

# Wait, I can catch a tropical disease in America?

Chris Baliga, MD

Infectious Diseases

March 8, 2024

# Objectives

- Understand the epidemiology, clinical features, diagnosis, and treatment of malaria
- Understand the epidemiology, clinical features, diagnosis, and treatment of dengue
- Understand the epidemiology, clinical features, diagnosis, and treatment of Angiostrongyliasis
- Understand the epidemiology, clinical features, diagnosis, and treatment of Melioidosis

# Disclosures

- None

# Is America ready for a new wave of tropical diseases?



By Carrie Arnold, MOSAIC

Updated 5:57 AM EDT, Thu August 13, 2015



# Is America ready for a new wave of tropical diseases?



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The New York Times

## U.S. Sees First Cases of Local Malaria Transmission in Two Decades

Five people, four in Florida and one in Texas, have acquired malaria in the United States in recent months.

By Emily Anthes

Published June 27, 2023 Updated July 3, 2023



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# Dengue will 'take off' in southern Europe, US, Africa this decade, WHO scientist says

By Jennifer Rigby

October 6, 2023 7:09 AM PDT · Updated a month ago





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Volume 29, Number 10—October 2023

*Dispatch*

### *Angiostrongylus cantonensis* Infection in Brown Rats (*Rattus norvegicus*), Atlanta, Georgia, USA, 2019–2022

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**Infectious Disease Experts Warn: Brace for Yellow Fever Resurgence in U.S.**

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# Bacteria that causes rare, serious illness melioidosis is endemic in parts of Mississippi Gulf Coast, CDC says

By Virginia Langmaid, CNN

Updated 11:14 PM EDT, Wed July 27, 2022

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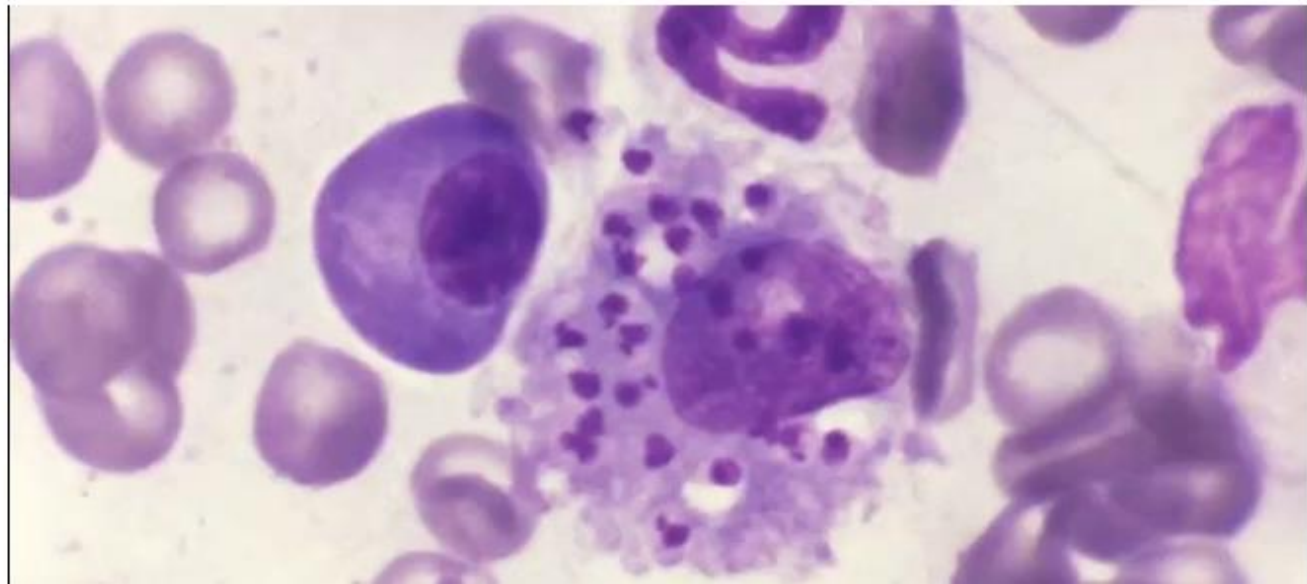
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## Tropical disease now endemic in U.S., CDC says. Imported dogs could bring deadlier form

 **Eduardo Cuevas**  
USA TODAY

Published 1:39 p.m. ET Oct. 19, 2023 | Updated 1:54 p.m. ET Oct. 20, 2023



# Classic: Case Files from Virginia Mason

- 43 year old surgeon returns from a trip to Laos. She taught at the university hospital in Vientiane, but did travel to rural areas as a tourist. She ate mostly the food provided by the NGO that sent her, but did occasionally eat out (mostly at tourist restaurants). Lots of mosquito bites.
- 1 week after returning develops high fevers, chills, nausea, diarrhea. She has severe myalgias and says “it hurts in my bones.”

# New: Case Files from Virginia Mason

- 43 year old surgeon returns from a trip to California. She went to Disneyland for 3 days and then visited family in Long Beach.
- 1 week after returning, she and her son develop high fevers, chills, nausea, diarrhea. She has severe myalgias and says “it hurts in my bones.”
- COVID test was negative

# New: Case Files from Virginia Mason

- 43 year old surgeon returns from a trip to Florida. She went to Disney World for 3 days and then visited family in Miami.
- 1 week after returning, she and her son develop high fevers, chills, nausea, diarrhea. She has severe myalgias and says “it hurts in my bones.”
- COVID test was negative

# What to know about dengue as cases are reported in Florida

By Amanda Musa, CNN

Published 6:47 AM EDT, Fri August 18, 2023



**AP**



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U.S. NEWS

## California officials confirm 2 cases of dengue, a mosquito-borne illness rarely transmitted in US

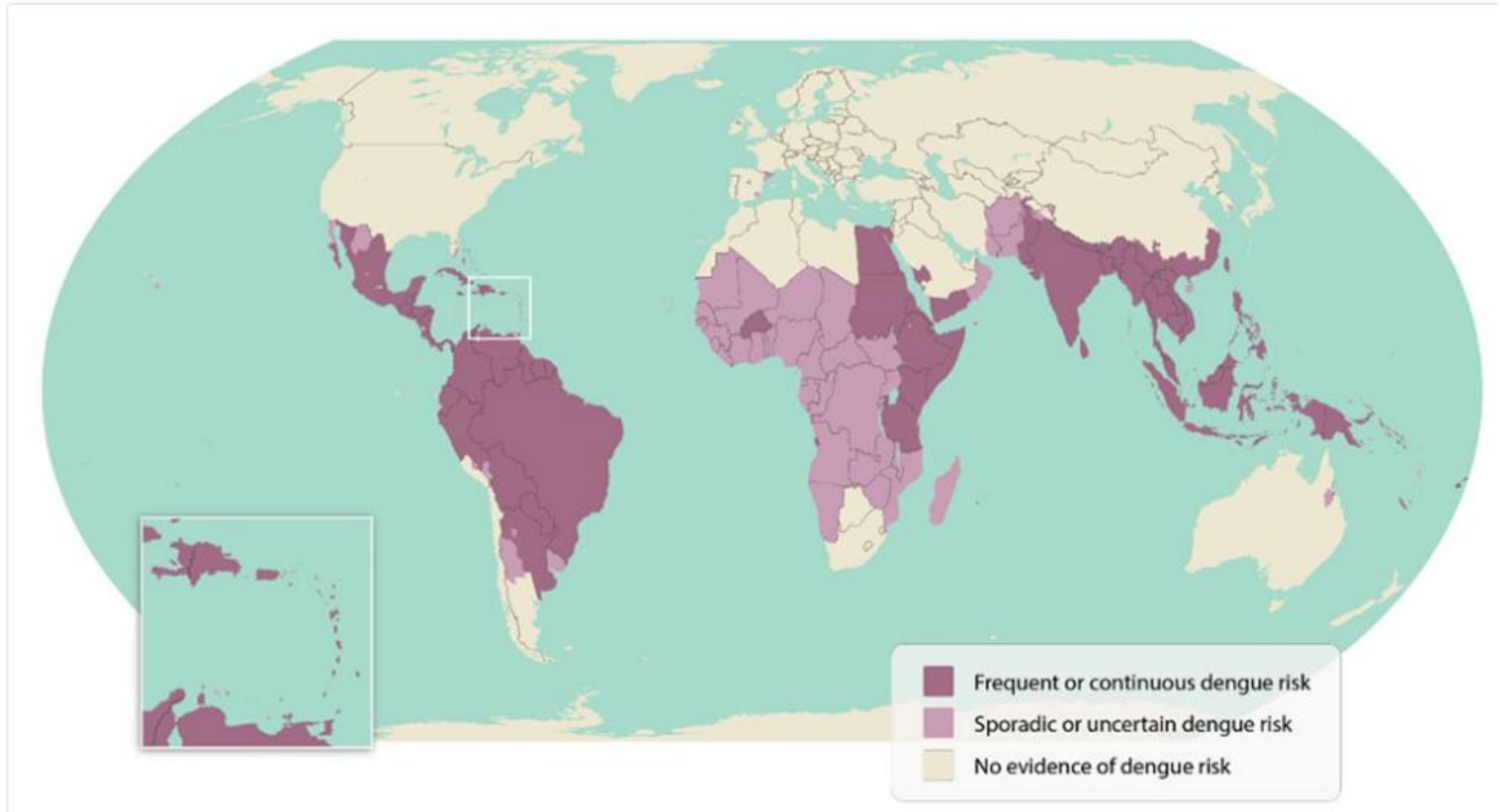
Updated 6:00 PM PDT, November 2, 2023

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# Dengue

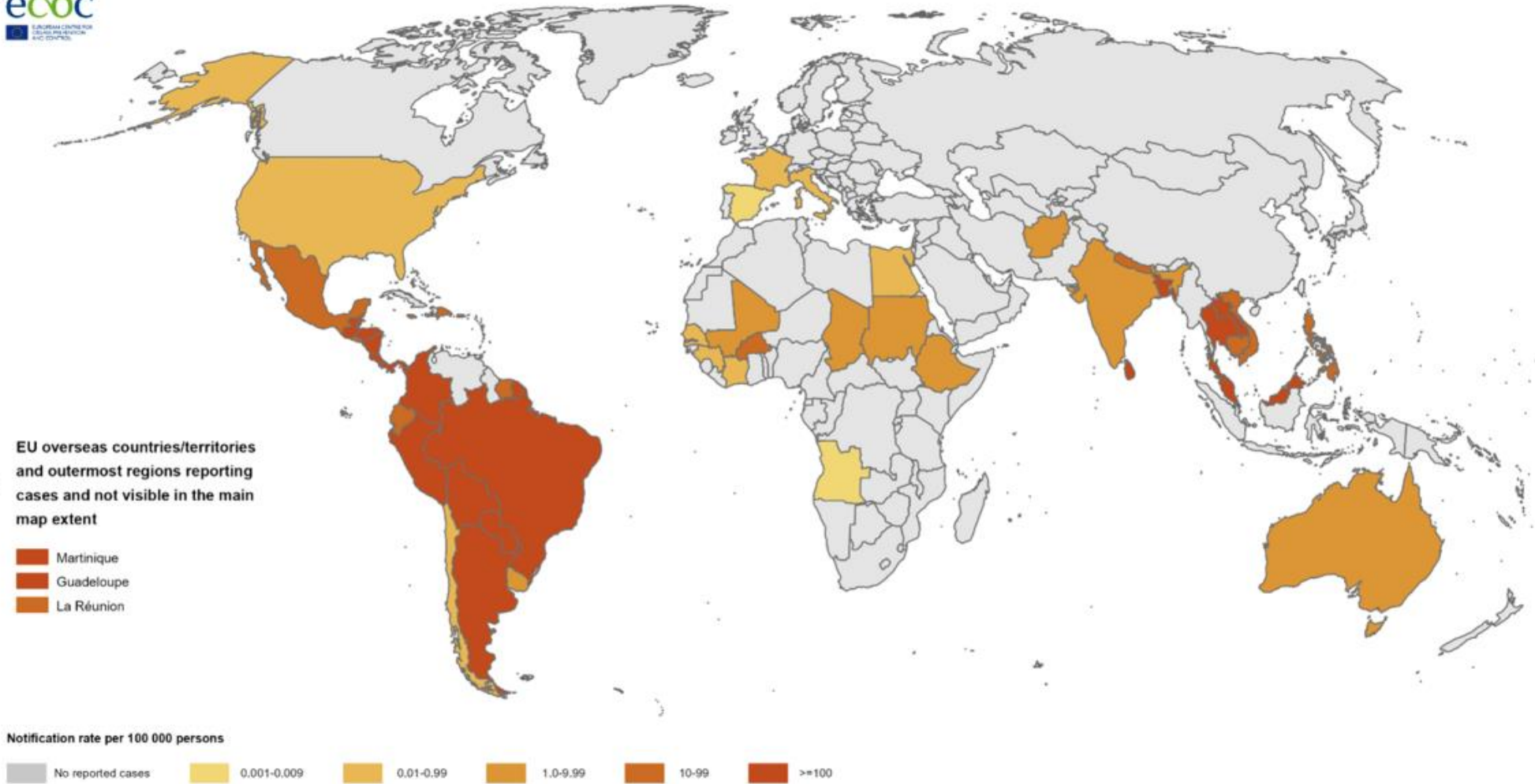
- Known since 1940s
- *Flavivirus*
- 4 strains (DENV1-4)
- Each strain does not provide protection against the other
- Infection with one strain followed by another increases the risk of a hemorrhagic fever syndrome
- 50-100 million infections annually

# CDC Dengue map

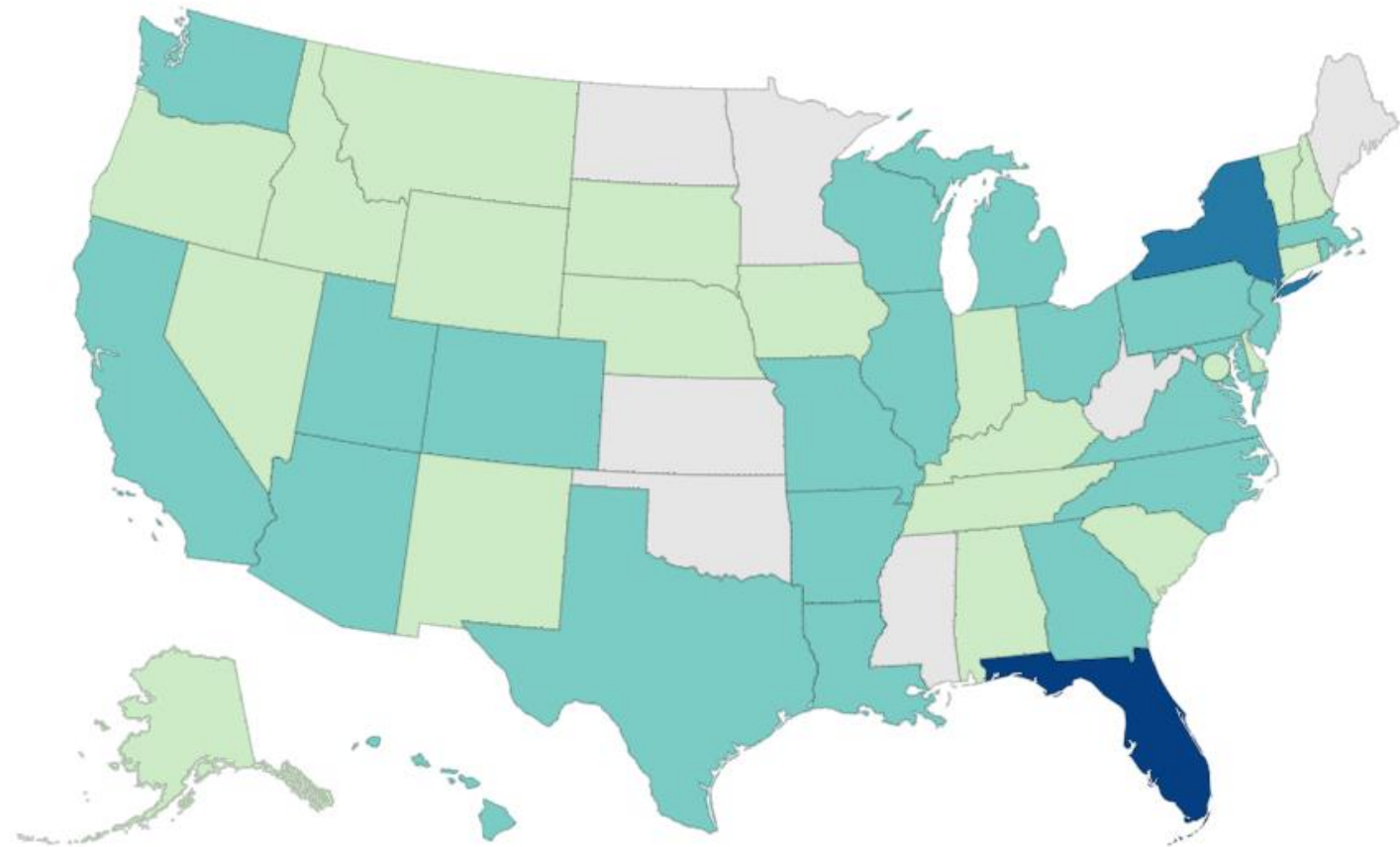




# European CDC Dengue Map



# All US Dengue Activity



Territories and freely associated states

- AS
- GU
- PR**
- VI
- MP
- FM
- PW
- MH

## Legend

○ No reported cases

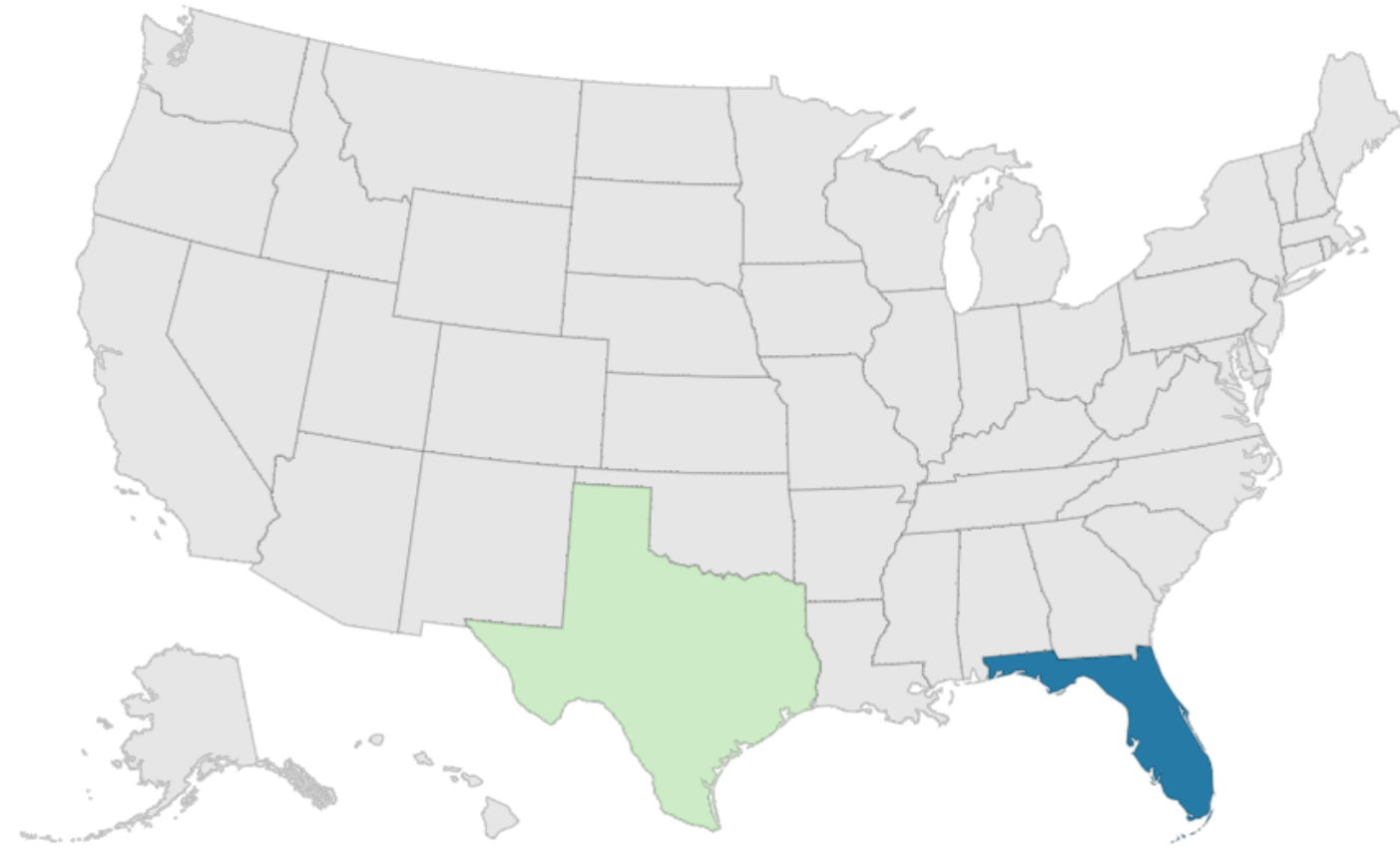
● 5 to 49

● 250+

● 1 to 4

● 50 to 249

# Locally Acquired Dengue US



Territories and freely associated states

AS GU **PR** VI MP FM PW MH

## Legend

○ No reported cases

● 5 to 49

● 250+

● 1 to 4

● 50 to 249

# Transmission



- Mosquitos! *Aedes aegypti*, *Ae. albopictus*
- Rarely blood transfusions
- Rarely Mother to Child (but not by breast feeding)

# Dengue Fever: Clinical Features

- In children, majority of cases are asymptomatic
- In adults, 86% are symptomatic

# Classic Dengue Fever: Clinical Features

- 3-14 days post bite
- “Break bone fever”
- High fever for 3-7 days, in 5% a second period of fever for 1-2 days after first episode
- Frontal headache
- Retroorbital pain
- Myalgias/arthralgias
- Rash, conjunctival injection
- Anorexia and nausea
- Hepatosplenomegaly
- Generalized lymphadenopathy

# Lab findings

- Leukopenia
- Thrombocytopenia
- Transaminitis

# Diagnosis

- Serology: widely available
- PCR: not so widely available
  
- PCR positive in first 5 days
- Serology positive starting at day 3, but more reliably after 5 days



# Dengue Hemorrhagic Fever and Shock Syndrome

- Begins 3-7 days into the illness
- Defervescence of fever leading to hypothermia
- Severe abdominal pain
- Hemorrhage: spontaneous bleeding or petechiae, “tourniquet test”
- Mental status change
- Shock (plasma leakage syndrome): hemoconcentration, pleural effusion, ascites
- Mortality without treatment 10%, with treatment 1%

# Tourniquet test

## How To Do a Tourniquet Test

1. Take the patient's blood pressure and record it, for example, 100/70.
2. Inflate the cuff to a point midway between SBP and DBP, and maintain for 5 minutes,  $(100 + 70) \div 2 = 85$  mm Hg
3. Reduce and wait 2 minutes.
4. Count petechiae below antecubital fossa.
  - A positive test is 10 or more petechiae per 1 square inch.



# Treatment

- Supportive
- IV Fluids
- Acetaminophen (avoid NSAIDs for bleeding risk)
- Mosquito avoidance for 1 week (the period of viremia) to prevent further transmission
- In hemorrhagic or shock syndrome iv fluids, correct lab abnormalities if possible.

# Classic: Case Files from Virginia Mason

- 43 year old surgeon returns from a trip to home to visit family in Lagos, Nigeria. Her family home is not airconditioned, and although they have nets, there are lots of mosquitos around.
- One the plane home, she developed rigors and fevers, but the fever broke and she felt fine until about a day later when the fever returned again.
- She didn't take malaria prophylaxis as she never got malaria as a child, but while there did hear of family members who had contracted malaria.

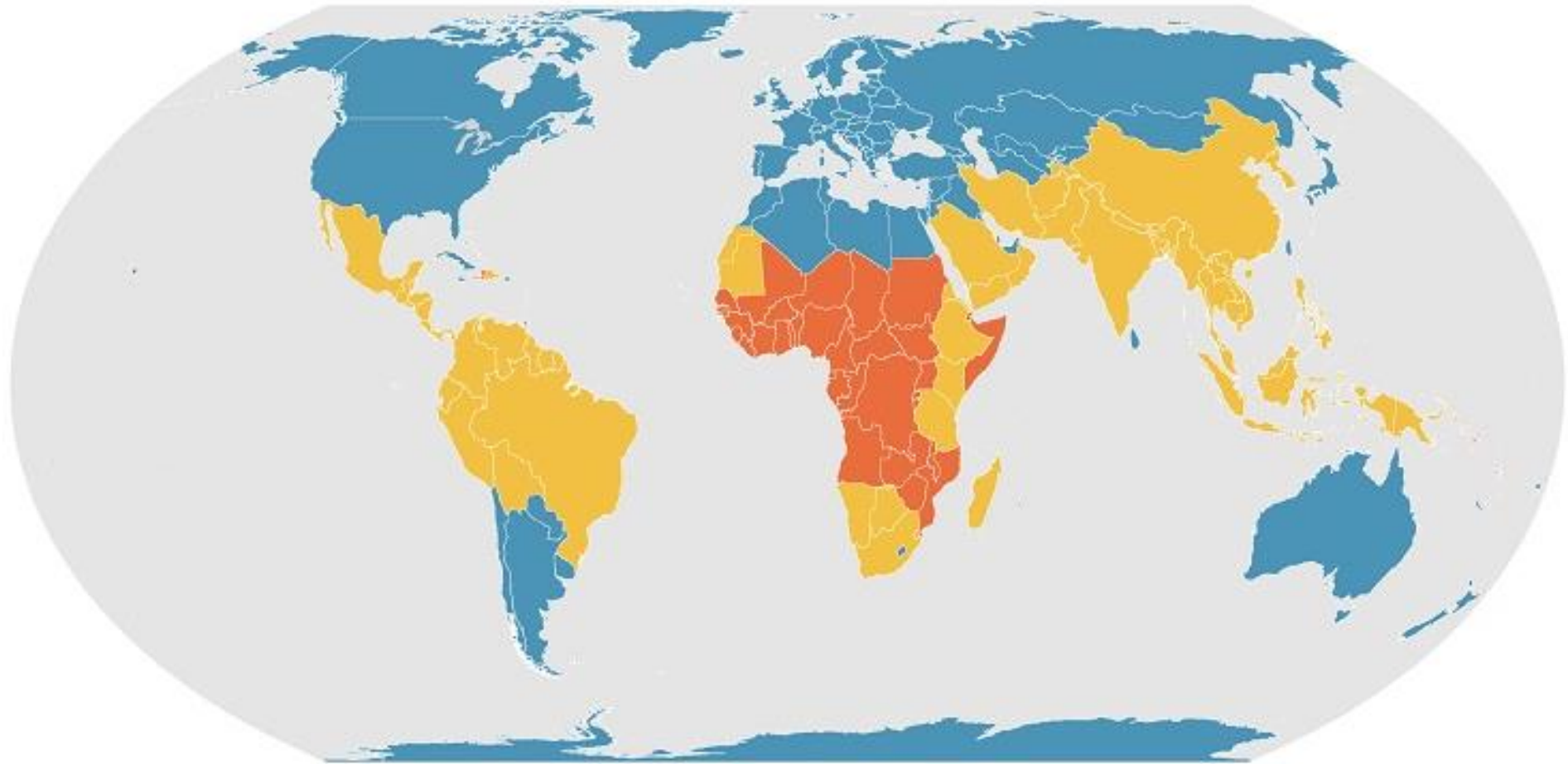
# New: Case Files from Virginia Mason

- 43 year old surgeon returns from a trip home to visit family in Sarasota, Florida. Her family home is not airconditioned, and although they have nets, there are lots of mosquitos around.
- One the plane home, she developed rigors and fevers, but the fever broke and she felt fine until about a day later when the fever returned again.
- She didn't take malaria prophylaxis as she never got malaria as a child, but while there did hear of family members who had contracted malaria.

HEALTH NEWS

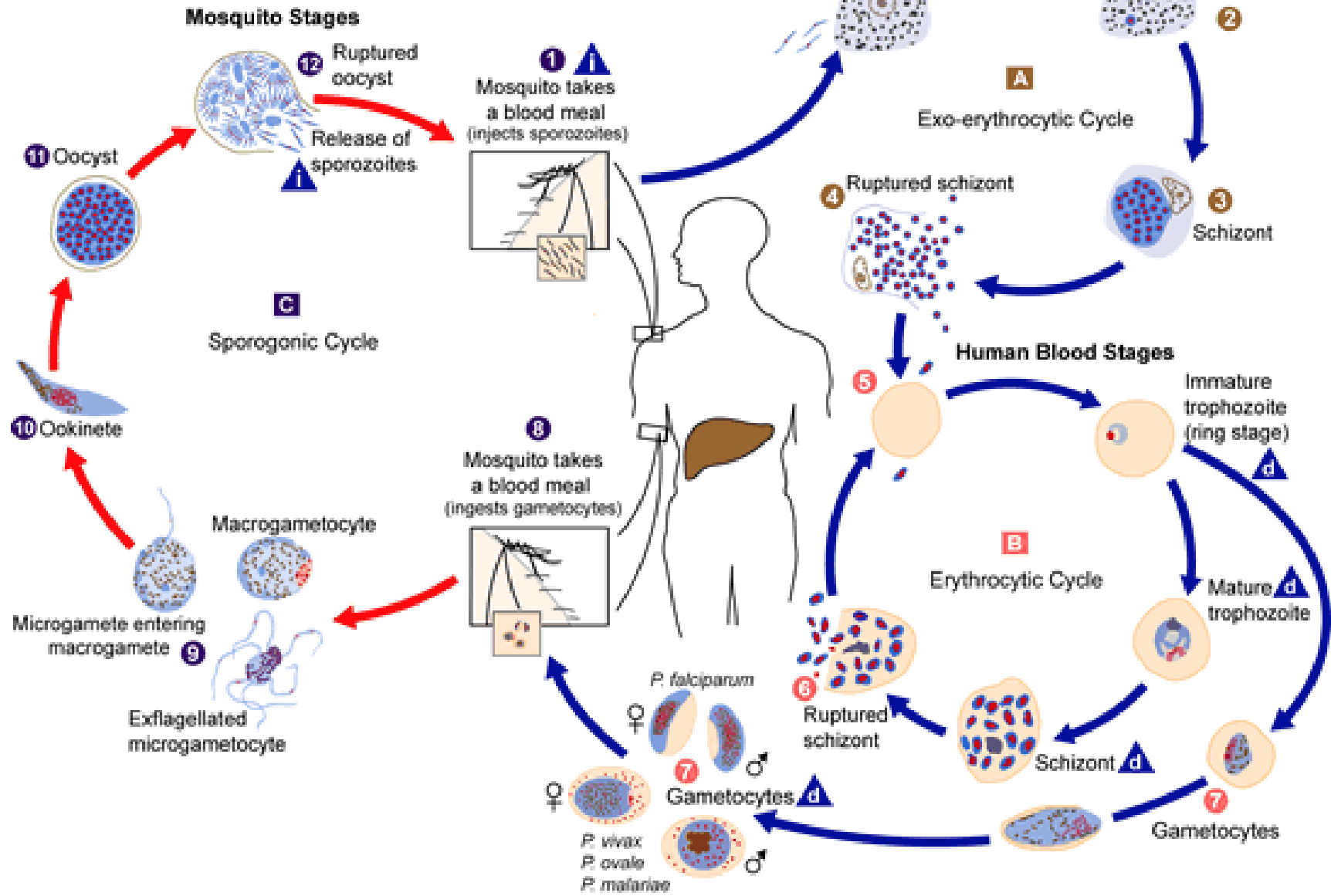
# **New malaria case in Florida brings national total to 8, the first U.S. acquired cases in 20 years**

# Malaria



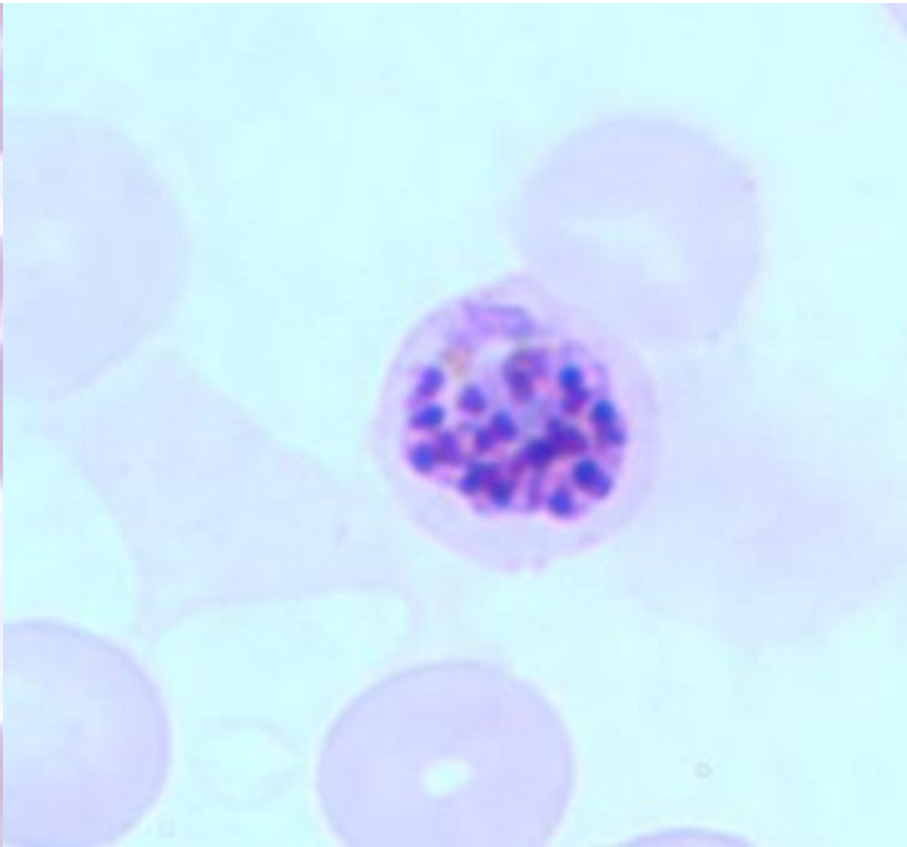
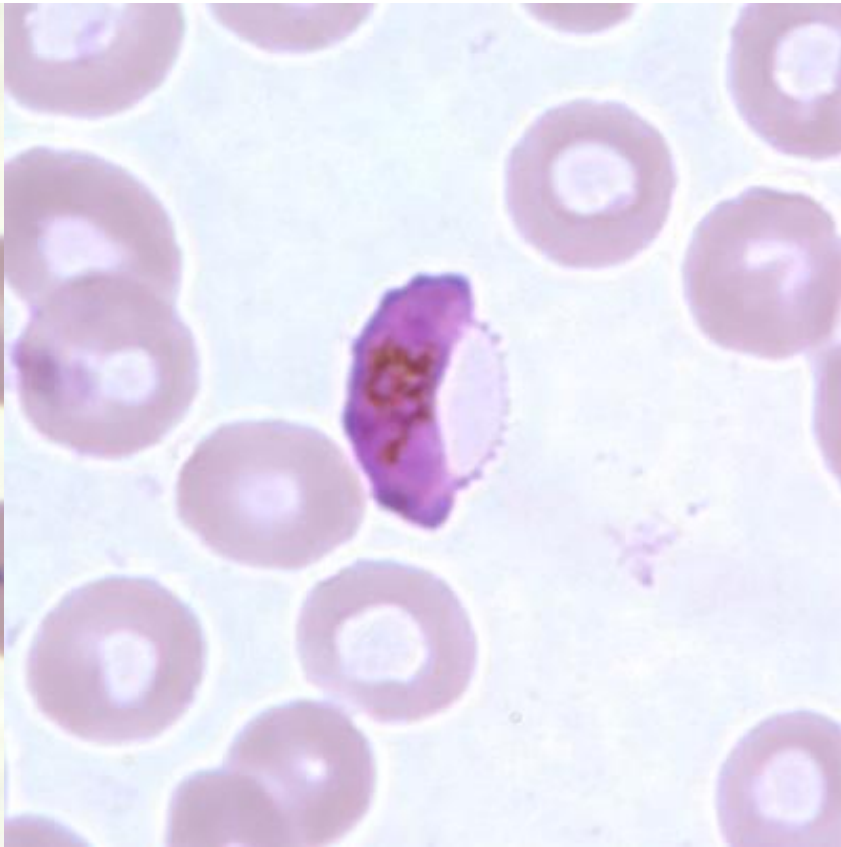
- Malaria transmission is not known to occur
- Malaria transmission occurs in some places
- Malaria transmission occurs throughout

**i** = Infective Stage  
**d** = Diagnostic Stage





# Thin blood smear findings



# Types of malaria

- ***P. vivax*** found mostly in Asia, Latin America, and in some parts of Africa. Because of the population densities especially in Asia it is probably the most prevalent human malaria parasite. *P. vivax* (as well as *P. ovale*) has dormant liver stages (“hypnozoites”) that can activate and invade the blood (“relapse”) several months or years after the infecting mosquito bite.
- ***P. falciparum*** found worldwide in tropical and subtropical areas, and especially in Africa where this species predominates. *P. falciparum* can cause severe malaria because it multiplies rapidly in the blood, and can thus cause severe blood loss (anemia). In addition, the infected parasites can clog small blood vessels. When this occurs in the brain, cerebral malaria results, a complication that can be fatal.
- ***P. malariae*** found worldwide, is the only human malaria parasite species that has a quartan cycle (three-day cycle). (The three other species have a tertian, two-day cycle.) If untreated, *P. malariae* causes a long-lasting, chronic infection that in some cases can last a lifetime. In some chronically infected patients *P. malariae* can cause serious complications such as the nephrotic syndrome
- ***P. ovale*** found mostly in Africa (especially West Africa) and the islands of the western Pacific. It is biologically and morphologically very similar to *P. vivax*. However, differently from *P. vivax*, it can infect individuals who are negative for the Duffy blood group, which is the case for many residents of sub-Saharan Africa. This explains the greater prevalence of *P. ovale* (rather than *P. vivax*) in most of Africa
- ***P. knowlesi*** found throughout Southeast Asia as a natural pathogen of long-tailed and pig-tailed macaques. It has recently been shown to be a significant cause of zoonotic malaria in that region, particularly in Malaysia. *P. knowlesi* has a 24-hour replication cycle and so can rapidly progress from an uncomplicated to a severe infection; fatal cases have been reported

# Clinical Features

- Incubation period is 7-30 days (shorter for falciparum and longer for *P. malariae*)

# Classic malaria paroxysm

- Cold stage - feeling cold and shivering
- Hot stage – fever, headache, vomiting, seizures in young children
- Sweating stage – diaphoresis, return to normal temperature, fatigue

Paroxysms classically occur every second day (tertian malaria) for falciparum, vivax, ovale and every third day (quartan malaria) for malariae

It should be noted classic symptoms are uncommon, and typical symptoms are episodic fevers, rigors, diaphoresis, headaches, nausea, vomiting, myalgia and malaise.

# Exam findings

- Fever
- Diaphoretic
- Splenomegaly
- Jaundice
- Hepatomegaly
- Tachypnea
- Anemia

# Lab findings

- Parasitemia on blood smear
  - Anemia
  - Thrombocytopenia
  - Elevated bilirubin
  - Elevated LFTs
- 
- Rapid antigen tests available, as are PCRs

# Severe malaria

- Cerebral malaria – impaired consciousness, coma, seizures
- Severe anemia (Hb < 7 g/dL) and hemoglobinuria
- Acute respiratory distress syndrome (ARDS), may occur even after the parasite counts have decreased in response to treatment
- DIC
- Shock
- Acute kidney injury
- Hyperparasitemia, > 5% of the red blood cells are infected by malaria parasites
- Metabolic acidosis often in association with hypoglycemia
- Jaundice

# Malaria Relapse

- Occurs with vivax and ovale
- P vivax and ovale create hypnozoites in the liver as a dormant stage
- Can reactivate months to years later



# Malaria Treatment – uncomplicated falciparum

- Coartem, artemether-lumefantrine, now commercially available and is preferred

If not available

- Malarone, atovaquone-proguanil
- Quinine plus doxycycline, tetracycline, or clindamycin
- Mefloquine

If from Central America west of the Panama Canal, Haiti, the Dominican Republic, Middle East, can be assumed to be chloroquine susceptible and then chloroquine or hydroxychloroquine can be used

# Malaria Treatment – severe falciparum

- IV artesunate is commercially available
- Until it is available as it is probably not stocked, can crush and give via feeding tube or as pills with an antiemetic as before
- Check parasite index every 12 hours until response for 2-3 days
- The check PI daily until negative

# Malaria treatment – uncomplicated *P vivax*, *P ovale*, *P malariae*, *P knowlesi*

- *P malariae* or *knowlesi* – chloroquine or artemether-lumefantrine
- *P vivax* in an area w/o chloroquine resistance – chloroquine
- *P vivax* in an area w/ chloroquine resistance – artemether-lumefantrine
- *P vivax* and *P ovale* need hypnozoite treatment with primaquine after treating acute infection to prevent relapse

# Classic: Case Files from Virginia Mason

- 43 year old surgeon returns from a trip to home to visit family in Vientiane, Laos. She ate lots of vegetables and salad from their garden.
- Once home she developed headache, nausea, and neck stiffness.
- LP showed elevated WBCs, but not polys or monocytes, but eosinophils

# New: Case Files from Virginia Mason

- 43 year old surgeon returns from a trip home to visit family in New Orleans. She ate lots of vegetables and salad from their garden.
- Once home she developed headache, nausea, and neck stiffness.
- LP showed elevated WBCs, but not polys or monocytes, but eosinophils

*DISTURBING* —

# Worm that jumps from rats to slugs to human brains has invaded Southeast US

Multiple rats in Atlanta test positive for calamitous, rapidly spreading parasite.

BETH MOLE - 9/22/2023, 1:34 PM

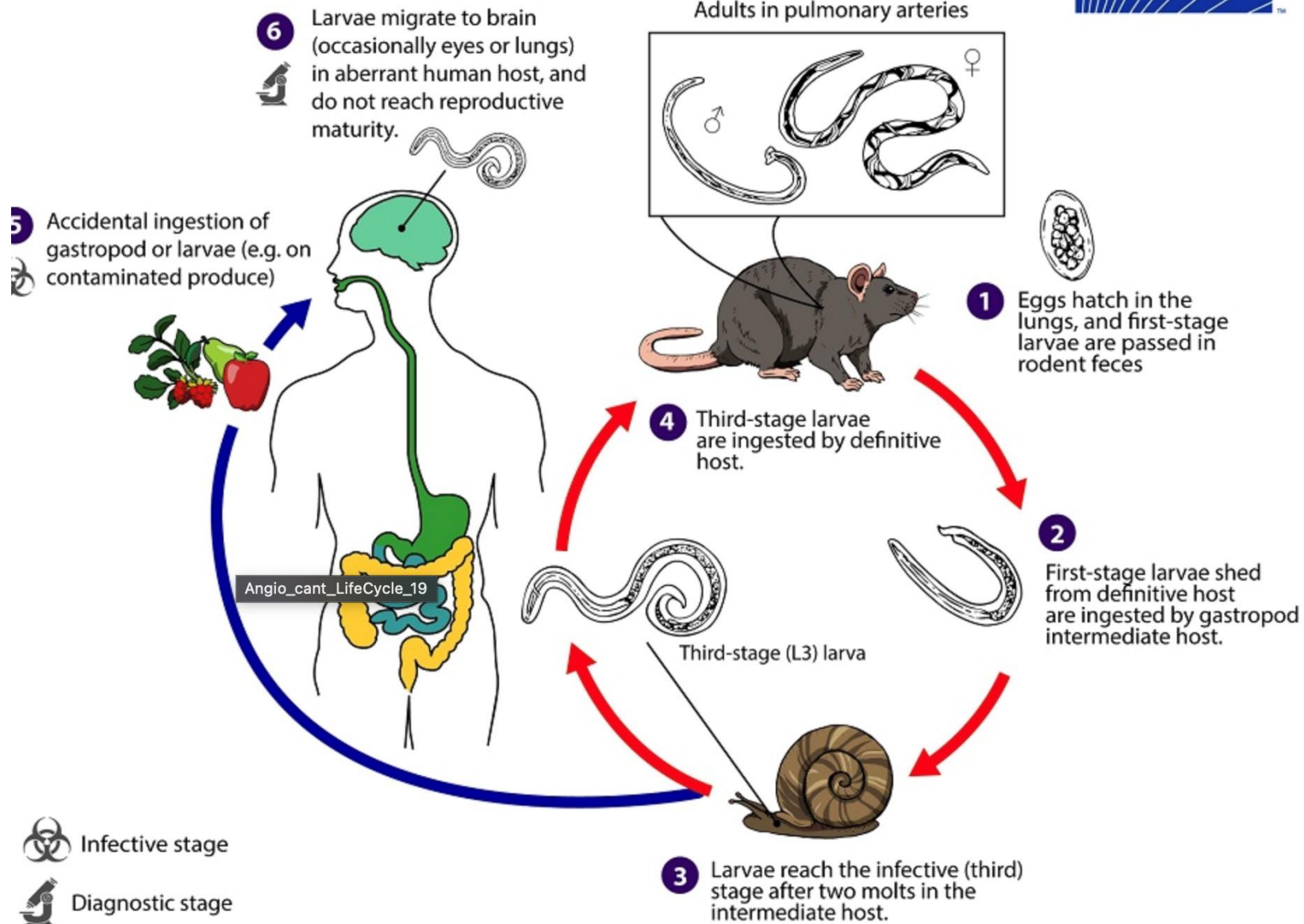
## Brain-Invading Rat Lungworm Found in Georgia

by LIZ NEPONENT

SEPTEMBER 28, 2023 AT 10:05 AM UTC

# Angiostrongylus cantonensis or rat lung worm







# Rat lung worm

- Found classically in SE Asia

In the US:

- Most famous for cases of eosinophilic meningitis in Hawaii
- Has become widespread in Louisiana
- Most recently identified in Atlanta
- CDC now says present in the US “South”
- Incubation period 1 day to 6 weeks

# Rat lung worm clinical features

- Headache
- Nausea and vomiting
- Neck stiffness
  
- CSF with eosinophils and not neutrophils or monocytes (although may not be dominant early or late in the course of disease); high protein, low to normal glucose
- May have eosinophilia in blood as well
  
- Usually resolves spontaneously over time. Pain meds and steroids

# Classic: Case Files from Virginia Mason

- 64-year-old with poorly controlled diabetes, just returned from a jungle trek through Thailand, presents to the ED with acute onset high fevers, septic shock, and imaging shows multiple large abscesses in her liver and kidneys.
- 18-year-old soldier, with no past medical history just returned from a joint exercise with the Thai military, comes to clinic with an ulcer on his shin where she got scraped while setting camp in a jungle.

# New: Case Files from Virginia Mason

- 64-year-old with poorly controlled diabetes, just returned from a visit to family along the Gulf Coast of Mississippi, presents to the ED with acute onset high fevers, septic shock, and imaging shows multiple large abscesses in her liver and kidneys.

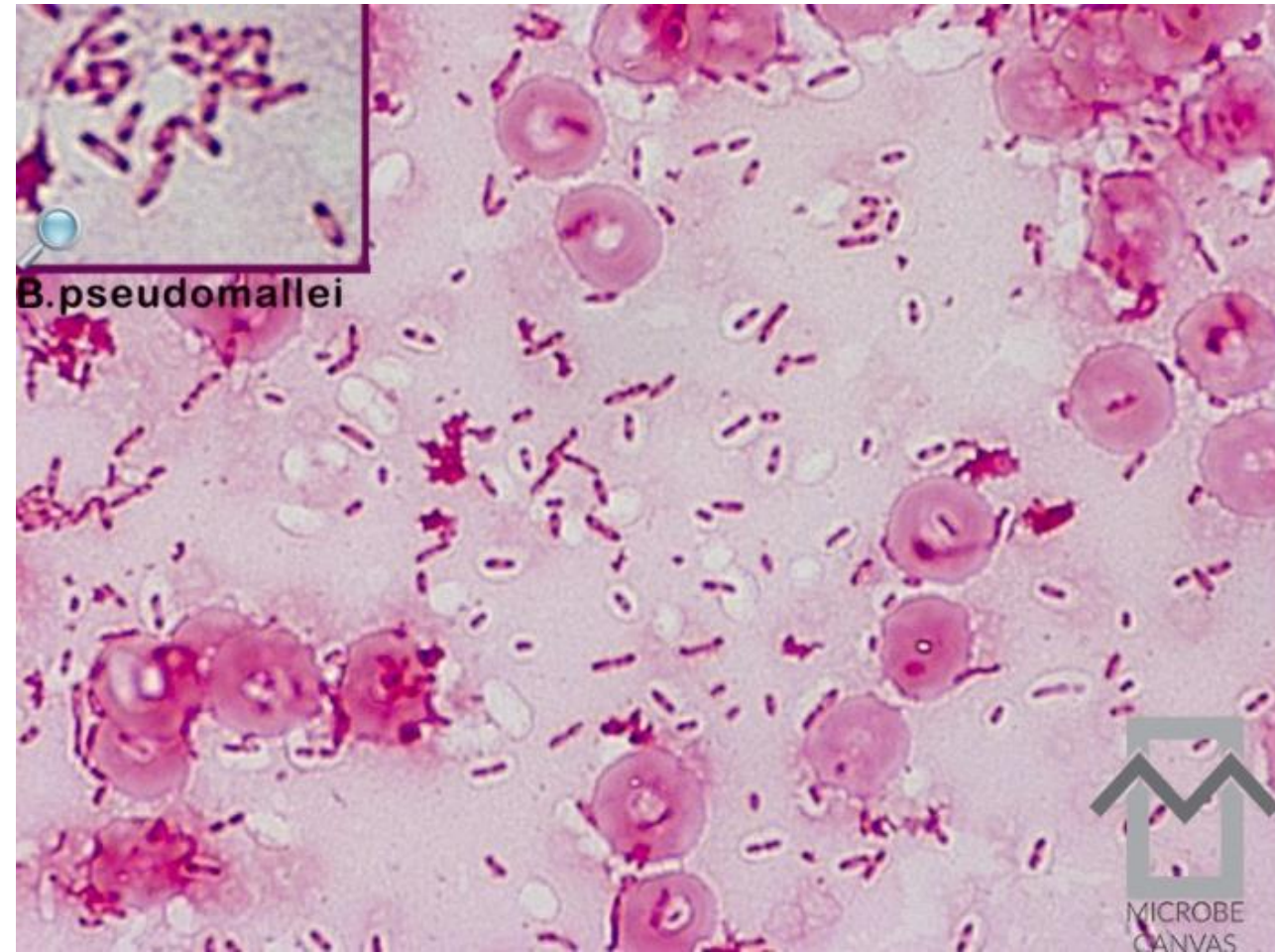
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# CDC Warns of Potentially Fatal Bacterial Illness on U.S. Gulf Coast

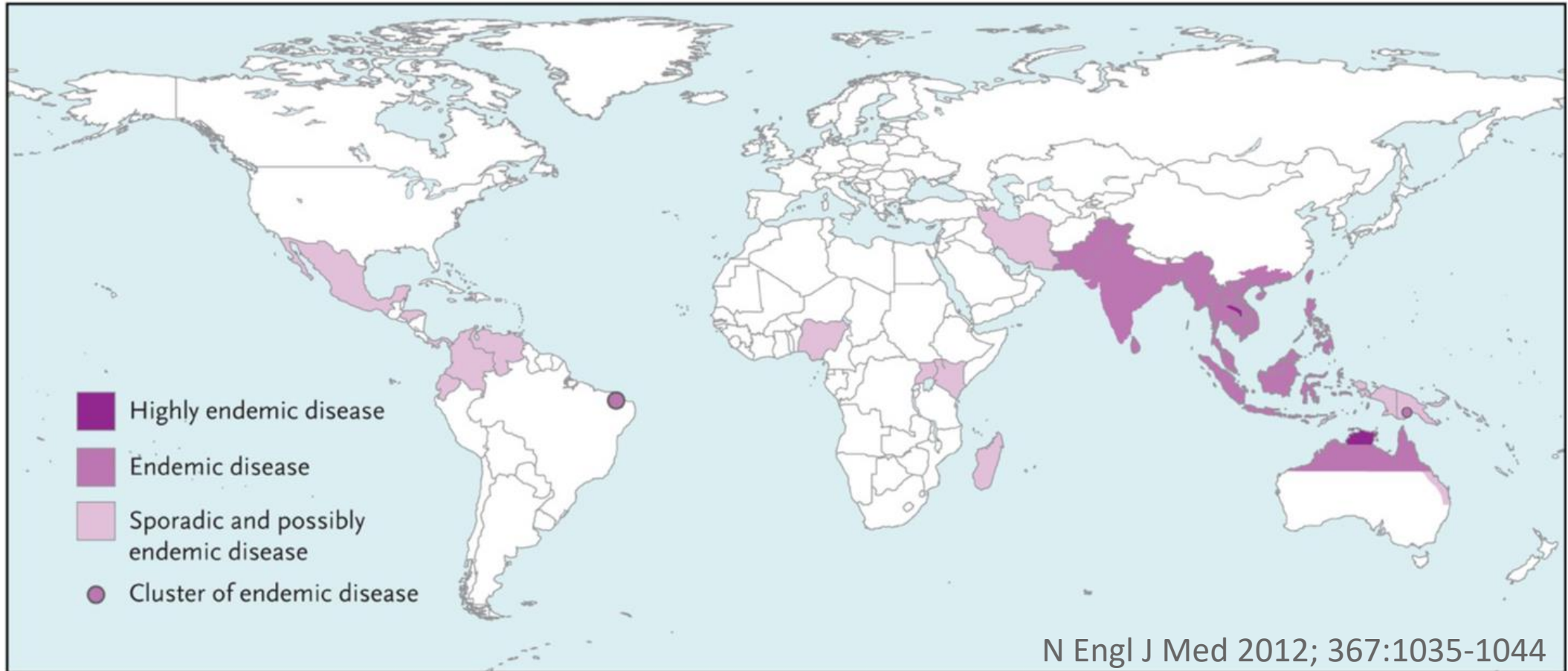
By [HealthDay](#) | June 2, 2023, at 8:50 a.m.

# Melioidosis

- Illness caused by *Burkholderia pseudomallei*
- Originally described in morphine addicts in Rangoon, then Burma, 1912, with caseous consolidation of lung and abscess in liver, spleen, kidney, and SQ tissues.
- Facultative intracellular gram-negative rod with a bipolar, safety pin appearance; motile



# Melioidosis – expected distribution



# Melioidosis

- Infection usually through direct inoculation, inhalation, or ingestion
- Patients become bacteremic and then abscesses can form in any organ (and often in multiple ones)
- Lives in the soil. In endemic regions, close association between rainy season and cases
- Risk factors: diabetes, hazardous alcohol use, renal disease, chronic lung disease



# Melioidosis – USA

- 2 unrelated cases noted along the Mississippi Gulf Coast in 2022, with soil and water samples in the area showing the bacteria
- Endemic but rarely reported in Puerto Rico
- 2021 4 non-travel cases in the US found to be related to aromatherapy spray from India
- Most cases imported from an endemic area

# Melioidosis – Clinical Features

- Most cases may be asymptomatic (based on serologic data)
- Severe cases occur in those with comorbidities
- **Acute Infection** – Pneumonia, skin and soft tissue, GU, bacteremia, abscesses in any organ. Mortality 10-40%
- **Chronic infection** – chronic pulmonary symptoms that may mimic TB or non-healing skin ulcer or abscess. 2% mortality
- **Latent infections** rare but have been described

# Melioidosis – Diagnosis and Treatment

- Grows in cultures
- Treatment uses an intensive parenteral therapy followed by po eradication therapy

## Intensive Therapy

- Non-critically ill patient w/o CNS Infection – ceftazidime preferred (50% reduction in mortality compared to old standard of Chloramphenicol, TMP-SMX, and doxycycline). If not pneumonia, also add TMP-SMX (high “PJP” dose)
- Critically ill patients or those with CNS disease– meropenem preferred (mortality benefit over ceftazidime in critically ill patients). If not pneumonia, also add TMP-SMX
- Drain abscess if possible
- IV antibiotics for at least 14 days, but can be up to 8 weeks in severely ill

## Eradication Therapy

- High dose TMP-SMX (or less preferred doxycycline or amoxicillin-clavulanate) for 3-6 months (relapse rates of 10% without this)