine
	Chloroquine-sensitive area	Chloroquine, hydroxychloroquine	ACT if sensitivity uncertain
	<i>P. vivax</i> / <i>P. ovale</i> (blood stage)	Chloroquine	ACT if chloroquine-resistant <i>P. vivax</i> (Papua New Guinea, Indonesia)
	<i>P. malariae</i> / <i>P. knowlesi</i>	Chloroquine	
Severe malaria	Severe malaria with any species	IV artesunate + oral ACT	- Every 12h for the first 24h; start interim oral ACT; switch to full oral when parasitemia $\leq 1\%$; otherwise continue every 24h - Interim: ACT, atovaquone-proguanil, quinine, mefloquine
Hypnozoites	<i>P. vivax</i> / <i>P. ovale</i> (liver hypnozoites)	Primaquine or tafenoquine	Check G6PD first (hemolysis risk); tafenoquine is a single oral dose; avoid both in pregnancy
Pregnancy	Chloroquine-sensitive	Chloroquine	No primaquine/tafenoquine (defer treatment of <i>P. vivax</i> / <i>P. ovale</i> hypnozoites until after delivery)
	Chloroquine-resistant	Quinine + clindamycin or artemether-lumefantrine	
	Severe malaria	IV artesunate	



Malaria Treatment

Blood transfusion can be considered for Hgb <7g/dL
No benefit from exchange transfusion

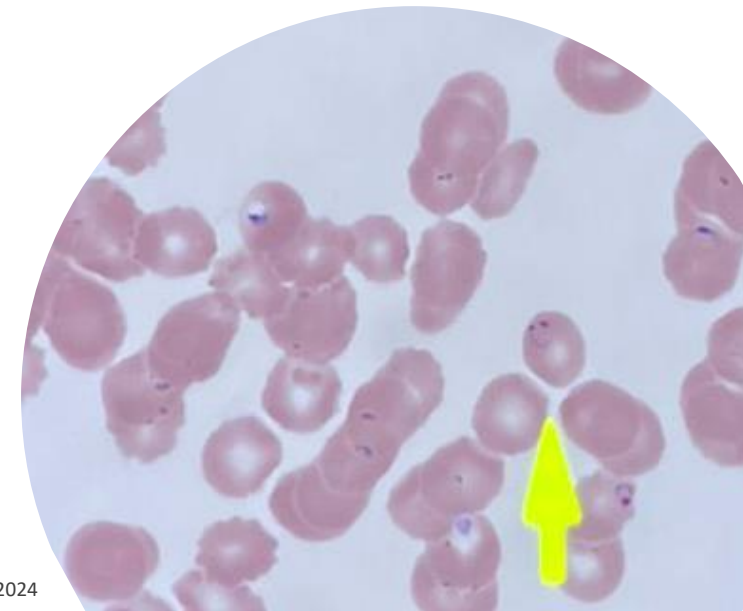
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Case 2



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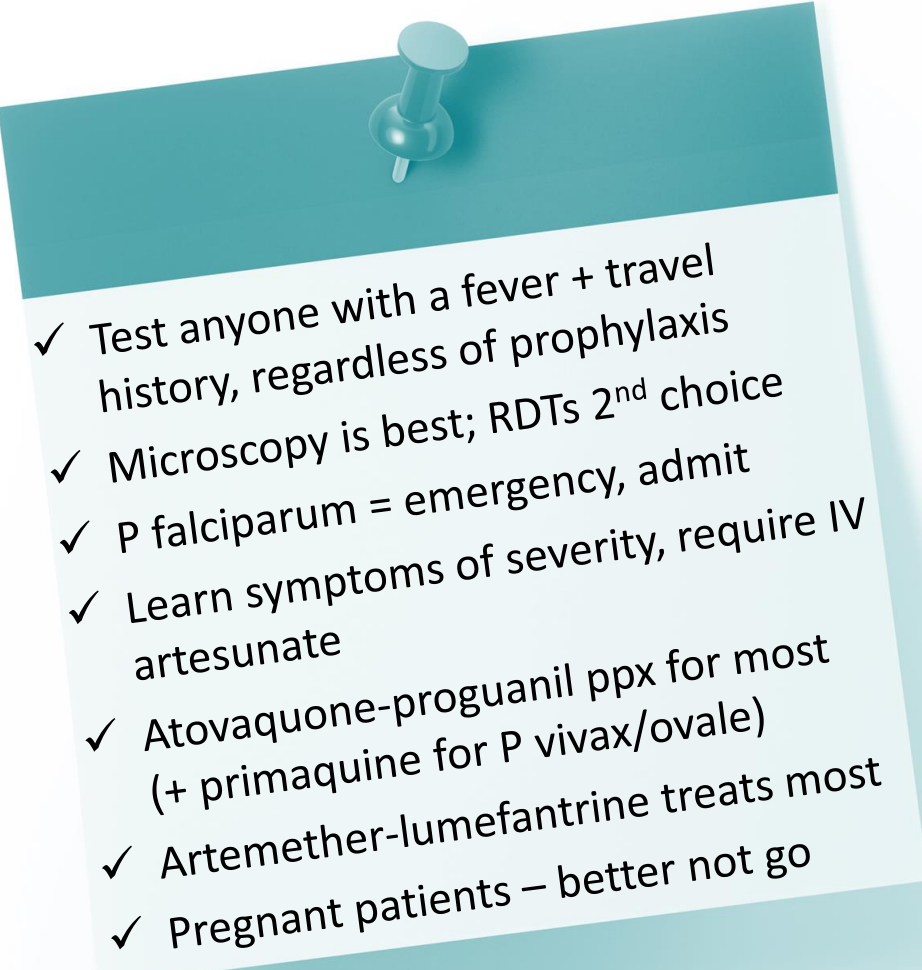
Malaria



- **Further management:**
 - *P. falciparum* is a medical emergency (rapid progression, ↑parasitemia that may seem low at first due to sequestration) → hospitalize, treat with IV artesunate
 - Blood transfusion can be considered for Hgb <7g/dL
 - No benefit from exchange transfusion
 - Follow-up
 - Daily smear for parasitemia until negative + treatment complete; more frequent as needed
 - Weekly visits with labs and smear until 4 weeks after
- **Prevention:** Vector avoidance, chemoprophylaxis; no vaccine available



Malaria

- 
- ✓ Test anyone with a fever + travel history, regardless of prophylaxis
 - ✓ Microscopy is best; RDTs 2nd choice
 - ✓ *P falciparum* = emergency, admit
 - ✓ Learn symptoms of severity, require IV artesunate
 - ✓ Atovaquone-proguanil ppx for most (+ primaquine for *P vivax*/ovale)
 - ✓ Artemether-lumefantrine treats most
 - ✓ Pregnant patients – better not go



Case 3



A 33-year-old woman is traveling to Nigeria for 3 weeks. She is 18-weeks pregnant and has a history of generalized anxiety disorder treated with sertraline. What is the best recommendation for malaria prophylaxis in this patient?

- A. Chloroquine
- B. Mefloquine
- C. Atovaquone-proguanil
- D. Doxycycline
- E. Cancel the trip



Malaria Prophylaxis



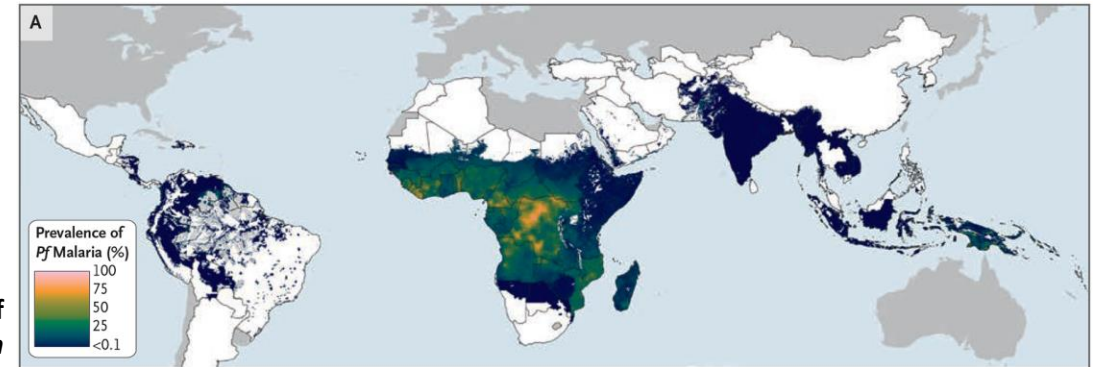
Malaria Prophylaxis

Where is the patient going?

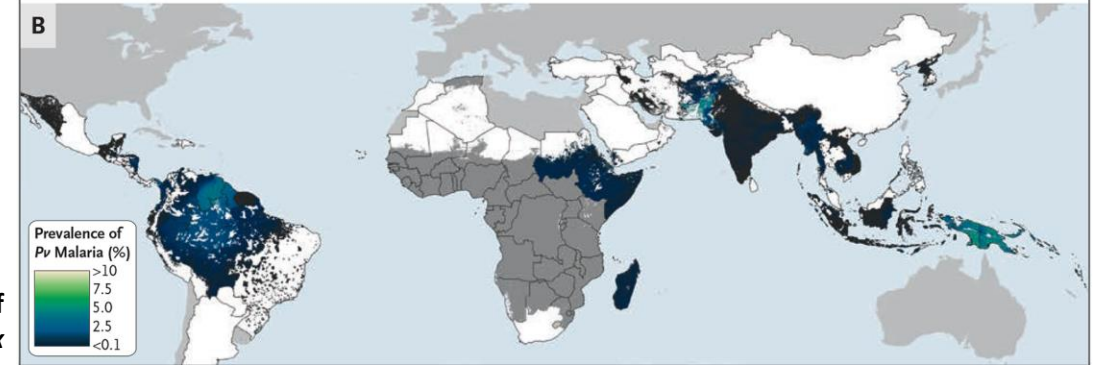
Species by region

- **Sub-saharan Africa** – *P. falciparum* (also *P. ovale* in some parts)
- **Americas** – Mostly *P. vivax*
- **Asia** – Mixed *P. falciparum* + *P. vivax*
- *P. malariae* and *P. knowlesi* more rare
 - *P. malariae* widespread; mostly Africa
 - *P. knowlesi* Southeast Asia

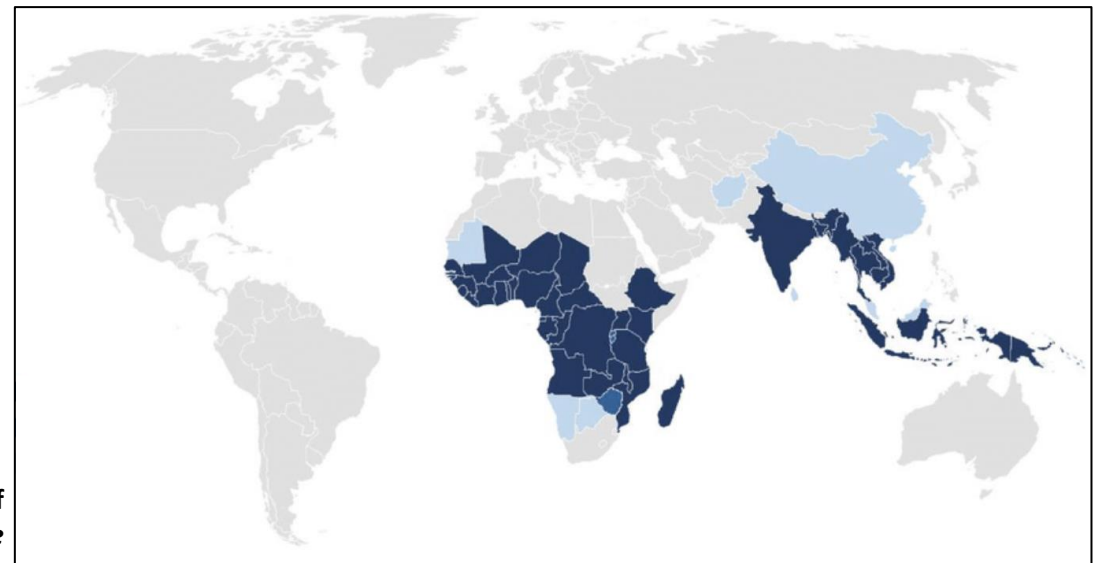
Distribution of
P. falciparum



Distribution of
P. vivax



Distribution of
P. ovale



Malaria Prophylaxis

Where is the patient going?

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- *P. malariae* and *P. knowlesi* more rare
 - *P. malariae* widespread; mostly Africa
 - *P. knowlesi* Southeast Asia

Resistance patterns

- **Chloroquine-resistance** – widespread throughout sub-Saharan Africa, most of South America, Southeast Asia, and Oceania
 - Sensitivity limited to Caribbean and Central America west of the Panama Canal
- **Mefloquine-resistance** – border regions between Thailand, Cambodia, and Myanmar

The liver hypnozoites of *P. vivax* and *P. ovale* are only targeted by primaquine or tafenoquine



Malaria Prophylaxis

Who is the patient and which agent(s) fit(s)?

Agent	Schedule	Pros	Cons	Pregnancy
Atovaquone-proguanil	Daily. Start 1-2 days before; daily there; 7 days after	Well tolerated; short post-travel course; preferred for most	Contraindicated in GFR <30 mL/min	Insufficient data
Doxycycline	Daily. Start 1-2 days before; daily there; 30 days after	Inexpensive; effective; covers some bacterial infections	Photosensitivity; GI upset	Contraindicated
Mefloquine	Weekly. Start 1-2 weeks before; weekly there; weekly for 4 weeks after	Weekly dosing; safe in pregnancy	Vivid dreams, mood changes, contraindicated in neuropsychiatric conditions; some resistance in SE Asia (Thailand, Cambodia, Myanmar borders)	Safe
Chloroquine	Weekly. Start 1-2 weeks before; weekly there; 4 weeks after	Weekly dosing; safe in pregnancy; well tolerated	Widespread resistance (sensitive <i>P. falciparum</i> in the Caribbean, Central America west of the Panama Canal); retinal toxicity	Safe
Primaquine	Daily. Start 1-2 days before; daily there; 7 days after	Effective against <i>P. vivax/ovale</i> hypnozoites	Must screen for G6PD deficiency (normal if ≥70% activity)	Contraindicated
Tafenoquine	Daily 3 days before; weekly there; once the week after			



Malaria Prophylaxis

Who is the patient and which agent(s) fit(s)?

Agent	Schedule	Pros	Cons	Pregnancy
Atovaquone-proguanil	Daily. Start 1-2 days before; daily there; 7 days after	Well tolerated; short post-travel course; preferred for most	Contraindicated in GFR <30 mL/min	Insufficient data
Doxycycline	Daily. Start 1-2 days before; daily there; 30 days after	Inexpensive; effective; covers some bacterial infections	Photosensitivity; GI upset	Contraindicated
Mefloquine			Vivid dreams, mood changes, dizziness, headache, numbness, tingling	Safe
Chloroquine			Panama Canal); retinal toxicity	Safe
Primaquine	Daily. Start 1-2 days before; daily there; 7 days after	Effective against <i>P. vivax/ovale</i> hypnozoites	Must screen for G6PD deficiency (normal if ≥70% activity)	Contraindicated
Tafenoquine	Daily 3 days before; weekly there; once the week after			

If extended time in *P. vivax/ovale* area, can consider **presumptive anti-relapse therapy (PART)**, also known as “terminal prophylaxis”, targeting hypnozoites:

- Primaquine: daily for 14 days starting after leaving the endemic area
- Tafenoquine: one single dose on day 7 after leaving the endemic area



Malaria Prophylaxis

Best for last-minute start:

- Atovaquone-proguanil, doxycycline, and primaquine (start 1-2 days before)

Options in pregnancy:

- Ideally, delay travel to malaria-endemic regions until after delivery, especially to areas with chloroquine-resistant *Plasmodium spp*
- If travel can't be avoided, then chloroquine (if no concern for resistance) or mefloquine (if no concern for neuropsychiatric illness)
- Atovaquone-proguanil is not indicated given not enough safety data
- Doxycycline (a tetracycline) is contraindicated
- Primaquine and tafenoquine are contraindicated



Case 3



A 33-year-old woman is traveling to Nigeria for 3 weeks. She is 18-weeks pregnant and has a history of generalized anxiety disorder treated with sertraline. What is the best recommendation for malaria prophylaxis in this patient?

- A. Chloroquine
- B. Mefloquine
- C. Atovaquone-proguanil
- D. Doxycycline
- E. Cancel the trip**



Malaria Prophylaxis

- 
- ✓ Atovaquone-proguanil for most
 - ✓ Mefloquine contraindicated with neuropsychiatric disease
 - ✓ Best for last minute start: atovaquone-proguanil and doxycycline
 - ✓ Primaquine/tafenoquine for primary or terminal prophylaxis of *P.vivax/ovale* areas, but G6PD first
 - ✓ Pregnancy: chloroquine or mefloquine

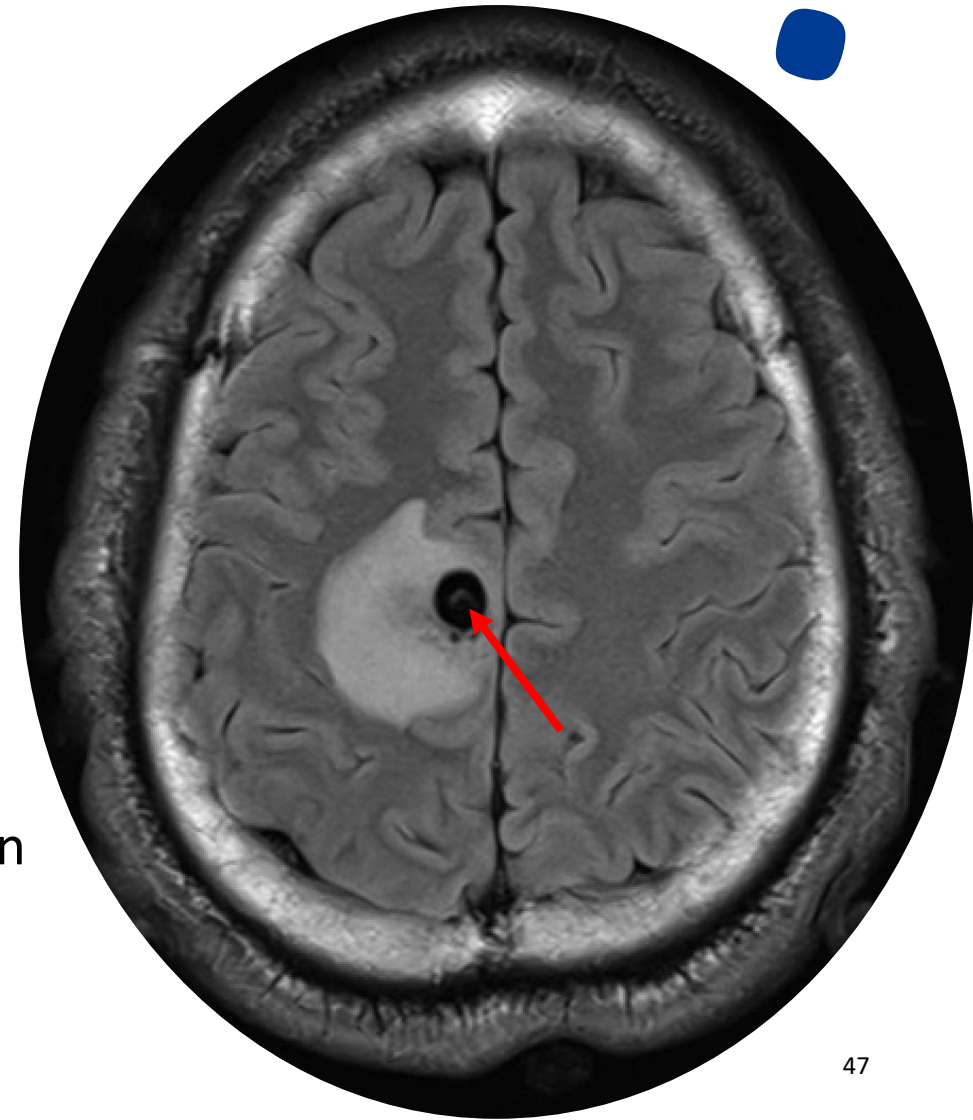


Case 4

A 27-year-old previously healthy male presents after a witnessed generalized tonic-clonic seizure. He is originally from Haiti and immigrated to the U.S. two years prior. He is afebrile and hemodynamically stable. Labs show elevated creatine kinase and transaminitis. Brain MRI is obtained.

What is **the next best step**?

- A. Neurosurgery consultation for drainage
- B. Ophthalmology consultation for dilated exam
- C. Initiate albendazole and dexamethasone
- D. Initiate praziquantel
- E. Initiate pyrimethamine, sulfadiazine, and leucovorin

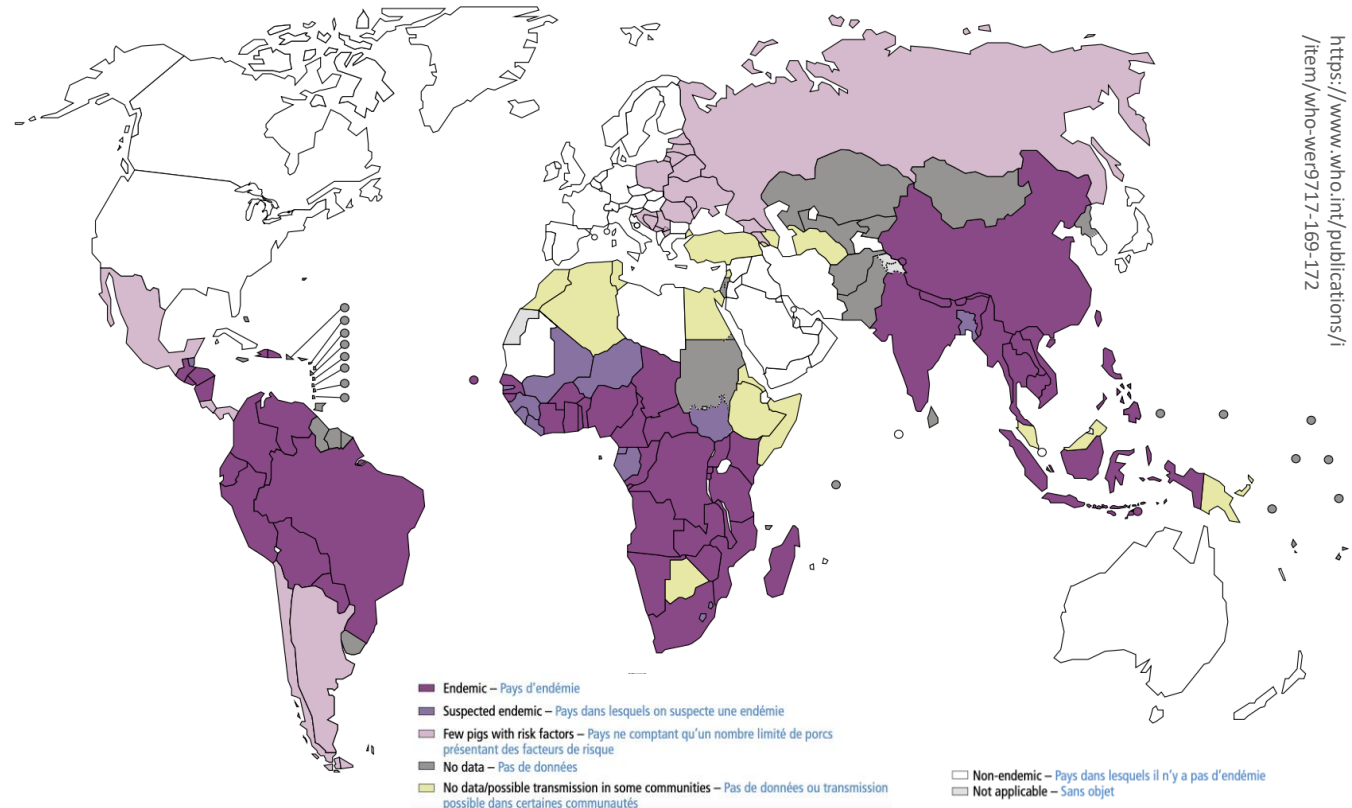
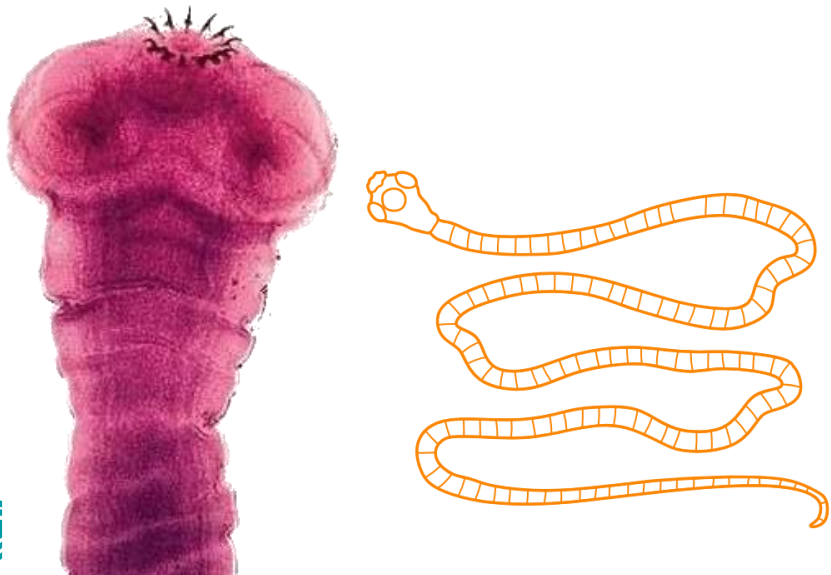


Neurocysticercosis



Neurocysticercosis

- **Cause:** *Taenia solium* (pork tapeworm) larvae
- **Transmission:** Fecal-oral ingestion of **eggs** from a tapeworm carrier (*not undercooked pork!*)
 - Ingestion of *T. solium* cysticerci in undercooked pork → intestinal taeniasis
 - Ingestion of *T. solium* eggs in contaminated foods → neurocysticercosis
- **Epidemiology:** Most common parasitic CNS infection worldwide; endemic in Latin America, sub-Saharan Africa, South/Southeast Asia
- **Risk factors:** Time in endemic areas, contacts with tapeworm



Neurocysticercosis

- Clinical Manifestations:**

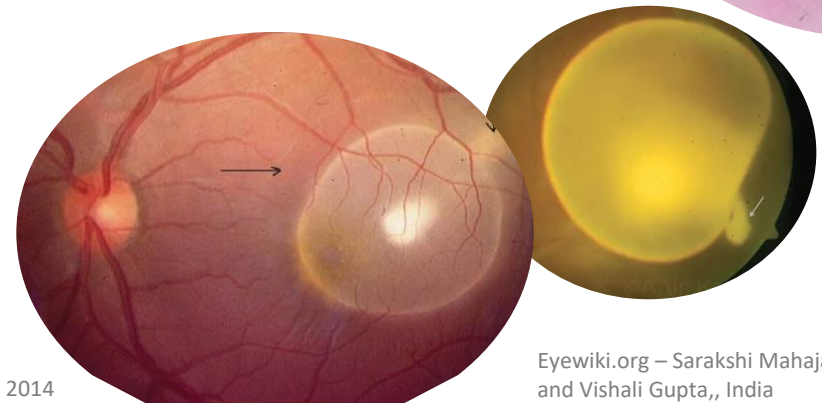
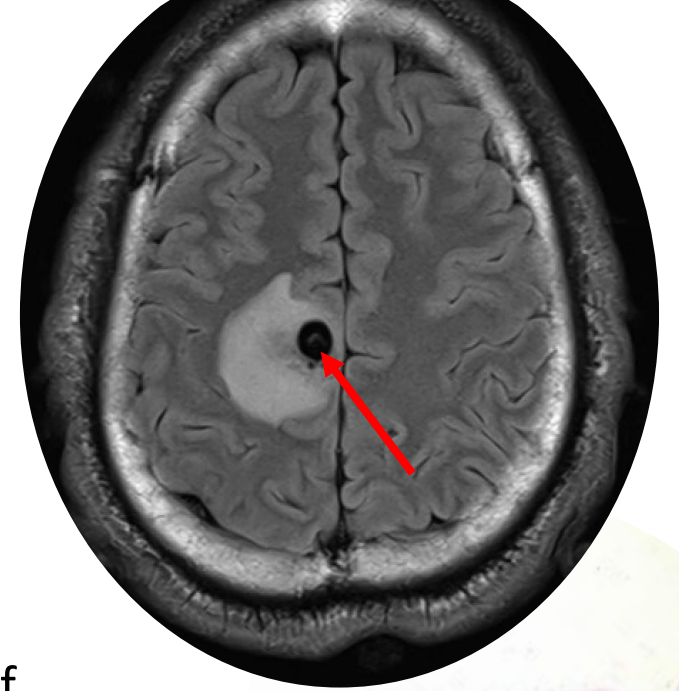
- Seizures** (most common, up to 80%) → accounts for 1/3 of seizures in endemic regions!
- Symptoms vary by number, stage, and location of cysts

	Location	Clinical Manifestation	Treatment
Parenchymal	Nonviable calcified	Seizures (80%) Headache Focal deficits Cognitive and behavioral changes	Antiepileptics only
	Single, small enhancing		Albendazole + steroids +/- antiepileptics
	Viable parenchymal		• 1-2 cysts: albendazole + steroids • >2 cysts: albendazole + praziquantel + steroids +/- antiepileptics
Extraparenchymal	Ventricular	Headache, ↑ICP (blurry vision, papilledema), obstructive hydrocephalus, nausea, vomiting, gait disturbance	- Surgical/endoscopic removal - CSF diversion (ventriculoperitoneal shunt) - Medical therapy if removal not feasible
	Subarachnoid (basal cisterns)	Arachnoiditis, vasculitis, chronic meningitis, stroke, hydrocephalus, cranial neuropathies	- CSF diversion (ventriculoperitoneal shunt) - Albendazole +/- praziquantel +/- steroids
	Spinal (subarachnoid or intramedullary)	Radiculopathy, myelopathy, arachnoiditis, paresis/paralysis	Steroids +/- antiparasitics +/- surgical removal
	Ocular / Orbital	Ocular pain, visual field defects, diplopia	Surgical removal



Neurocysticercosis

- **Diagnosis: Clinical suspicion + travel history + imaging**
 - **Imaging:** Brain MRI/CT with viable cysts (“hole with dot” classic), degenerating ring-enhancing cysts with edema, calcifications
 - If subarachnoid NCC, image spine too
 - **Serology:** Negative does not rule out!
 - *T. solium* antibody: specific, but sensitivity depends on type of disease; serum > CSF
 - *T. solium* antigen: CSF > serum; reflects viable parasite
 - *T. solium* PCR: CSF > serum
 - **CSF analysis:** lymphocytic/eosinophilic pleocytosis, ↑protein, ↓ glucose
 - Classic parenchymal lesions do not need LP (only if subarachnoid, ventricular, or uncertain)
 - **Tissue analysis**
 - **Fundoscopic exam**



Neurocysticercosis

- **Management:** Depends on stage, number, and location of the cysts

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	Ocular / Orbital	Ocular pain, visual field defects, diplopia	Surgical removal. <u>No</u> antiparasitics!



Neurocysticercosis

- 
- **Management:** Depends on stage, number, and location of the cysts
 - Calcified cyst(s): anti-epileptics
 - Viable cyst(s)
 - 1-2 cysts: albendazole + dexamethasone
 - >2 cysts: albendazole + praziquantel + dexamethasone
 - Intraventricular or intraocular cyst(s): surgical or endoscopic removal
 - Causing CSF flow obstruction: CSF diversion with ventriculoperitoneal shunt

Killing a cysticercus triggers an intense inflammatory response

Any time antiparasitics are given, give concomitant steroids to reduce inflammation as the cyst is killed

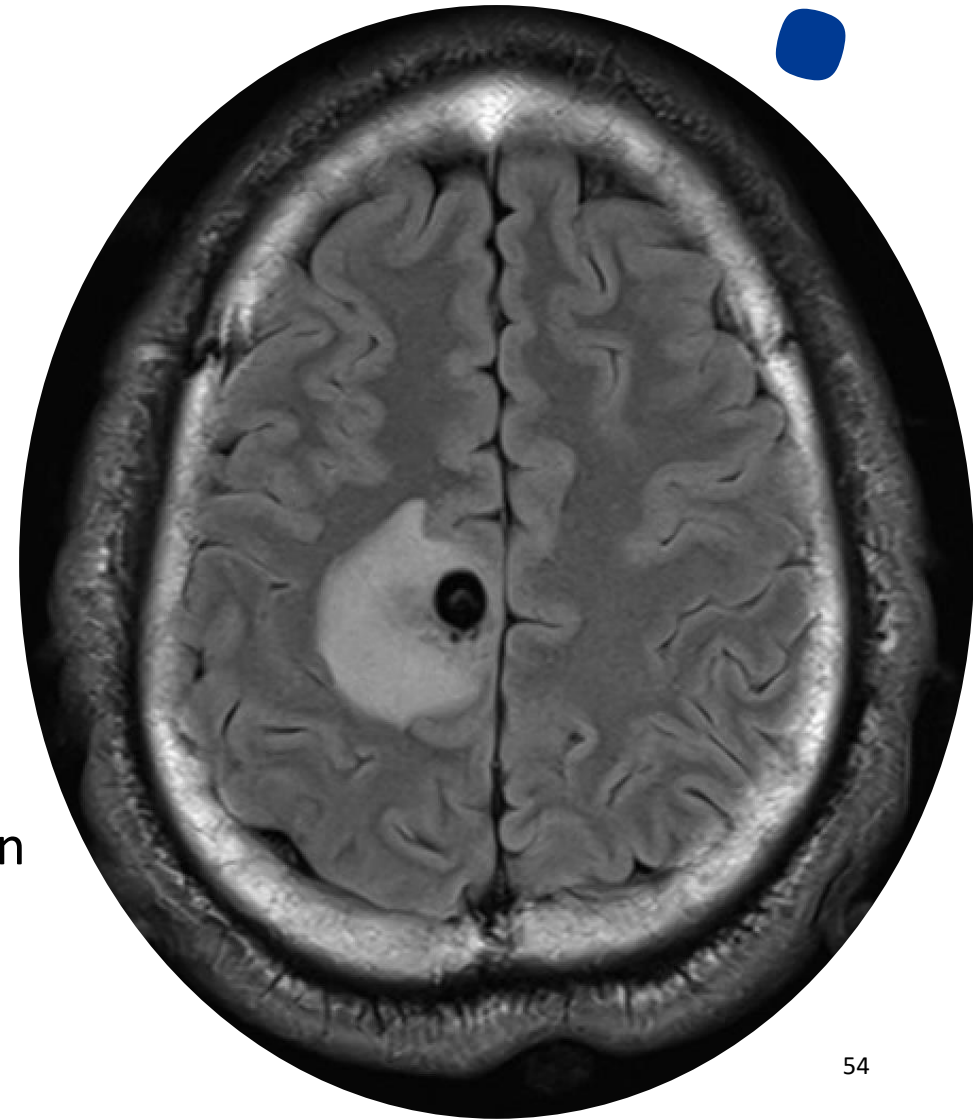


Must rule out and surgically remove intraocular cysts prior to starting antiparasitics

Case 4

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- C. Initiate albendazole and dexamethasone
- D. Initiate praziquantel
- E. Initiate pyrimethamine, sulfadiazine, and leucovorin



Neurocysticercosis

- 
- ✓ Think NCC with new-onset seizures + endemic areas
 - ✓ Imaging can sometimes be pathognomonic and enough
 - ✓ Serology does not rule it out
 - ✓ Caution with antiparasitics – often needs steroids first!
 - ✓ Screen household contacts for tapeworm (stool O&P)



Case 5



A 42-year-old man from Sierra Leone (immigrated 20 years ago) with alcohol use disorder undergoes laparotomy for a perforated, bleeding gastric ulcer. The liver appears nodular intra-operatively. He is afebrile, hemodynamically stable, with abdominal distension. Labs show eosinophilia (2,580/ μ L), ALP 262 U/L, and normal AST, ALT, and bilirubin. CT confirms a nodular hepatic contour without discrete lesions or biliary abnormalities. What is the **most likely infectious diagnosis**?

- A. Fascioliasis (*Fasciola hepatica*)
- B. Chronic liver fluke infection (*Clonorchis*/*Opisthorchis*)
- C. Echinococcosis (*Echinococcus granulosus*)
- D. Schistosomiasis (*Schistosoma mansoni*)
- E. Tuberculosis



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- D. Schistosomiasis (*Schistosoma mansoni*)**
- E. Tuberculosis

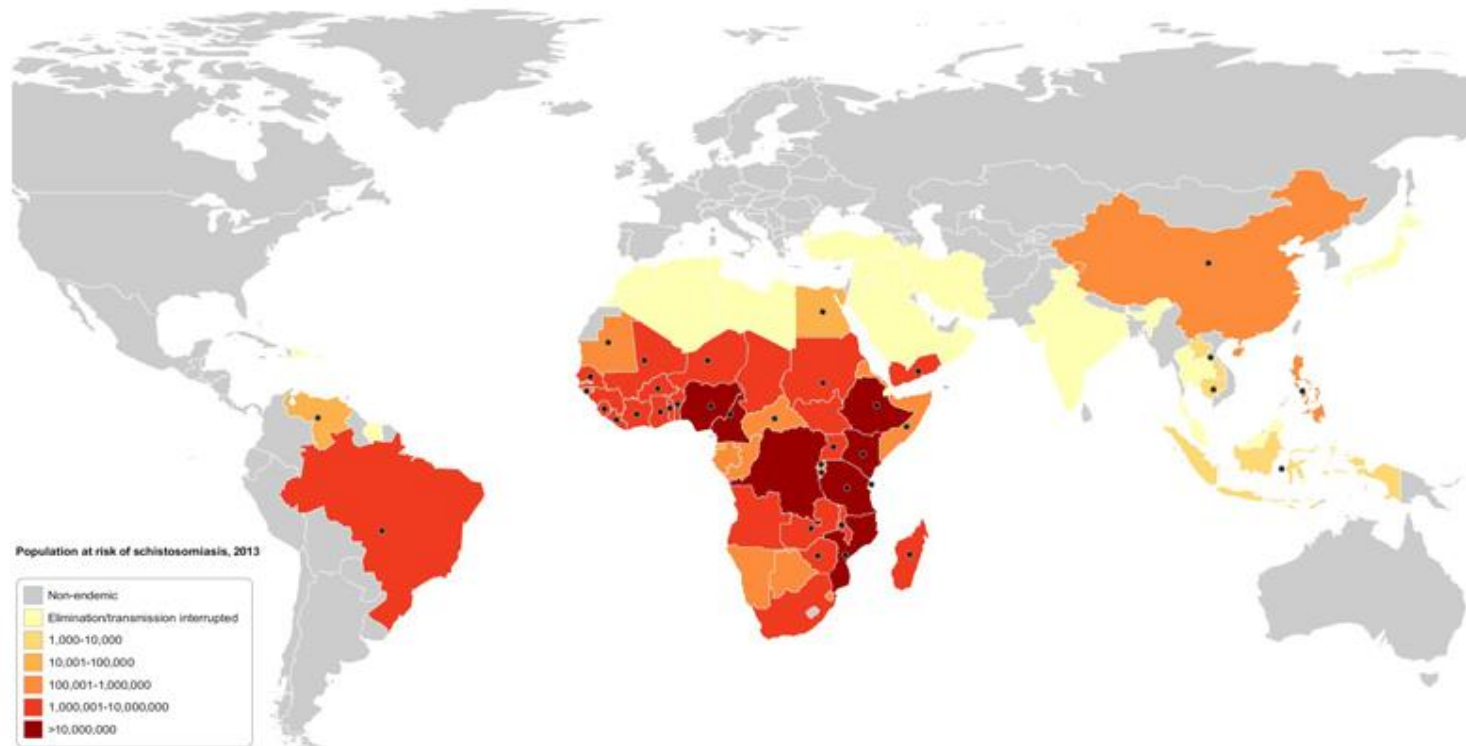


Schistosomiasis



Schistosomiasis

- **Cause:** Trematode *Schistosoma* (blood fluke); many species (*S. mansoni*, *S. haematobium*, *S. japonicum*, *S. mekongi*, *S. intercalatum*)
- **Transmission:** Skin entry by cercariae in freshwater contaminated by eggs in human urine/feces
- **Epidemiology:** Africa, Middle East, Southeast Asia, South America (Brazil, Venezuela)



Schistosomiasis

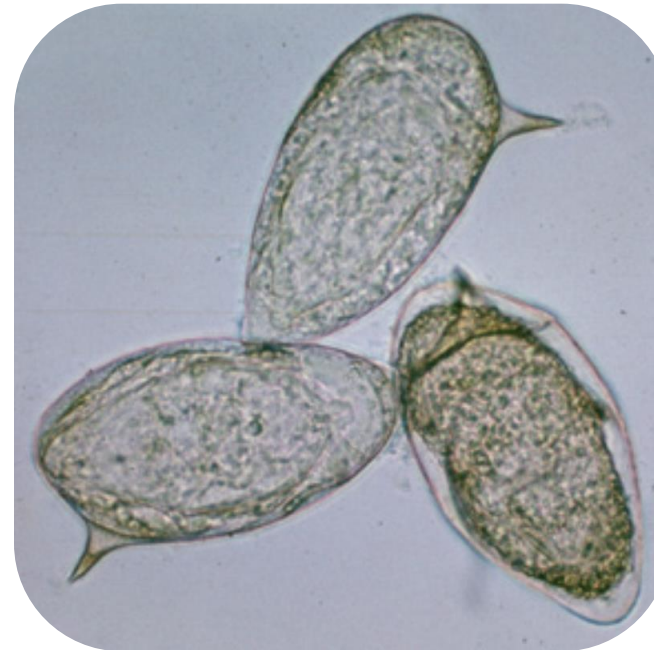
- **Pathophysiology:** Adult worms live in mesenteric/pelvic venules, live for decades, release tens of eggs → eggs spread hematogenously, trapped, trigger granulomatous inflammation, fibrosis
- **Clinical Manifestations:** Most are asymptomatic
 - **Acute infection:** exposure <12 weeks
 - Cercarial dermatitis: “Swimmer’s itch”, hypersensitivity to non-human *Schistosoma*
 - Katayama fever: Fever, urticaria, cough, diarrhea, eosinophilia
 - **Chronic disease:** ≥12 weeks to years; prolonged exposure, migrants
 - **Intestinal:** Abdominal pain, diarrhea, bowel strictures, ulcerations
 - **Hepatosplenic:** Periportal fibrosis, portal HTN, nodular hepatomegaly, splenomegaly
 - **Urogenital:** Hematuria, bladder fibrosis, polyps, risk of SCC, infertility
 - Other sites: CNS, pulmonary

Species	Region	Manifestation
<i>S. mansoni</i>	Sub-Saharan Africa (Nigeria), South America (Brazil), Caribbean, Middle East	Intestinal tract, hepatosplenic
<i>S. haematobium</i>	Sub-Saharan Africa, Middle East	Urogenital tract, CNS (spinal cord)
<i>S. japonicum</i>	Asia (China, Indonesia, Philippines)	Intestinal tract, hepatosplenic, CNS (cerebral)
<i>S. mekongi</i>	Asia (Cambodia, Laos)	Intestinal tract, hepatosplenic
<i>S. intercalatum</i>	Central and West Africa	Intestinal tract, hepatosplenic

Schistosomiasis

- **Diagnosis:**

- **Serologies:** Non-endemic areas; ≥ 12 weeks after infection; not species-specific; stay +
- **Detection of eggs:** Endemic areas; ≥ 12 weeks after infection; stool or urine
- **Labs:** Eosinophilia ($\pm$), thrombocytopenia (splenomegaly), LFTs usually normal
- **Imaging** (US, CT, MRI): periportal fibrosis, nodular liver, splenomegaly, bladder masses
- **Histopathology:** Granulomas, eosinophils surrounding eggs
- Not routinely used: Urine/serum antigen, PCR



www.cdc.gov/dpdx/schistosomiasis/index.html



Schistosomiasis

- **Treatment:**

- Praziquantel 40 mg/kg x1, repeat in 6-12 weeks – only kills the adult worms
- Katayama fever may require steroids
- If asymptomatic treat to prevent complications
- Manage sequelae (portal hypertension, hematuria, etc); may not reverse with anthelmintics

- **Prevention:**

- Avoid swimming/wading in freshwater in endemic areas
- Screen immigrants/travelers if high risk or eosinophilia

- **Follow-up:**

- Clinical symptoms
- Eosinophilia: May worsen first, then improve
- Egg microscopy: After 12 weeks
- Serology stays +
- Imaging: Abnormalities may not reverse



Schistosomiasis

- 
- ✓ ≥ 12 weeks to detect eggs and Ab
 - ✓ Chronic disease from immune reaction to trapped eggs (includes intestinal, hepatosplenic, urogenital)
 - ✓ Screen migrants and travelers if $\uparrow$ exposure or eosinophilia
 - ✓ Praziquantel kills worms, prevents more eggs, may not reverse damage
 - ✓ Ab remains + , no test of cure



Schistosomiasis + **BONUS**

- **Positive Strongyloides antibody screening**

		INFECTIOUS DISEAS...
Positive !	09/17/24	Strongyloides Ab, IgG



✓ Remember to screen for other endemic conditions!

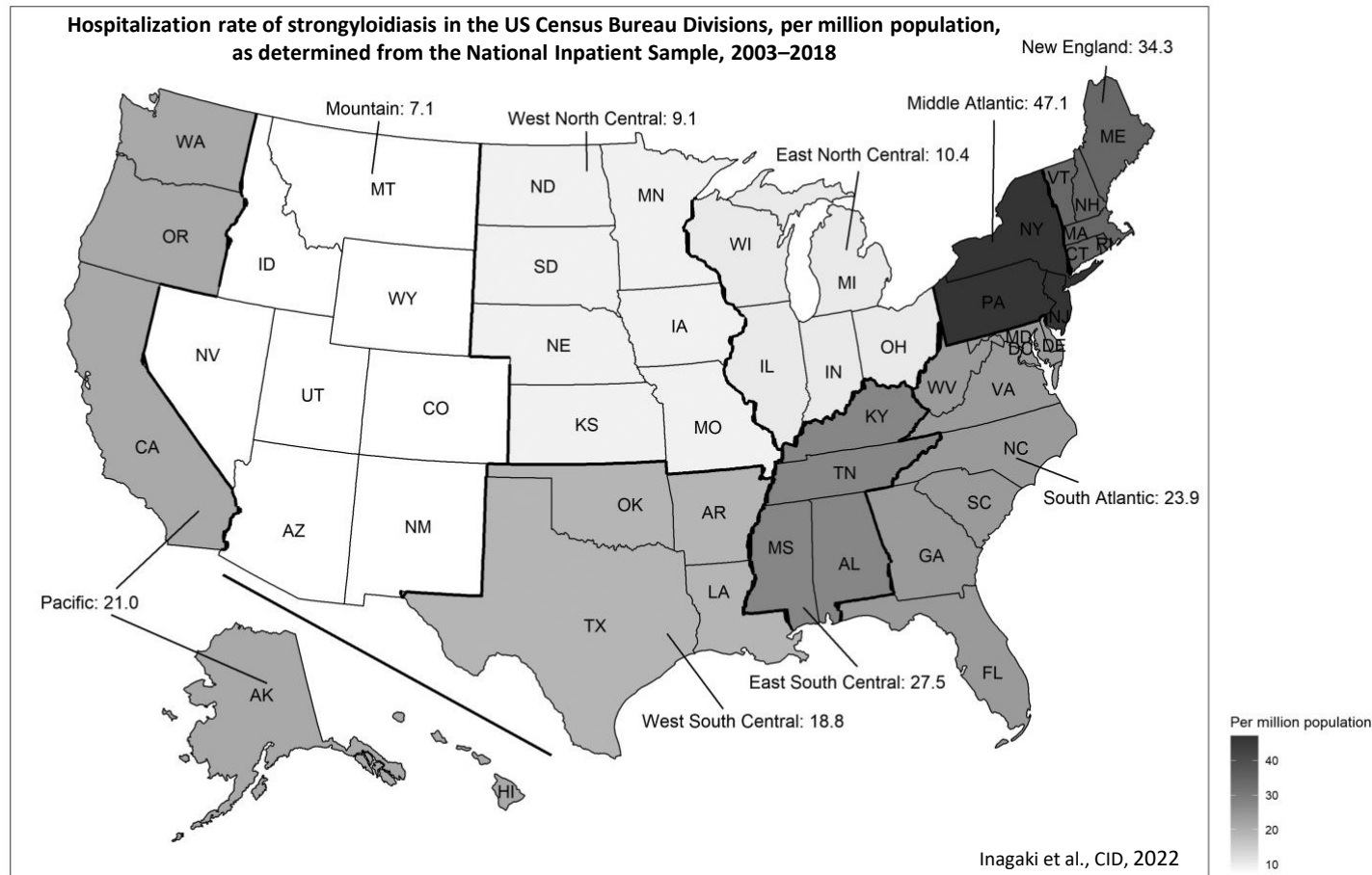


Strongyloidiasis



Strongyloidiasis

- **Cause:** Parasite *Strongyloides stercoralis* (intestinal nematode)
- **Transmission:** Skin penetration by larvae in contaminated soil, walking barefoot
- **Epidemiology:** Tropics/subtropics; parts of the U.S. (Appalachian region)



Strongyloidiasis

- **Pathophysiology:** Larvae penetrate skin → migrate via blood to lungs → ascend and are swallowed → mature in small intestine → new larvae shed in stool or re-enter through bowel/perianal skin (autoinfection, lifelong)
- **Clinical Manifestations:**
 - Most asymptomatic
 - **Acute:** Itchy serpiginous rash (“larva currens”), GI upset, cough/wheeze (Loeffler-like)
 - **Chronic:** On/off diarrhea, abdominal pain, eosinophilia
 - **Hyperinfection syndrome:** In immunosuppressed (steroids, HTLV-1, transplant > HIV, malnutrition) → disseminated infection, **Gram-negative bacteremia**, sepsis, usually without eosinophilia



Strongyloidiasis

- **Diagnosis:**
 - Stool exam: Low sensitivity (larvae, not eggs)
 - Serology (**Strongyloides IgG**): Most sensitive for screening
 - Eosinophilia: Common but may be absent in severe disease
- **Treatment:**
 - **Ivermectin** 200 mcg/kg daily for 1-2 days
 - Repeat in 2 weeks if immunocompromised
 - Alternative: Albendazole (less effective)



Screen patients from endemic regions for Strongyloidiasis before starting immunosuppression!
If time-sensitive, treat preemptively (don't wait for result)

Strongyloidiasis

- 
- ✓ Think Strongyloidiasis with eosinophilia or GI/pulmonary symptoms + travel history
 - ✓ Always screen before steroids or other immunosuppression
 - ✓ If time-sensitive, treat preemptively (don't wait for result)

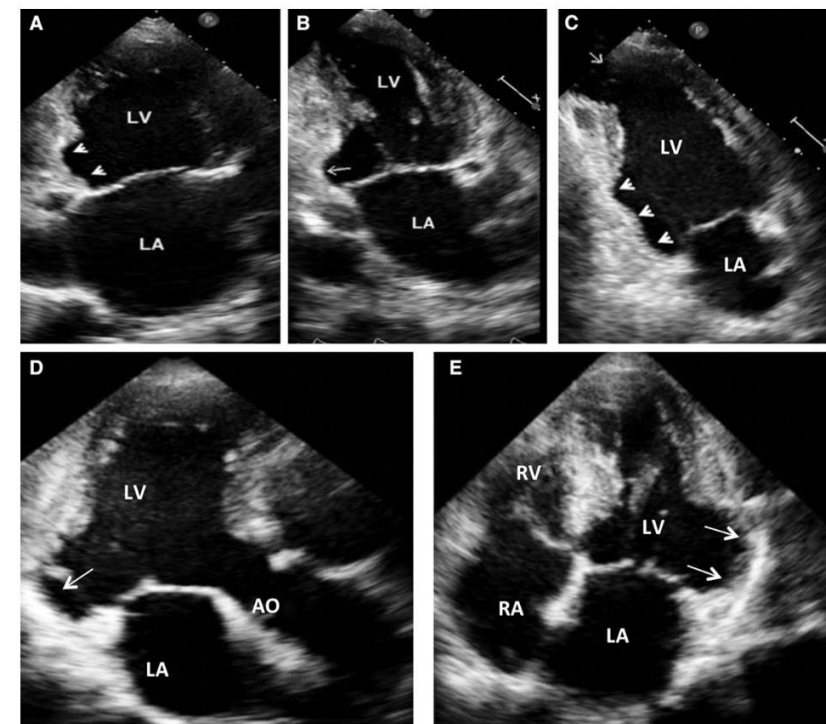


Case 6



A 36-year-old man with no past medical history presents with 6 months of progressive exertional dyspnea and leg swelling. He emigrated from El Salvador at age 16. He is afebrile and hemodynamically stable, with bibasilar crackles and bilateral pitting edema. Routine labs, including troponin, are unremarkable. Echocardiography shows a moderately dilated LV (LVEF 32%) with segmental wall-motion abnormalities in the apical and inferolateral walls, plus an apical aneurysm. The RV is mildly dilated. What is the most appropriate **next step**?

- A. Obtain *Trypanosoma cruzi* serum PCR
- B. Obtain *Trypanosoma cruzi* serologies
- C. Endomyocardial biopsy
- D. Obtain brain MRI
- E. Start empiric benznidazole therapy

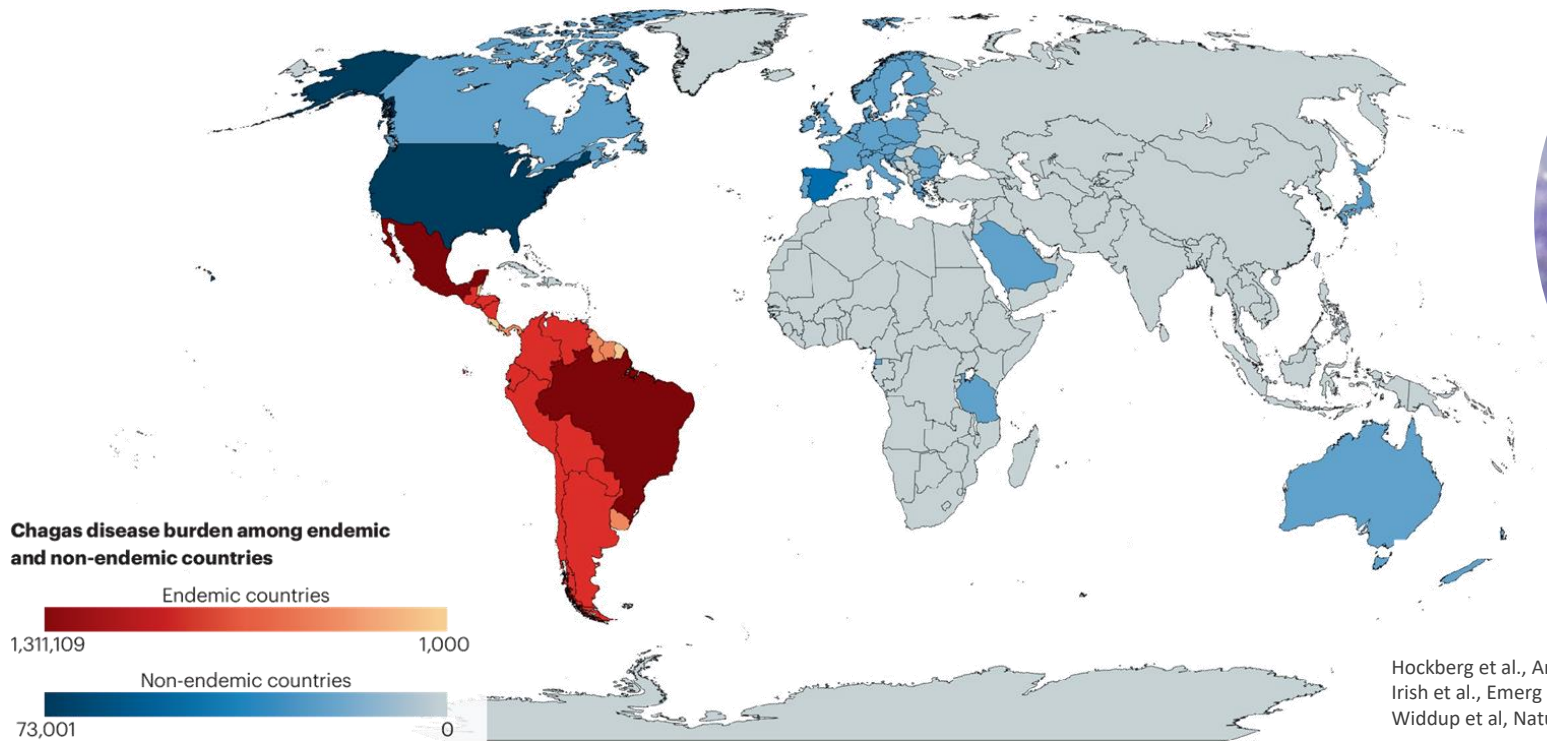


Chagas Disease (American Trypanosomiasis)



Chagas Disease (American Trypanosomiasis)

- **Cause:** *Trypanosoma cruzi* (protozoan)
- **Transmission:** Bite of the triatomine (“kissing”) bugs; congenital, blood transfusion, organ transplant, rarely contaminated food (sugar cane, açaí bowls)
- **Epidemiology:** Endemic **in** Latin America, **not** in Caribbean
 - U.S.: 288,000 infected, 57,000 Chagas cardiomyopathy, 43,000 women reproductive age
 - Most blood banks screen



Hockberg et al., Ann Intern Med, 2023
Irish et al., Emerg Infect Dis, 2022
Widdup et al, Nature Biotech, 2025



Chagas Disease (American Trypanosomiasis)

- **Clinical Manifestations:**

- **Acute:** Weeks-months
 - Often mild or **asymptomatic** (most are unaware)
 - Possible fever, lymphadenopathy, hepatosplenomegal
 - Conjunctivitis, Romaña sign (periorbital swelling)



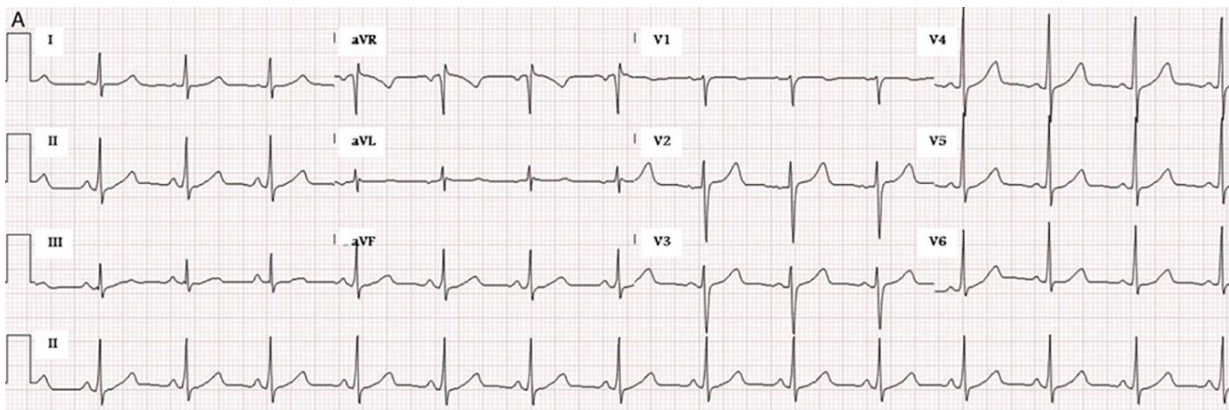
CDC/Dr. Mae Melvin



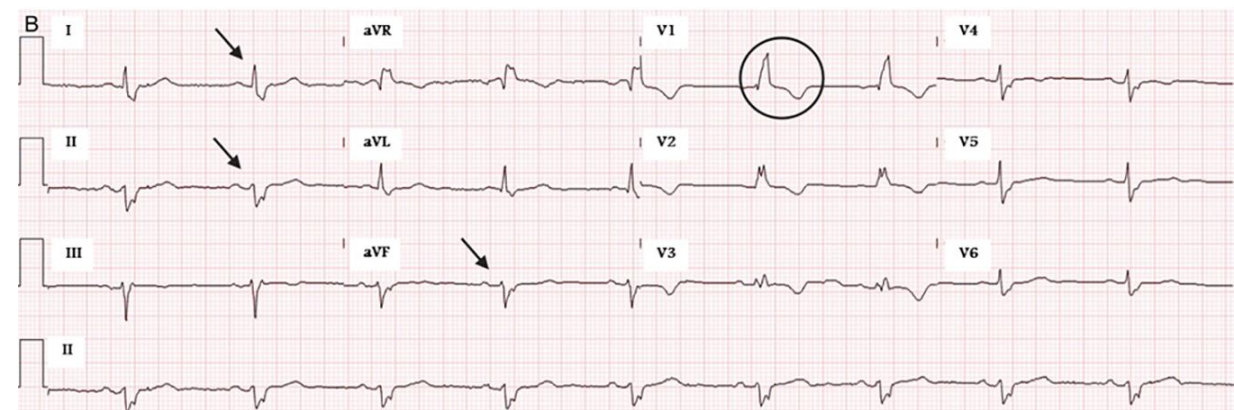
Chagas Disease (American Trypanosomiasis)

- **Clinical Manifestations:**

- **Chronic:** Develops in 20-30%, over years-decades (usually ages 30-40)
 - Subclinical in 70-80%
- **Cardiac:** arrhythmias, cardiomyopathy, heart failure, LV apical aneurysm, thrombus
 - EKG abnormalities in ~40% – RBBB, left anterior or posterior fascicular block
 - In LA, 327 prior residents of endemic areas with RBBB and LAFB → 17.9% positive for Chagas



Normal EKG



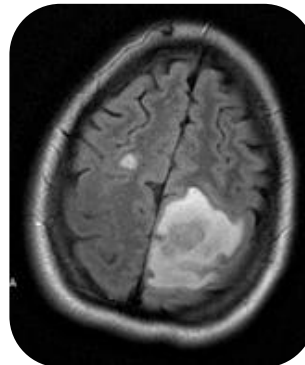
RBBB in V1 (circle) with left axis deviation in the limb leads (arrows) secondary to a left anterior fascicular block.



Chagas Disease (American Trypanosomiasis)

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 - EKG abnormalities in ~40% – RBBB, left anterior or posterior fascicular block
 - In LA, 327 prior residents of endemic areas with RBBB and LAFB → 17.9% positive for Chagas
 - **GI:** megaesophagus, megacolon
 - **CNS:** necrotizing multifocal encephalitis, mass lesions ("chagomas"); reactivation in HIV, other immunocompromise (DDx toxoplasmosis)



CDC.gov



CDC.gov; Radiopaedia.org



Chagas Disease (American Trypanosomiasis)

- **Who to screen:**

- Patients born or who lived in endemic areas ≥ 6 months
- Relatives of a seropositive case who share residence, children of seropositive mothers
- Pregnant women (congenital transmission)
- Immunocompromised
- Blood and organ donors
- Patients with evidence of exposure to the triatomine bug

- **Diagnosis:**

- Acute: blood smear, PCR
- Chronic: serology (*T. cruzi* IgG) - two different tests recommended (ELISA **plus** IFA or WB)
- *T. cruzi* serum PCR used in acute infection or reactivation. Low sensitivity in chronic disease because of low/intermittent parasitemia
- Endomyocardial not a first-line test for Chagas cardiomyopathy in the general setting



Chagas Disease (American Trypanosomiasis)

- **Management:**

- Antiparasitic: **Benznidazole** (first-line) or **nifurtimox** – watch for toxicity
 - Most effective early in disease; reduces progression and congenital transmission
 - Once advanced cardiomyopathy, no benefit [BENEFIT trial (Morillo et al., NEJM 2015)]

Treatment indicated	Treatment not indicated
○ Acute infection ○ Congenital infection ○ Reactivation ○ Age <18 ○ Women of reproductive age ○ Immunocompromised ○ Age <50 without advanced cardiomyopathy (>50 can consider)	○ Advanced cardiomyopathy ○ Pregnancy ○ Hepatic disease ○ Renal disease

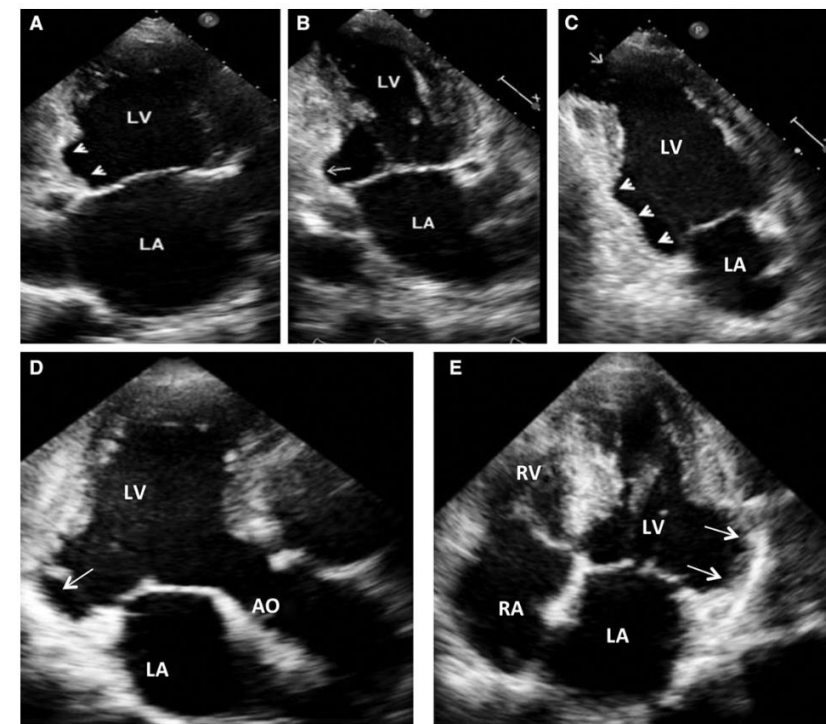


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Chagas Disease (American Trypanosomiasis)

- 
- ✓ Acute phase often missed
 - ✓ Chronic progresses over decades
 - ✓ Screen if from endemic area
 - ✓ Consider in unexplained heart failure in young patient
 - ✓ Treat if acute, young, reproductive-aged women, no advanced disease
 - ✓ No role for antiparasitics once advanced heart disease



Case 7



A 34-year-old man presents with 16 days of crampy abdominal pain and 6-8 loose stools per day streaked with blood and mucus. He returned from rural India 3 weeks ago, where he often ate street food and drank untreated well water. He is afebrile and hemodynamically stable with mild diffuse abdominal tenderness. Labs show mild leukocytosis without eosinophilia. Which of the following is the **most appropriate treatment** for the most likely diagnosis?

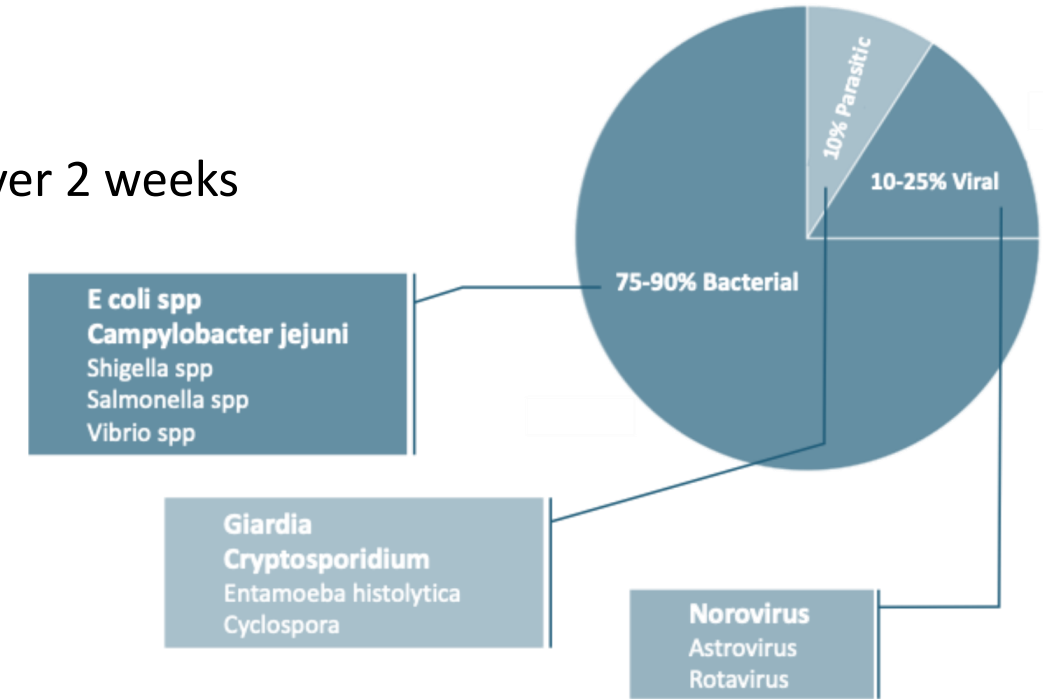
- A. Oral tinidazole
- B. Oral metronidazole followed by paromomycin
- C. Oral trimethoprim-sulfamethoxazole
- D. Oral azithromycin
- E. Oral albendazole



Traveler's Diarrhea

Traveler's Diarrhea

- Most common travel-related illness; attack rates 30-70% over 2 weeks
- Mostly mild, 3% severe
- Antibiotics ↓ duration by 1-2 days if bacterial
 - Risk of *C. diff*, colonization with resistant organisms
 - Fluoroquinolone-resistance on the rise
- Think parasites if lasting ≥14 days
- Prevention: food/water precautions, vaccination; bismuth
- Sequelae (up to 6 months): post-infectious malabsorption, lactase deficiency, bacterial overgrowth, and IBS; unmasked IBD



SEVERITY	DEFINITION	ANTIBIOTICS	NON-ANTIBIOTICS
Mild	Tolerable, does not interfere with activities	Not recommended	- Bismuth subsalicylate - Loperamide
Moderate	Distressing, interferes with activities	May be used	- Loperamide as monotherapy or as adjunct
Severe	Incapacitating , prevents activities; dysentery	Recommended	- Loperamide as adjunct; not recommended if blood or fever

ANTIBIOTIC	DOSE	NOTES
Azithromycin	1,000 mg once	Preferred , especially if dysentery or fever, or in Southeast Asia (fluoroquinolone-resistance)
	500 mg QD for 3 days	
Ciprofloxacin	750 mg once	If unresolved after 24h of single dose, initiate the 3-day regimen
	500 mg BID for 3 days	
Levofloxacin	500 mg QD for 1-3 days	If unresolved after 24h, 3 days
Rifamycin SV	388 mg BID for 3 days	If unable to receive the above. Not if invasive (<i>Campylobacter</i> , <i>Shigella</i> , <i>Salmonella</i> , etc.)
Rifaximin	200 mg TID for 3 days	

Traveler's Diarrhea – Parasitic Causes

Organism	Incubation & Exposure	Manifestations	Diagnosis	Treatment
<i>Giardia duodenalis</i> (most common)	1-3 weeks Untreated water	Non-inflammatory, malabsorptive - greasy foul stools, bloating, flatulence, weight loss; prolonged	Stool Ag/PCR; O&P x3	Tinidazole/metronidazole; nitazoxanide
<i>Entamoeba histolytica</i>	2-4+ weeks Fecal-oral, food/water	Inflammatory, invasive - gradual, bloody , mucoid; liver abscess	Stool Ag/PCR; Ab for invasive disease; abdominal US	Metronidazole/tinidazole, followed by luminal agent (paromomycin)
<i>Cryptosporidium</i>	~1 week Pools ; fecal-oral	Non-inflammatory, profuse watery; often self-limited; severe/chronic in HIV	Modified acid-fast; stool Ag/PCR	Supportive; nitazoxanide; ART in HIV
<i>Cyclospora cayetanensis</i>	1-2 weeks Imported produce	Non-inflammatory, watery, prolonged/relapsing	Modified acid-fast; PCR; request on O&P	TMP-SMX
<i>Cystoisospora belli</i>	~1 week	Non-inflammatory, watery, can be chronic; eosinophilia ; in HIV	Modified acid-fast	TMP-SMX

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- C. Oral trimethoprim-sulfamethoxazole
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Traveler's Diarrhea

- 
- ✓ Most common travel illness
 - ✓ Bacterial > viral > parasitic (suspect the latter when duration ≥ 14 days)
 - ✓ Empiric antibiotics if incapacitating or blood; azithromycin is 1st line
 - ✓ Parasites: Giardia (untreated water) > Cryptosporidium (pools) > E. histolytica
 - ✓ Think E. histolytica with contaminated food/water, bloody/mucoid stools. Treat with metronidazole/tinidazole, then luminal agent (paromomycin)



Scratching the Surface



Scratching the Surface

Ma et al., NEJM, 2016

Bohati et al., NEJM, 2015

Marty et al., NEJM, 2005

Muehlstaedt, NEJM, 2008

Richards et al., Trop Med Infect Dis, 2020

Cutaneous Larva Migrans

- Dog and cat hookworms (*Ancylostoma spp*)
- Make 25% of travel skin lesions
- Itchy creeping eruption
- Barefoot in sand
- Days to weeks after exposure
- Caribbean, Latin America, Asia
- Clinical diagnosis
- Ivermectin or albendazole
- Surgery not ideal (it migrates)



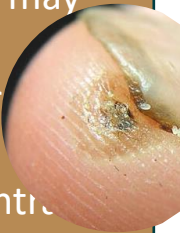
African Tick-Bite Fever

- *Rickettsia africae*, bite from *Amblyomma* tick
- Most common Rickettsial disease in travelers
- Sub-Saharan Africa (outdoors)
- One or many eschars, regional LAD, fever, myalgias, rash
- Mild-moderate, no deaths
- Often clinical diagnosis
- Doxycycline



Myiasis & Tungiasis

- **Myiasis:** Fly larvae (*Dermatobia* in Latin America, *Cordylobia* in Africa)
 - Painful, furuncles, central punctum; may feel or see larva
- **Tungiasis:** sand flea *Tunga penetrans*, burrows in soil (feet or periungual)
 - Itchy painful papules, white halo center, black dot
- Cure for both: Manual or surgical extraction



Scrub Typhus

- *Orientia tsutsugamushi*; chigger mite bites
- “Tsutsugamushi Triangle” (SE Asia)
- Necrotic eschar classic but not always
- Acute fever, headache, myalgia, rash, LAD, GI symptoms; severe → multiorgan failure
- Often clinical diagnosis
- Can be fatal; treat empirically
- Doxycycline



Take-home Messages

Approach to Travel-related Illness

- History first: frame the differential by timeline, syndrome, and geography/exposure
- ~40% of post-travel illness is non-tropical - keep common causes in mind

Nonmigrant Travelers

- Dengue is the most common tropical infection in travelers from Latin America; while malaria from Africa
- Exclude malaria in every febrile returning traveler, even on prophylaxis - thick/thin smear is the gold standard; *P. falciparum* is an emergency, severe disease (criteria) requires IV artesunate
 - Chemoprophylaxis: atovaquone-proguanil for most; in pregnancy better cancel (or chloroquine/mefloquine)
- Know dengue warning signs - it can worsen as the fever breaks; treat supportively, avoid NSAIDs/ASA

Migrants & Immigrants

- Screen and consider treatment for asymptomatic infection if from endemic areas: Strongyloides (especially before immunosuppression), Schistosomiasis, Chagas
- New-onset seizure → think neurocysticercosis (get ophthalmology consult)
- Unexplained cardiomyopathy → think Chagas (think first if treatment indicated)



Look for these!



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Thank you

Carolina Geadas
cgeadas@bwh.harvard.edu