# Travel Medicine and Infections in Returning Travelers

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MIDC
METRO INFECTIOUS DISEASE CONSULTANTS

# Disclosures

The planner and speakers of this conference have no relevant financial relationships with any commercial interests to be disclosed. There is no external financial support for this activity.

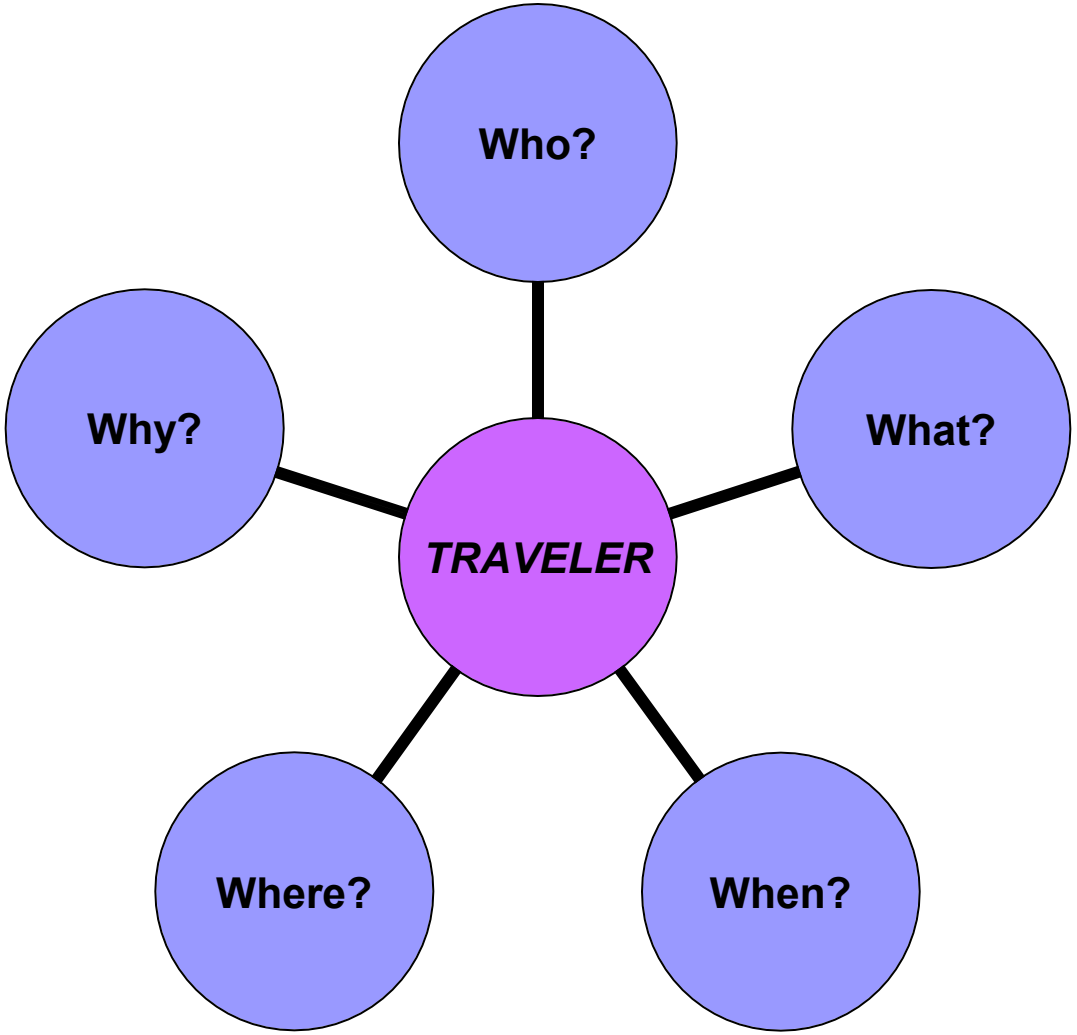
# Objectives

- Develop a strategy for taking a thorough and relevant travel history
- Identify, treat, and prevent human infections associated with travel within the United States
- Recognize, treat, and discuss prevention of infections associated with International Travel

“If you reject the food, ignore the customs, fear the religion and avoid the people, you might better stay at home.”

- James Michener

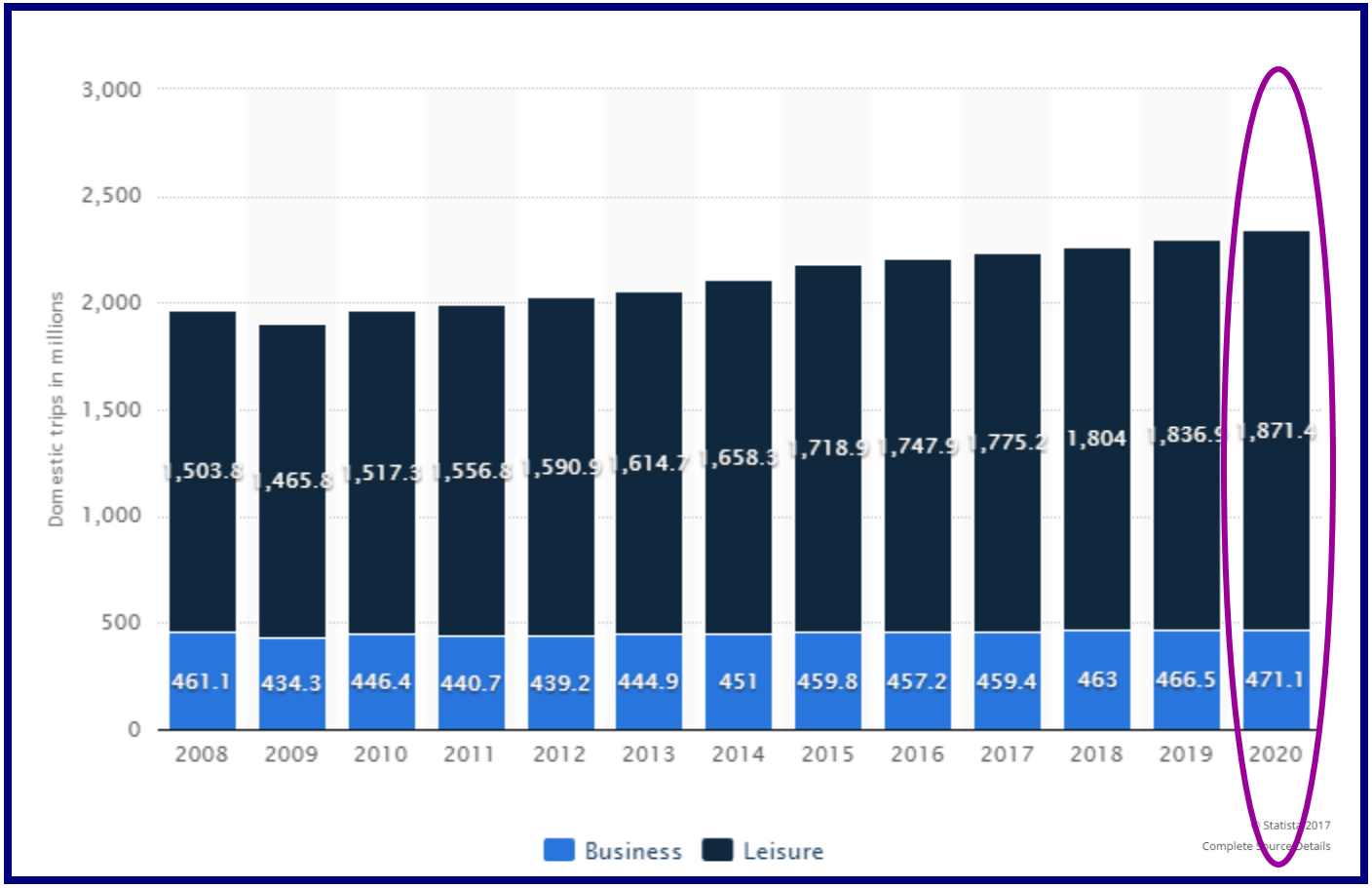
# Ask Questions About Travel



# Obtain a Travel History

- Who?
  - Sexual Partners
  - Inmates, Shelters
- What?
  - Activities
  - Exposures (Foods, Animals)
- When?
  - Time of year
  - Duration
- Where?
  - Travel Itinerary
  - Accommodations
- Why?
  - Leisure
  - Work

# Domestic Trips in the United States




**1,871,400 Leisure**

**471,100 Business**

https://www.statista.com/statistics/207103/forecasted-number-of-domestic-trips-in-the-us/

# Tick-borne Infections

***Ixodes scapularis***

**Deer Tick**

***Amblyomma americanum***

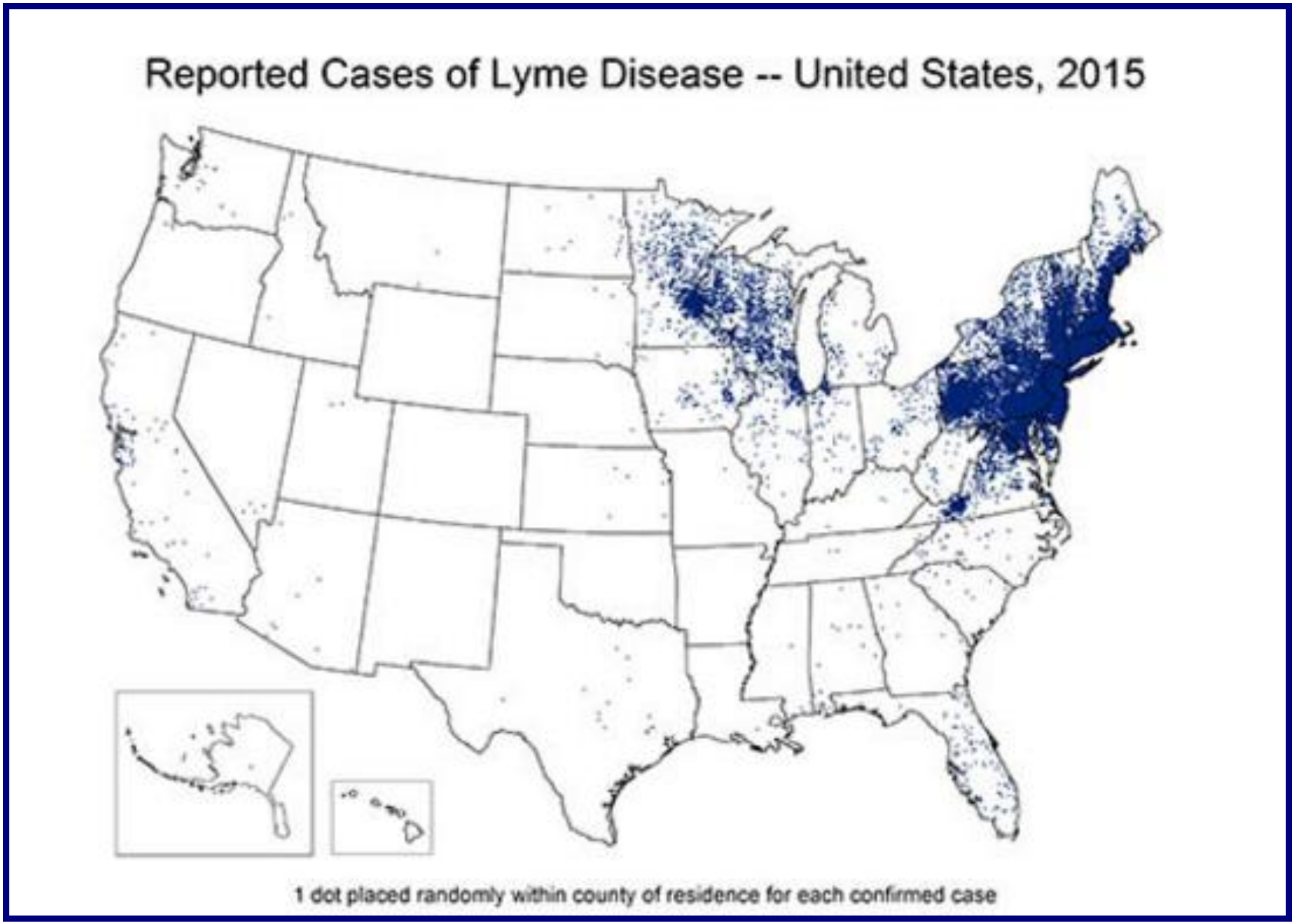
**Lone Star Tick**

***Dermacentor variabilis***

**Dog Tick**

# Lyme Disease

- *Borrelia burgdorferi*
- Vector: *Ixodes scapularis* (deer tick)
- Northeast, Mid-Atlantic, Upper Midwest
  - Most common tick-borne illness in U.S.




https://www.cdc.gov/lyme/stats/index.html

# Lyme Disease

- Early infection
  - Erythema Migrans
  - Constitutional symptoms
- Early disseminated disease
  - Multiple Erythema Migrans, constitutional symptoms
  - Neurologic (12-14%)
    - Cranial nerve palsies (CN VII)
    - Aseptic meningitis
    - Radiculitis
  - Carditis (1%)
    - A-V block
- Late Lyme disease
  - Arthritis
  - Neurologic
    - Encephalitis, Encephalopathy, sensory peripheral neuropathy

# Lyme Disease


Erythema Migrans (target lesion)

# Diagnose Lyme Disease

- Early Infection
  - Clinical diagnosis
- Early Disseminated Infection
  - Clinical findings
  - Positive Serology
    - EIA and Western Blot
- Late Infection
  - Clinical condition
  - Positive serology
  - CSF testing for Lyme antibody
  - Synovial fluid *B. burgdorferi* PCR

# Erythema Migrans Treatment

Doxycycline 100mg BID x14 days
Amoxicillin 500mg TID x14 days
Cefuroxime 500mg BID x14 days

- Alternative treatments
  - Azithromycin 500mg x10 days
  - Clarithromycin 500mg BID x21 days

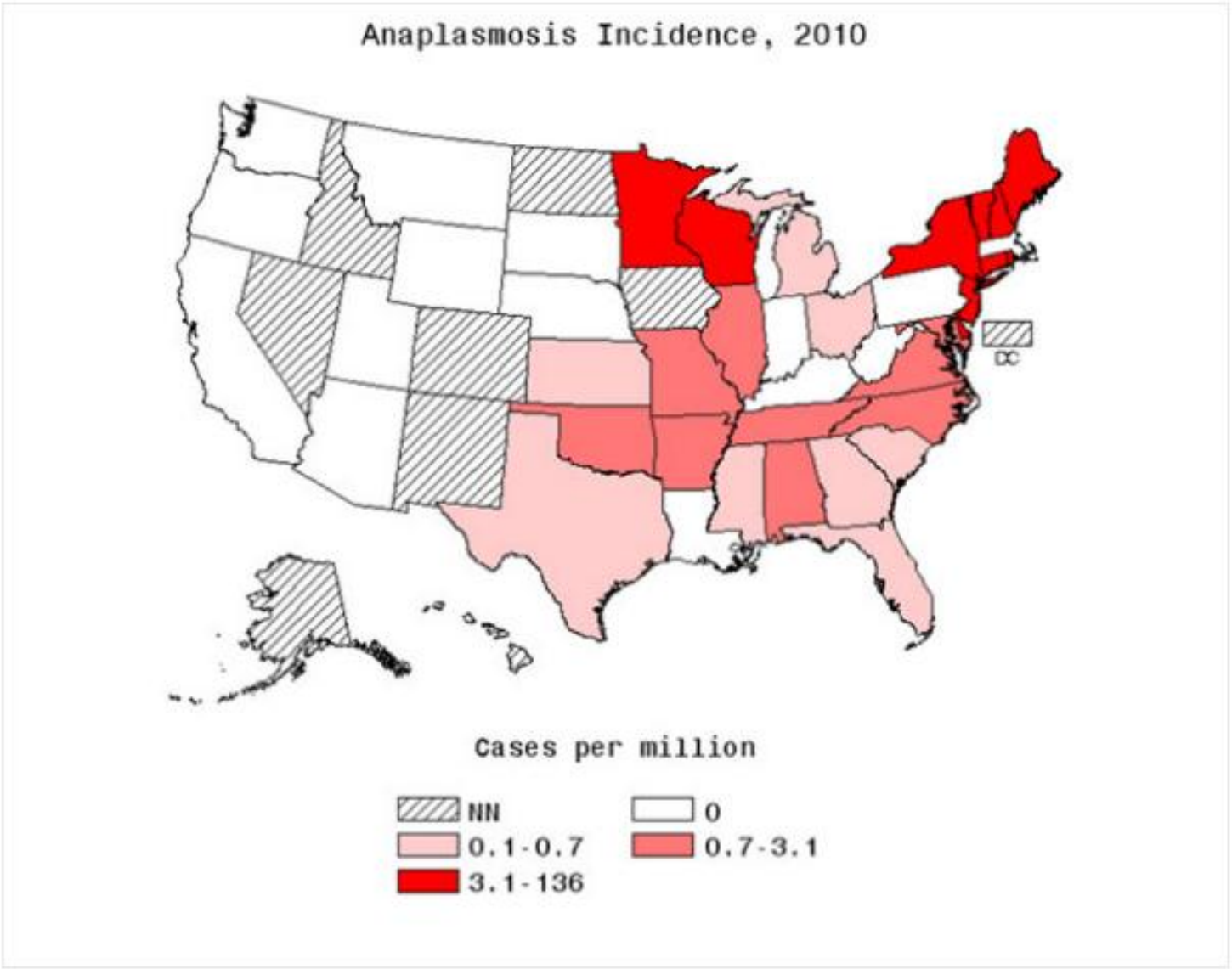
# Lyme Disease Treatment

- Cranial Nerve Palsy
  - Oral regimen (14-28 days)
- Meningitis
  - Intravenous ceftriaxone (10-28 days)
- Cardiac Disease
  - Ceftriaxone until heart block resolves
  - Oral regimen to complete course (14-21 days)
- Late Lyme Arthritis
  - Oral regimen (28 days)

# Anaplasmosis

## Human granulocytotrophic anaplasmosis (HGA)

- *Anaplasma phagocytophilum*
- Vector: *Ixodes scapularis* (deer tick)
- Northeast, Upper Midwest




https://www.cdc.gov/anaplasmosis/stats/index.html

# Anaplasmosis

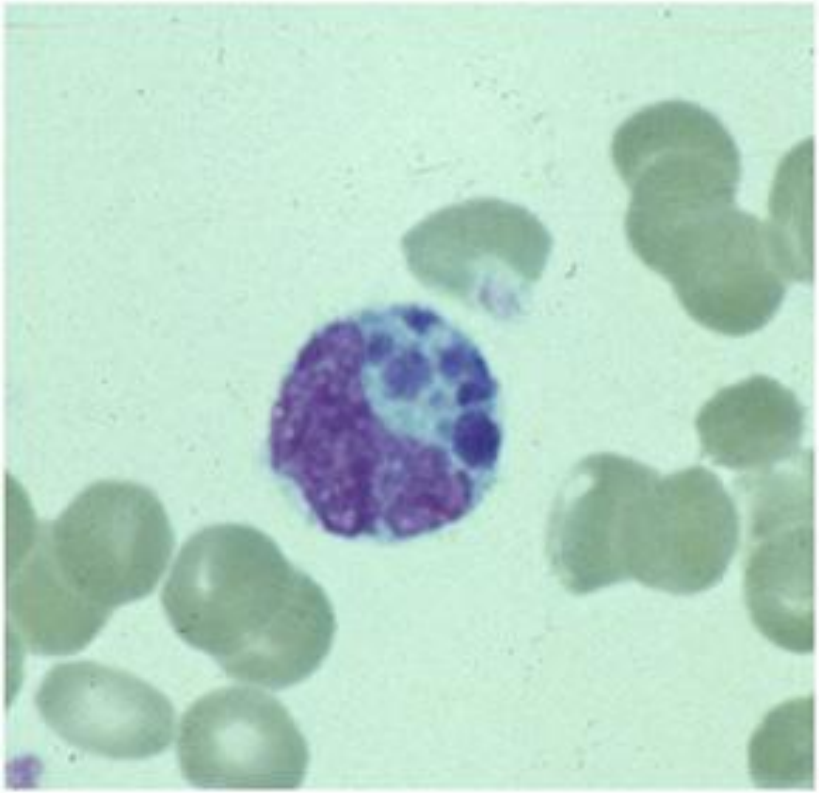
- Incubation period of 1-2 weeks
- Symptoms
  - Fever
  - Headache
  - Myalgias
  - Nausea, vomiting
- Maculopapular rash (~10%)
- Laboratory abnormalities
  - Elevated liver enzymes
  - Leukopenia, thrombocytopenia

# Anaplasmosis Diagnosis and Treatment

- Serology
  - Single titer > 1:256, or four-fold increase in titer
  - Acute testing often negative
- PCR on whole blood

Doxycycline (10 day course)
Alternative: Rifampin

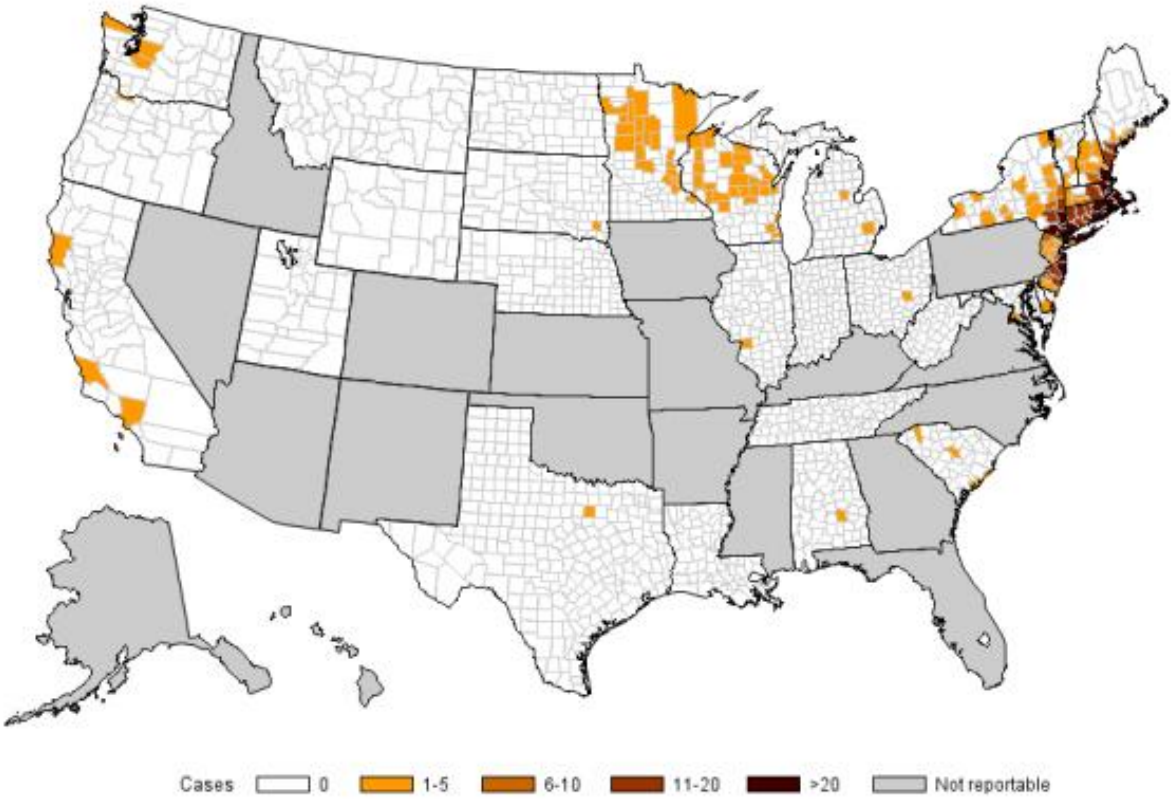
# Anaplasmosis



Morulae in granulocyte

# Babesiosis

- *Babesia microti*
- Vector: *Ixodes scapularis* (deer tick)
- Northeast, Midwest, West Coast
- Most commonly transfused pathogen




**Number of reported cases of babesiosis, by county of residence — 31 states, 2014***

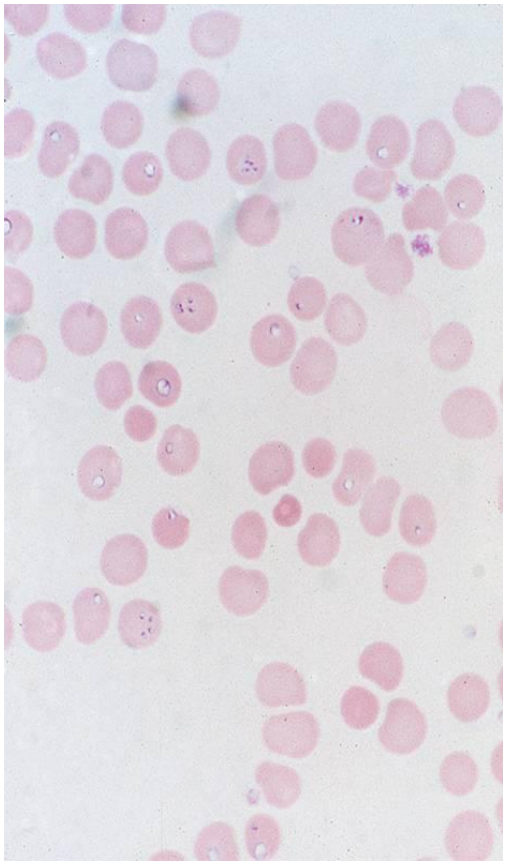
# Babesiosis

- Symptoms
  - Fever, flu-like symptoms, cough
- Laboratory abnormalities
  - Hemolytic anemia, thrombocytopenia
  - Elevated liver enzymes
- Severe illness
  - Elderly, immunocompromised, asplenic patients
  - Parasitemia >10%
  - Severe hemolysis
  - Liver, kidney, or respiratory failure

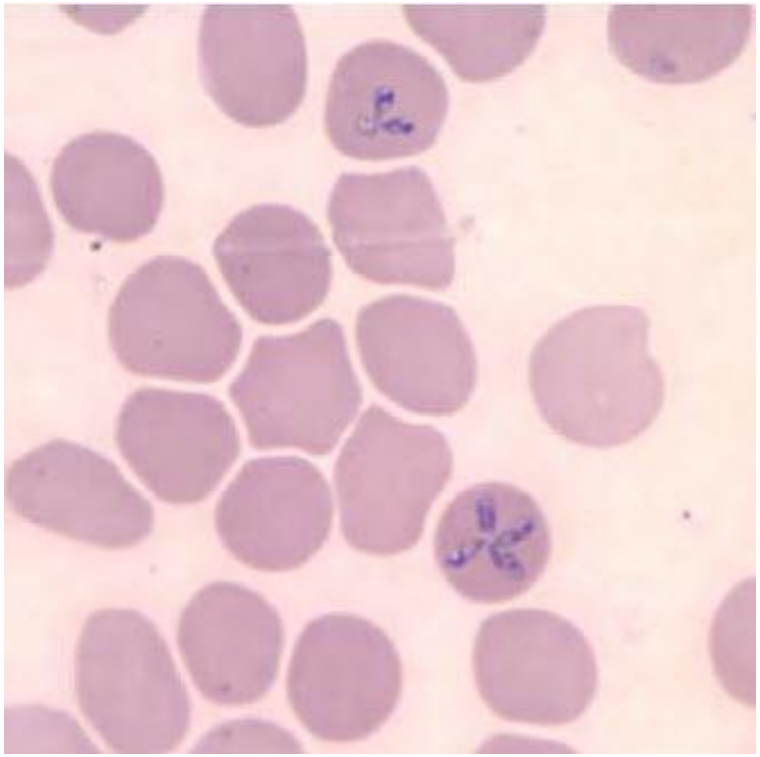
# Babesiosis Diagnosis

- Thick and thin blood smears
  - Intraerythrocytic ring forms
  - Maltese cross
- PCR on whole blood
  - Most sensitive
- Serology
  - IFA IgM >1:64
  - Four-fold increase in titer

# Babesiosis



Intraerythrocytic ring forms



Maltese Cross (tetrad)

# Babesiosis Treatment

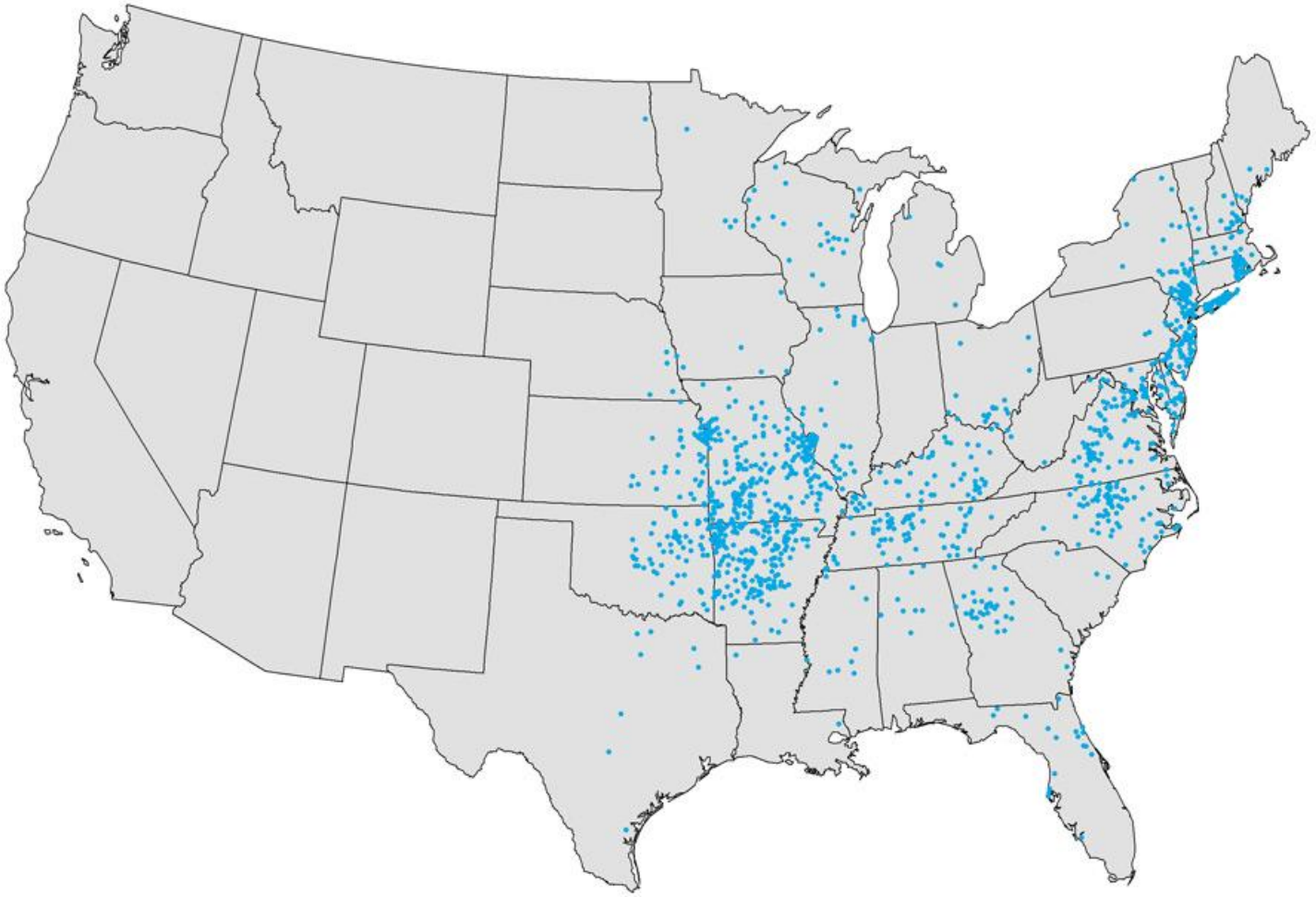
- Asymptomatic
  - No treatment required
  - Atovaquone and azithromycin (7 days)
    - persistent parasitemia
- Mild-moderate disease
  - Atovaquone and azithromycin (7-10 days)
  - Adverse drug reactions (15%)
- Severe disease
  - Clindamycin + quinine (7-10 days)
  - Adverse drug reactions (72%)
- Critically Ill
  - Exchange blood transfusions
    - Parasitemia >10%, severe anemia, liver, kidney, respiratory failure

# Ehrlichiosis

Human monocytotropic ehrlichiosis (HME)

- *Ehrlichia chaffeensis*
- Vector: *Amblyomma americanum* (Lone Star tick)
- Southeastern and South-Central states
- ~800-1,000 cases annually

# U.S. Reported Cases of Ehrlichiosis (2015)



https://www.cdc.gov/ticks/tickbornediseases/ehrlichiosis.html

# Ehrlichiosis

- Symptoms
  - Fever, headache, abdominal pain, nausea
  - Meningitis (20%)
  - Maculopapular rash (~30%)
- Laboratory abnormalities
  - Elevated liver function tests, thrombocytopenia, leukopenia
- Severe illness
  - Elderly, immunocompromised, asplenic patients
  - Liver, kidney, or respiratory failure
  - Coagulopathies

# Ehrlichiosis Diagnosis and Treatment

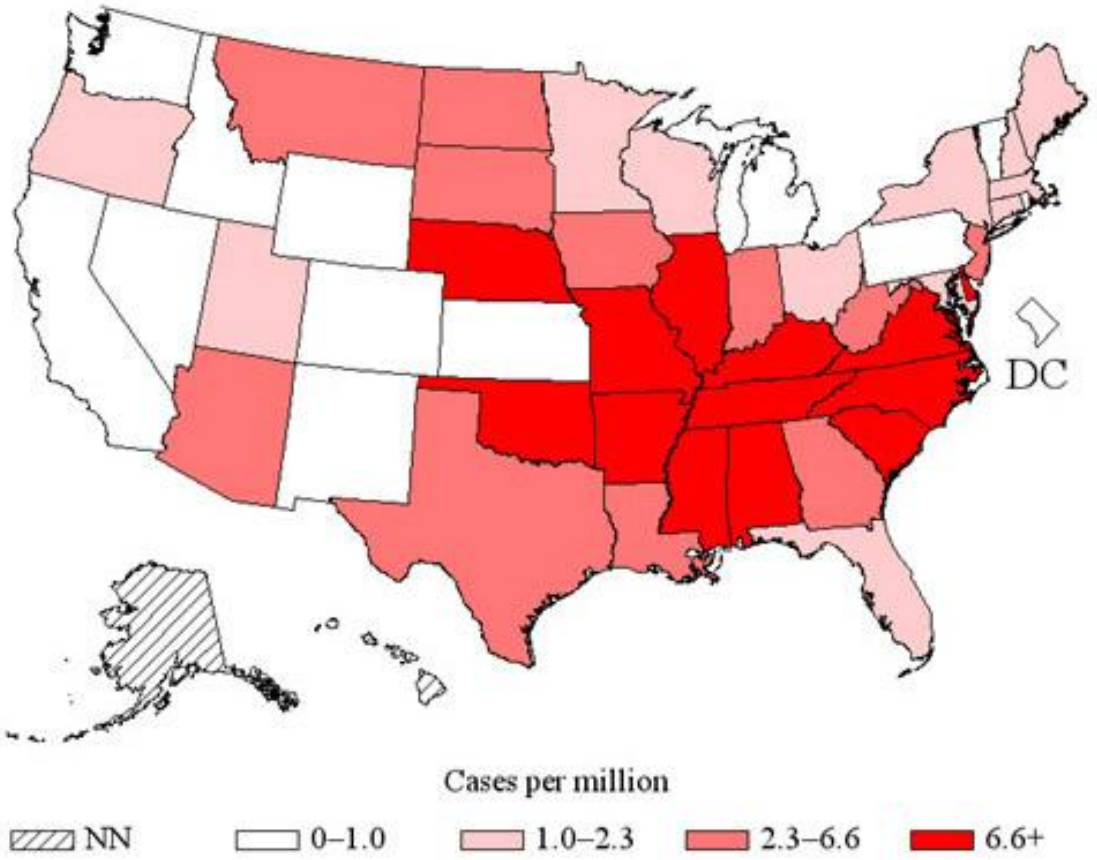
- Serology
  - Single titer > 1:256, or four-fold increase in titer
  - 85% negative during first week
- PCR whole blood

Don’t wait for confirmation, treat if suspected!
Doxycycline (10 day course)
Alternative: Rifampin

# Rocky Mountain Spotted Fever (RMSF)

- *Rickettsia rickettsii*
- Vector: *Dermacentor variabilis* (dog tick), *Dermacentor andersoni* (wood tick)
- South-central, Southeastern, Mid-Atlantic
- 500-1000 cases reported annually

# Incidence for Spotted Fever Rickettsiosis (2014)




https://www.cdc.gov/rmsf/index.html

# Rocky Mountain Spotted Fever

- Incubation period 3-12 days
- Symptoms
  - Fever, headache, malaise
  - Petechial rash develops 3-5 days later
    - Found on palms and soles
  - Neurologic involvement common
- Laboratory abnormalities
  - Hyponatremia, thrombocytopenia, elevated liver function tests

Petechial rash of RMSF

# RMSF Diagnosis and Treatment

- Serologic testing
  - Seroconversion 7-10 days after onset
  - IFA is the standard, cross reactivity seen

Do not wait for confirmatory testing!
Doxycycline (7 days)
Alternative: Chloramphenicol

# Prevention of Tick-borne Infections

- Avoid Tick Contact
- Tick Removal
  - 24-36 hours for Lyme Disease
  - 4-6 hours for RMSF
- DEET
- Permethrin
  - clothes, tents

# West Nile Virus (WNV)

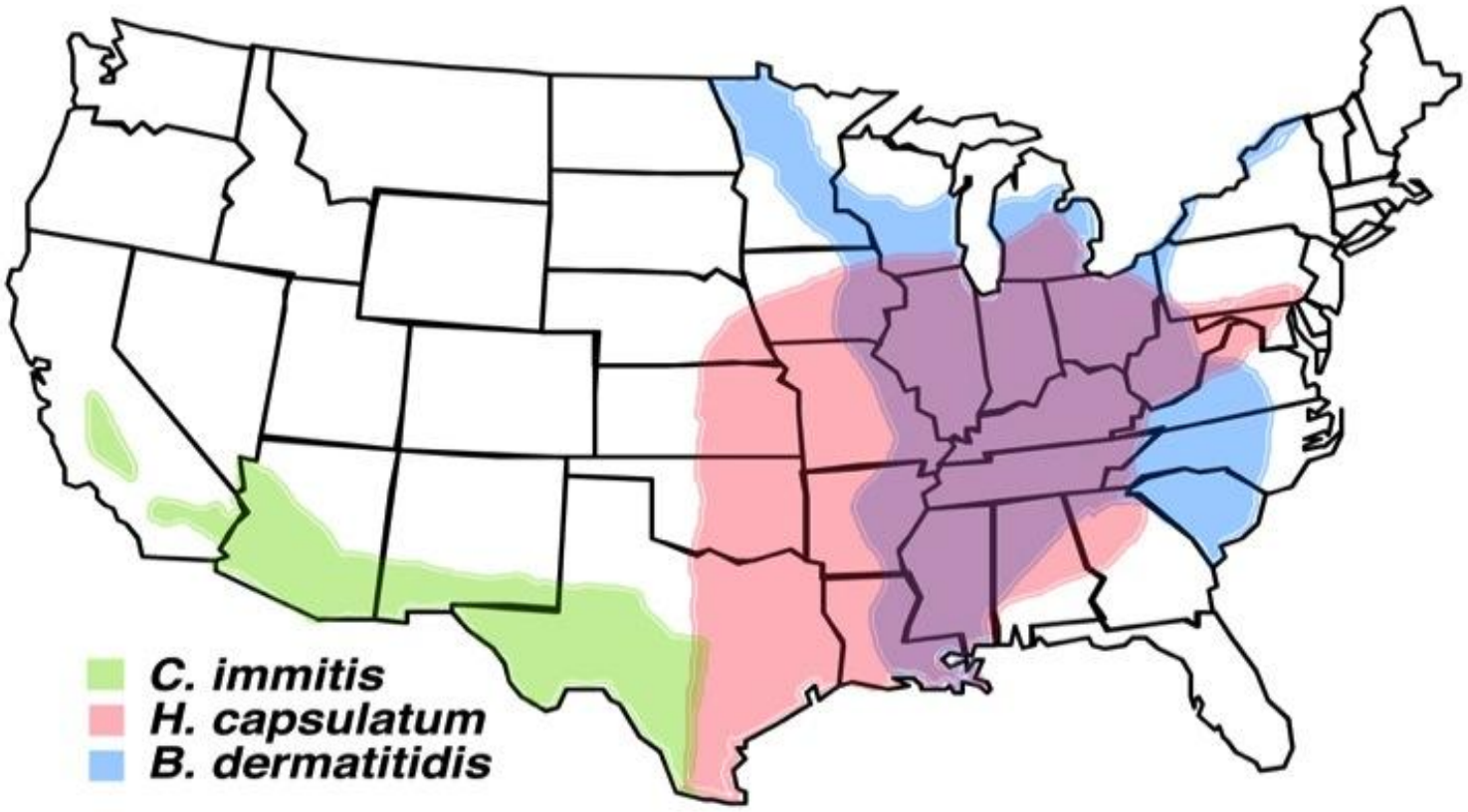
- Mosquito-borne flavivirus
  - Highest risk June-November
- Asymptomatic Infection (80%)
- WNV Fever (20%)
  - Fever, headache, rash
- WNV neuroinvasive infection (1%)
  - Encephalitis
  - Aseptic Meningitis
  - Myelitis

# WNV Diagnosis and Treatment

- WNV IgM antibody
  - Serum, CSF
  - Cross-reactivity with other flaviviruses

Treatment: Supportive Care
Report WNV to Health Department

# Endemic Mycoses



# Blastomycosis

- *Blastomyces dermatitidis*
  - Dimorphic fungus
  - Moist, acidic soil
- Southeast and South-Central states, Midwest
  - Hunters, farmers, manual laborers
  - Wisconsin reports highest incidence

# Blastomycosis

# Blastomycosis

- Infection by Inhalation
  - Pneumonia
  - Disseminated disease
- Diagnosis
  - Culture
  - Urinary antigen, serum antigen
    - Cross-reactivity seen
  - Large yeast with broad based bud
- Serologic testing not recommended

# Blastomycosis

- Pulmonary disease (70-75%)
  - Asymptomatic (50%)
  - Acute disease resembles bacterial pneumonia
  - Chronic disease resembles malignancy or tuberculosis
- Cutaneous
  - Papules on the face
  - Ulcerative lesions
- Bones
  - Osteomyelitis
- Genitourinary
  - Prostatitis, epididymitis
- CNS infection is rare

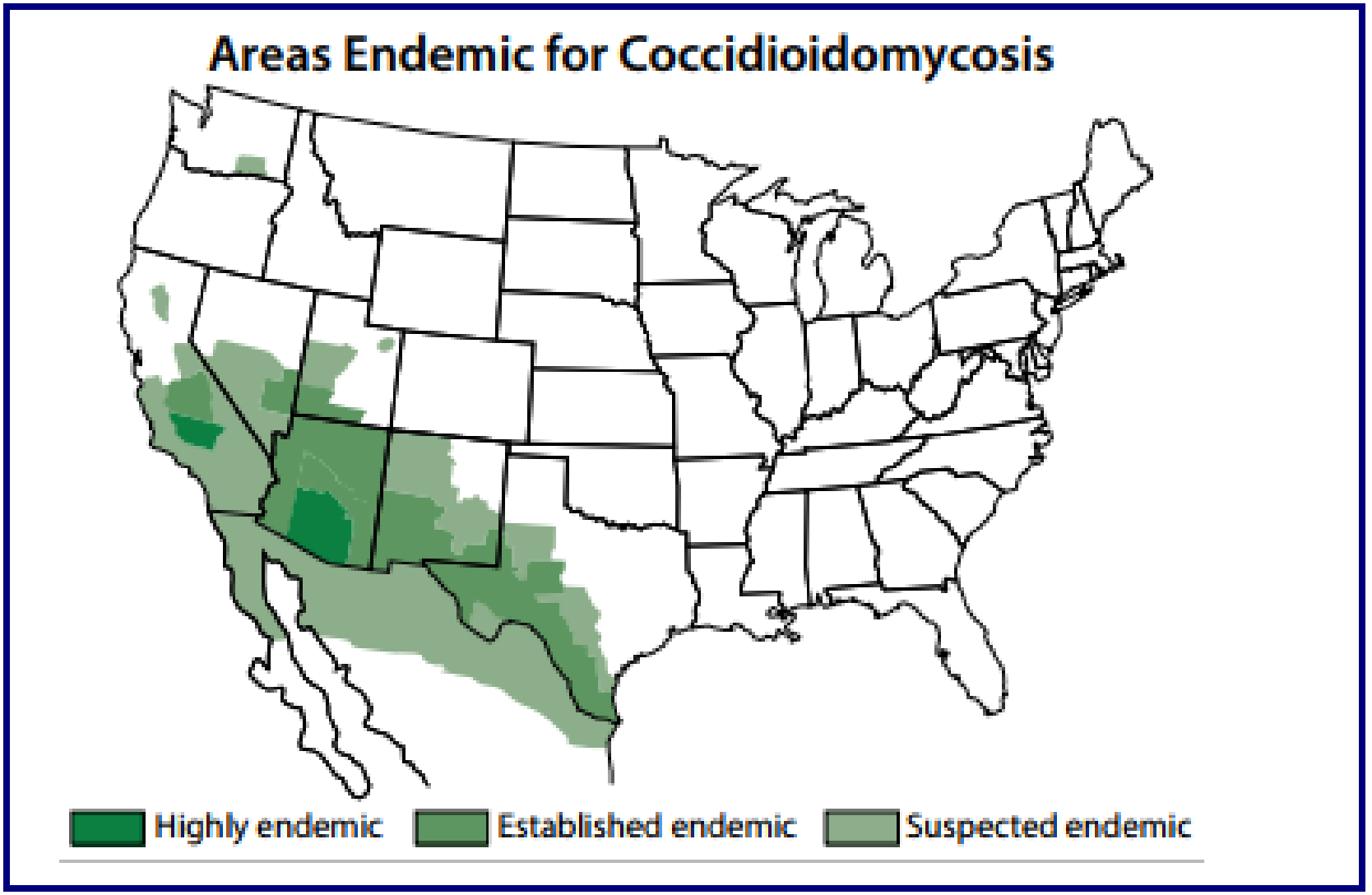
# Blastomycosis Treatment

- Severe Pulmonary Infection
  - Amphotericin B, itraconazole
- Disseminated Infection
  - Itraconazole
- Duration of therapy: 6-12 months

# Coccidioidomycosis

- *Coccidioides immitis*
  - Dimorphic fungus
  - Warm, dry environments, deserts
- San Joaquin Valley
  - Most cases in CA, AZ
- Approximately 150,000 infections/year

# Coccidioidomycosis



# Coccidioidomycosis

- Infection by inhalation
- Presents as acute or sub-acute pneumonia
  - Incubation period 7-21 days
  - Cough, fever and infiltrate
  - Asymptomatic with X-ray findings
- Skin lesions
  - Erythema Nodosum
- Bone infection
- CNS infection
  - Sub-acute or chronic

# Coccidioidomycosis Diagnosis and Treatment

- Diagnosis
  - Spherule identification
  - Positive fungal culture
  - Positive serologic testing

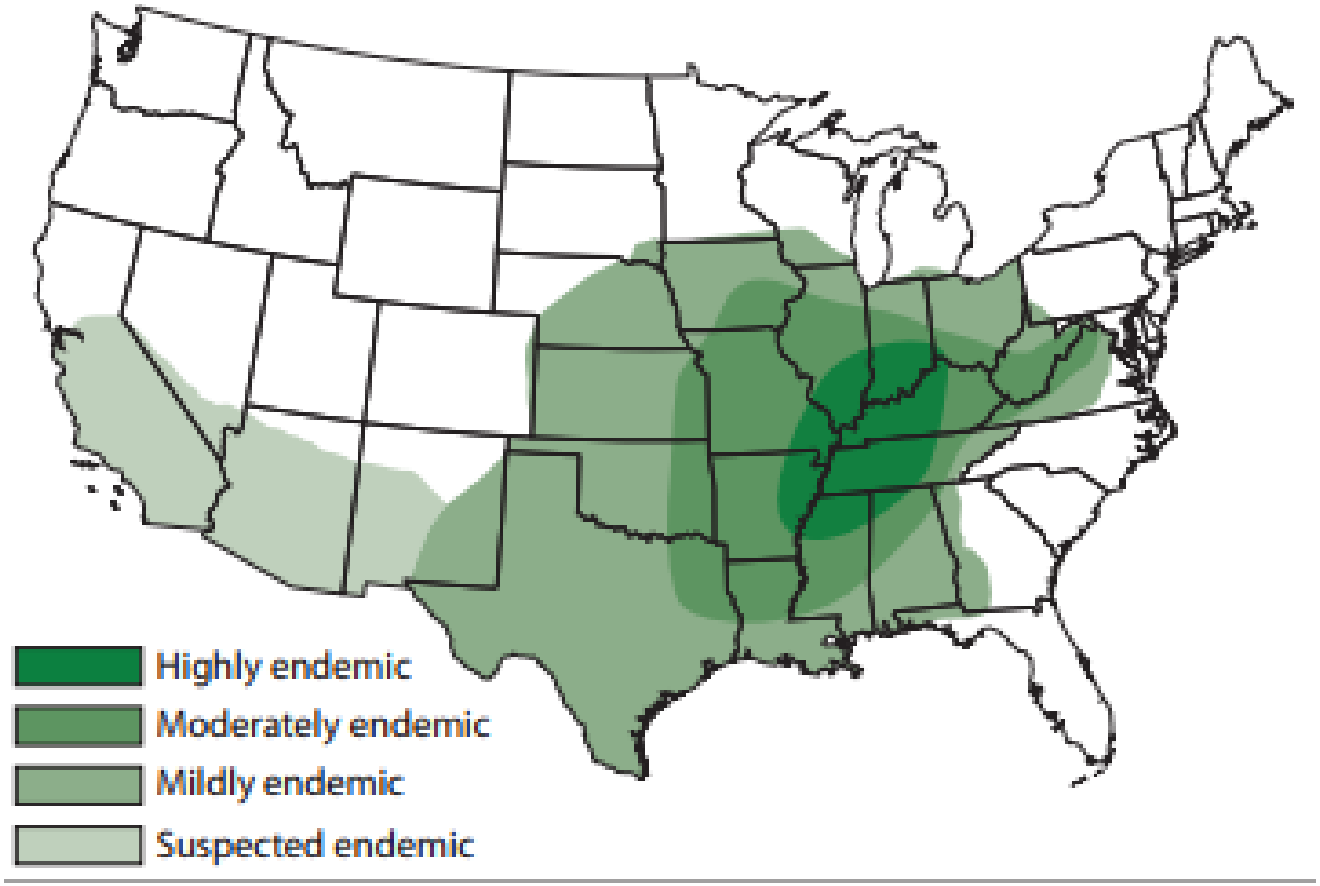
Treatment

- Most resolve symptoms without treatment
- Fluconazole, itraconazole
- Duration: 3-6 months

# Histoplasmosis

- *Histoplasma capsulatum*
  - Dimorphic fungus
  - Soil, associated with birds and bats
- Ohio and Mississippi River Valleys
- 6.1 cases/100,000 persons in the Midwest

# Histoplasmosis



# Histoplasmosis

- Infection by inhalation
  - Acute Infection
  - Reactivation
- Pulmonary Infection
  - Acute, chronic
- Disseminated
  - Bone marrow, gastrointestinal tract
- CNS
  - Meningitis, abscess
- Mediastinitis
- Pericarditis
- Ocular

# Histoplasmosis Diagnosis and Treatment

- Diagnosis
  - Urinary or Blood Antigen

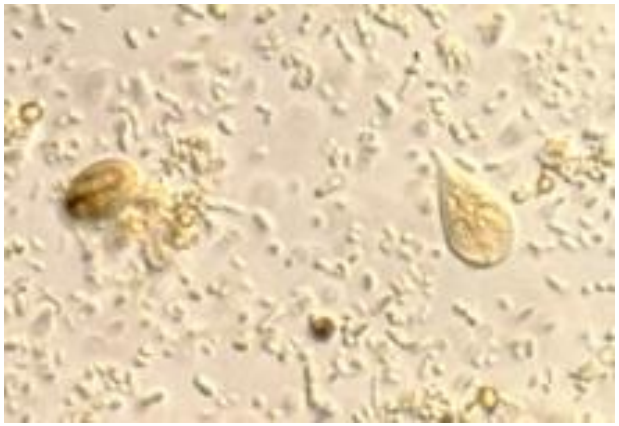
Severe pulmonary infection

- Amphotericin B, itraconazole

Mild-moderate pulmonary infection

- Usually self-limited
- Itraconazole

# Other Infections



*Giardia lamblia*

Deer mouse

*Naegleria fowleri*

# Giardiasis

- *Giardia lamblia*
  - Flagellated, bi-nucleated protozoan
- Most common intestinal parasite in North America
- Contaminated water or food, fecal-oral route
  - Surface water easily contaminated
  - Highly contagious
    - 10 cysts to be infective

# Giardiasis

- Incubation period 1-2 weeks
- Presentation
  - Acute diarrhea
  - Chronic diarrhea with malabsorption
- Symptoms
  - Abdominal pain
  - Nausea, vomiting
  - Large volume stool, watery, foul smelling

# Giardiasis Diagnosis

- Direct fluorescent assay of stool
  - Most sensitive and specific
- Fecal ova and parasite exam
- Antigen testing, PCR tests
- Duodenal aspirate to examine for trophozoites

# Treatment

Metronidazole 250mg PO TID x7 days

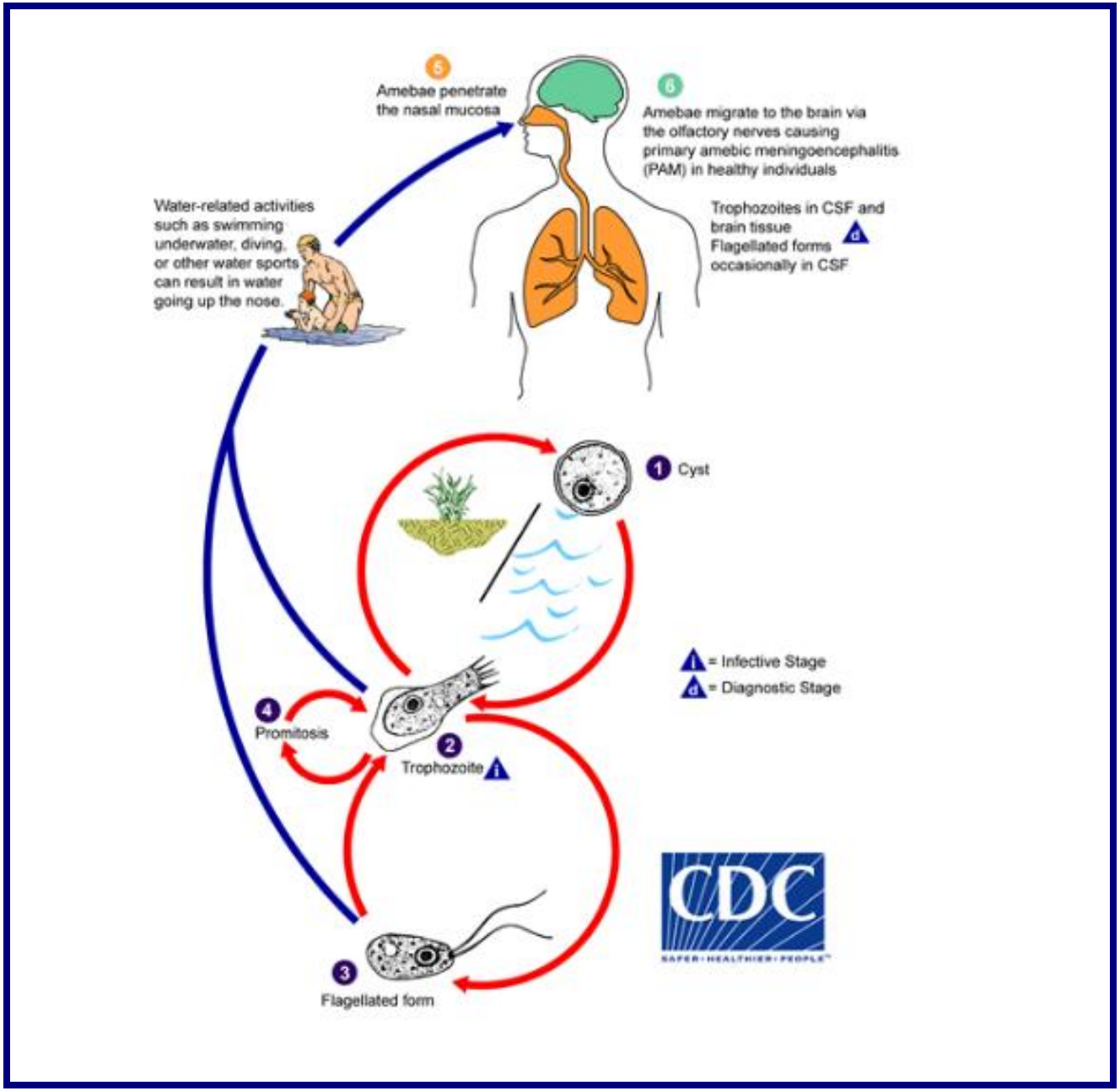
Tinidazole 2g PO x1 dose

Nitazoxanide 500mg PO BID x3 days

Paromomycin in pregnancy

# Primary Amebic Meningoencephalitis (PAM)

- *Naegleria fowleri*
  - "brain eating ameba"
- Found in warm, fresh water
- Enters via nasal mucosa
- 4 survivors in 143 U.S. cases since 1962


5
Amebae penetrate the nasal mucosa
6
Amebae migrate to the brain via the olfactory nerves causing primary amebic meningoencephalitis (PAM) in healthy individuals
Water-related activities such as swimming underwater, diving, or other water sports can result in water going up the nose.
Trophozoites in CSF and brain tissue
Flagellated forms occasionally in CSF
d
1 Cyst
i = Infective Stage
d = Diagnostic Stage
4 Promitosis
2 Trophozoite i
3 Flagellated form
CDC
SAFER · HEALTHIER · PEOPLE™

# PAM

- Symptoms begin 1-9 days after exposure
  - Death 1-18 days after symptom onset
- Symptoms
  - Headache, fever, nausea
  - Seizures, altered mental status, coma
- Diagnosis
  - High level of suspicion
  - *N. fowleri* organisms, nucleic acid, or antigen in CSF or tissue
- No standard treatment

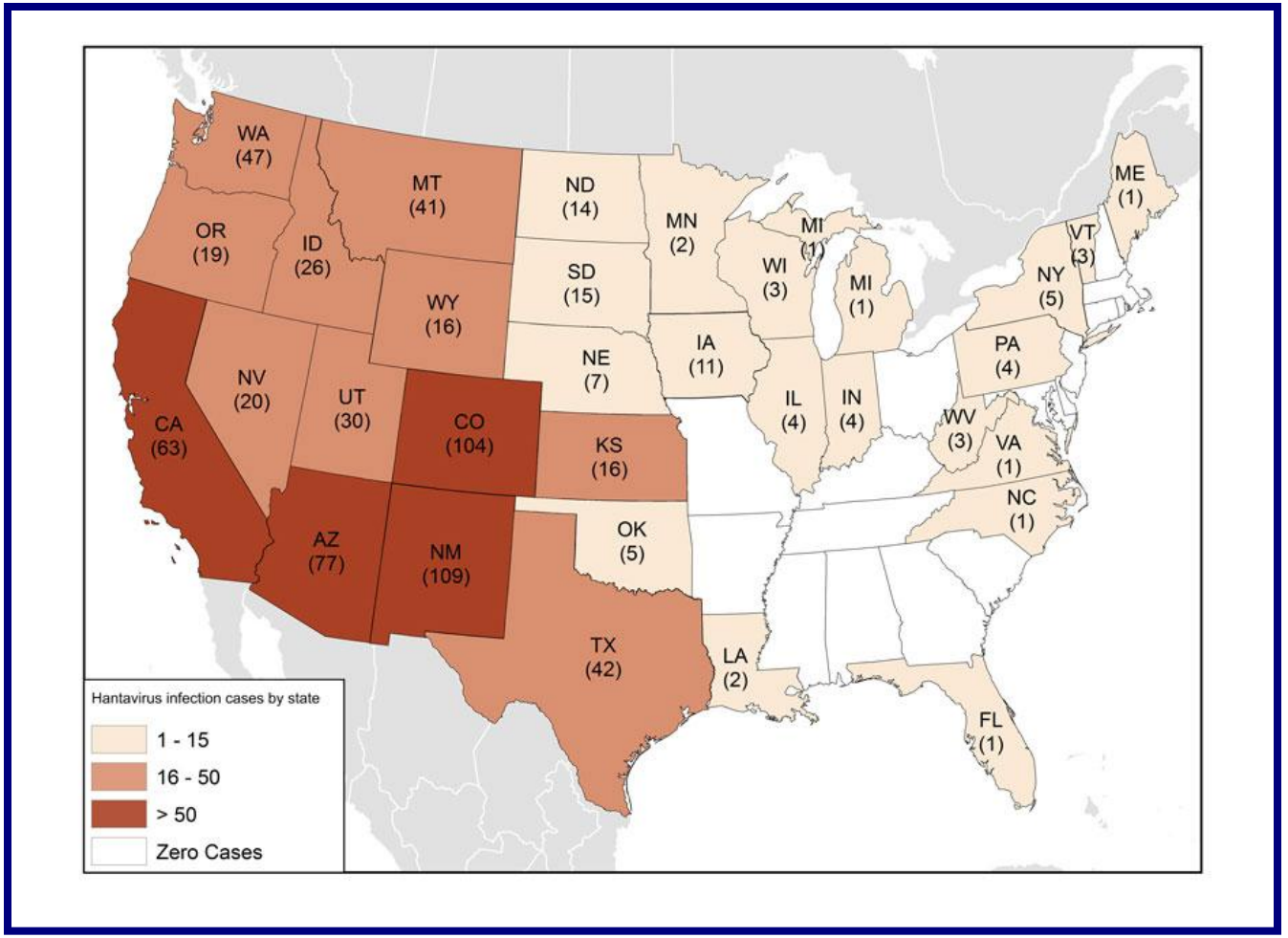
# Hantavirus

- Sin Nombre virus
  - Discovered in 1993 after four-corners outbreak
- Reservoir: North American deer mouse
- Inhalation of virus that has been excreted in urine, saliva, or feces of rodents
- Risk Factors: high rodent density in home, handling rodents, occupational or recreational exposure

# Hantavirus Symptoms

- Early Symptoms
  - Fevers, headache, myalgias
- Hantavirus Pulmonary Syndrome
  - 4-10 days after symptom onset
  - Cardiopulmonary symptoms, ARDS
  - Thrombocytopenia, leukocytosis, DIC
  - 50% mortality

# Hantavirus Pulmonary Syndrome




https://www.cdc.gov/hantavirus/surveillance/state-of-exposure

# Hantavirus Diagnosis and Treatment

- Hantavirus-specific IgM
  - Rising IgG
- Hantavirus-specific RNA by PCR
- Hantavirus-specific antigen
  - Tissue

Treatment: Supportive Care

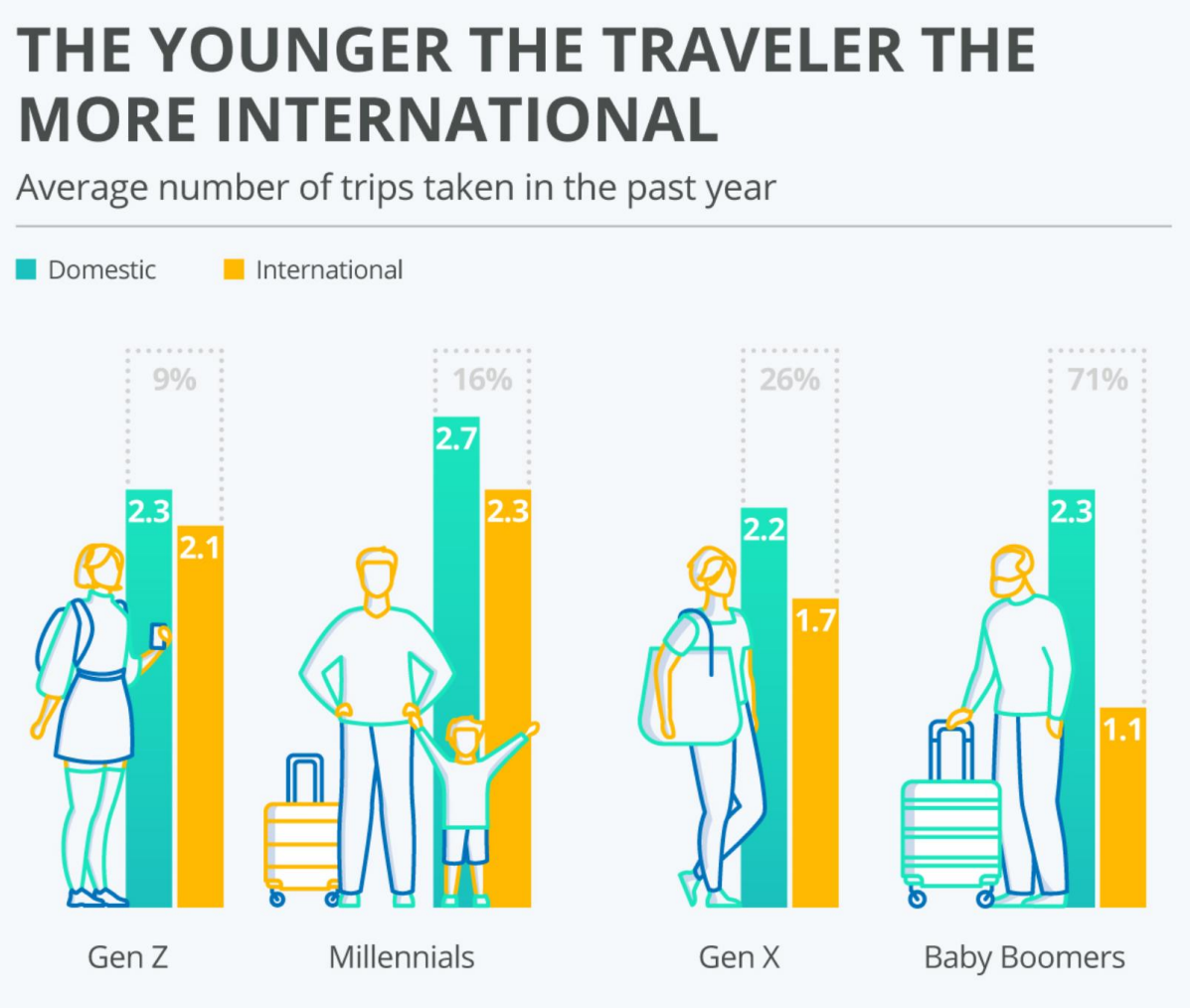
# Hantavirus Prevention

- Avoid rodent exposures
  - Recreational
  - Occupational
    - Agriculture, construction, forestry, cleaning
- Rodent Control
- Educational Materials

# Hansen's disease (Leprosy)

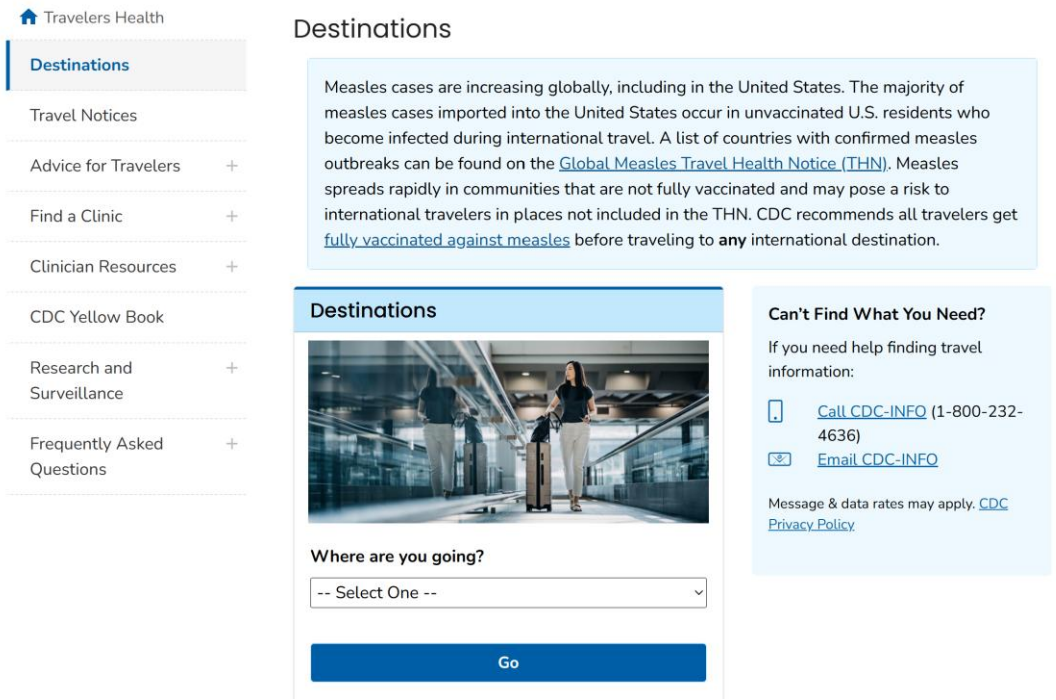
- *Mycobacterium leprae*
- Spread by droplet inhalation
  - 2-5 year incubation period
- Hypo-pigmented skin lesions, loss of sensation in peripheral nerves
- 95% of the population is immune
  - Indigenous in LA, TX, MS, HI
- Armadillo is natural reservoir
  - Direct contact
  - Meat consumption

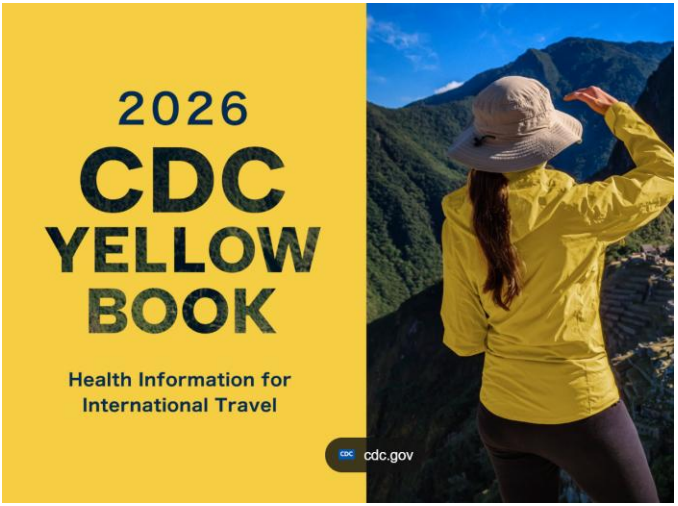
# International Travel Trends




www.statista.com/chart/32657/average-number-of-trips-by-generation/

# Travel Health Resources




www.cdc.gov/travel

# Travel Related Vaccinations

## Required

Yellow fever

Meningococcal

## Routine

Tetanus/Diphtheria

Measles

Polio

Pneumococcal

Varicella

## Recommended

Hepatitis A

Typhoid

Hepatitis B

Meningococcal

Rabies

Japanese Encephalitis

Cholera

# Traveler's Diarrhea

- Enterotoxigenic E. coli (ETEC)
  - Salmonella, shigella, Campylobacter
  - Rotavirus, norovirus
- Sudden onset, watery diarrhea with fevers, nausea, vomiting, cramping
  - 5-15 days after arrival
  - Duration 1-5 days
- 20-60% of 2-week travelers will experience this

# High-Risk Groups Traveler's Diarrhea

- Transplant
- Malignancy
- Inflammatory Bowel Disease
- Chronic Kidney Disease
- Ileostomy, colostomy
- AIDS

# Traveler's Diarrhea

## Treatment

**Ciprofloxacin**
**500 mg po 3 days**

**Levofloxacin**
**500 mg po 1-3 days**

**Azithromycin**
**1000 mg po once**

**Rifaximin**
**200 mg TID x3 days**

## Prophylaxis

**Bismuth subsalicylate**
**(Pepto Bismol)**
**2 tab PO QID**

**Norfloxacin**
**400 mg po daily**

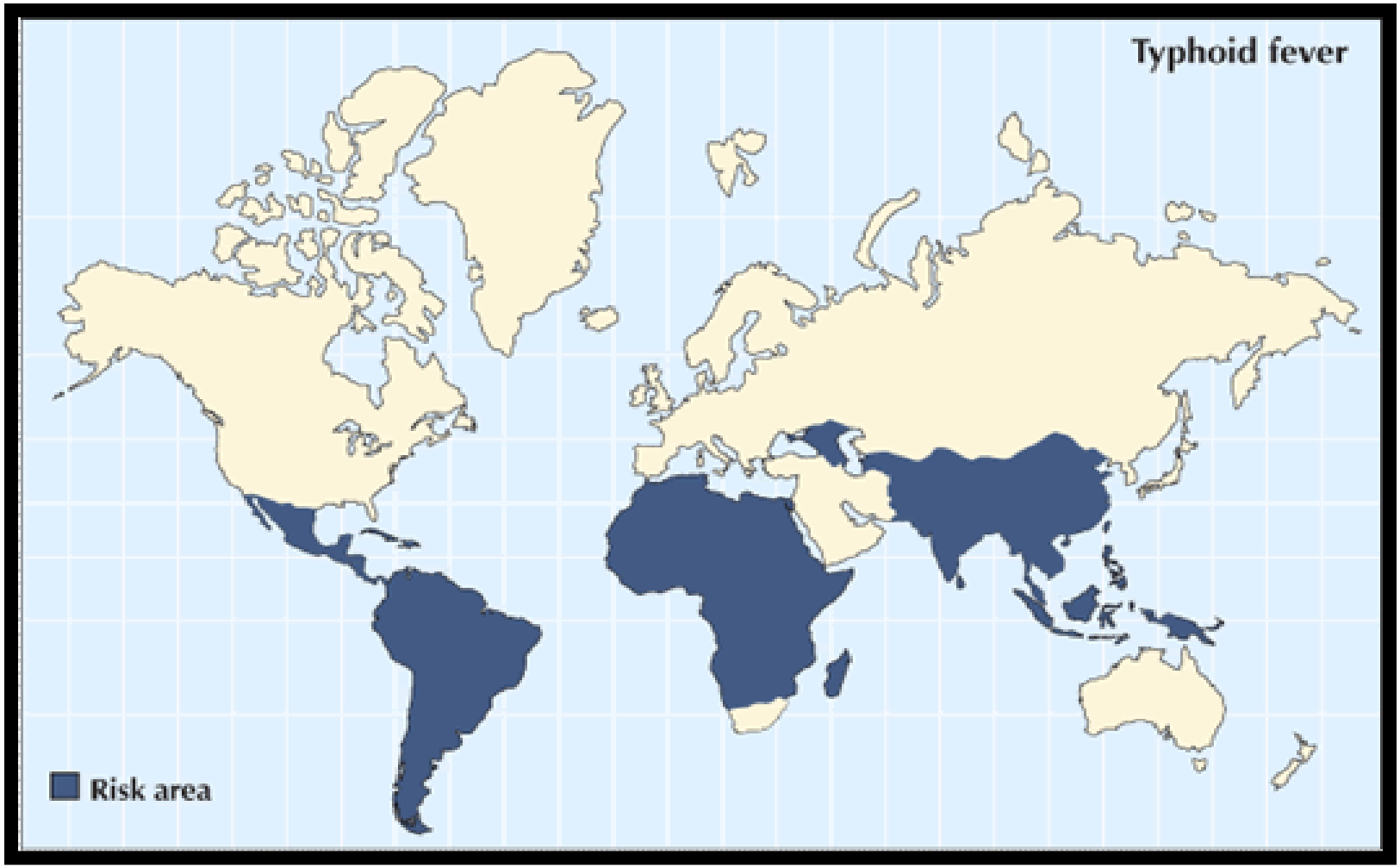
**Ciprofloxacin**
**500 mg po daily**

**Rifaximin**
**200 mg QD or BID**

# Typhoid Fever

- Enteric fever
  - Caused by *Salmonella enterica serovars typhi and paratyphi*
- Transmission : contaminated food and water
- 1-10 cases/100,000 travelers per month
- Oral live attenuated vaccine: 4 doses
  - Protection for 5 years
- Injectable polysaccharide vaccine: 1 dose
  - Protection for 2 years
- Vaccine protects from S. Typhi but not S. Paratyphi
  - 50-70% efficacy

# Typhoid Fever Distribution



# Malaria

- Acute febrile illness with headache, confusion, nausea, vomiting
  - RBCs rupture and release schizonts
  - Fevers and chills in intervals
- Suspect in any febrile traveler returning from an endemic area

# Malaria

- Caused by intraerythrocytic *Plasmodium* protozoa
- Anopheles mosquito
- Chemoprophylaxis as indicated by the CDC
  - Resistance patterns
  - Tolerability of drug

CDC Malaria Hotline: 770-488-7788

# Malaria prophylaxis

- Prevent bites!
- Chemoprophylaxis
  - Chloroquine resistance
    - Atovaquone-proguanil (2 days before through 7 days after)
    - Mefloquine weekly
    - Doxycycline

***Aedes aegypti***

**Yellow fever mosquito**

# Yellow Fever

- Caused by yellow fever virus
  - Single-stranded RNA virus
  - 2 genotypes in South America (Jan-May), 5 genotypes in Africa (July-Oct)
- Asymptomatic to multisystem viral hemorrhagic fever
  - Up to 15% cases
- Treatment is supportive

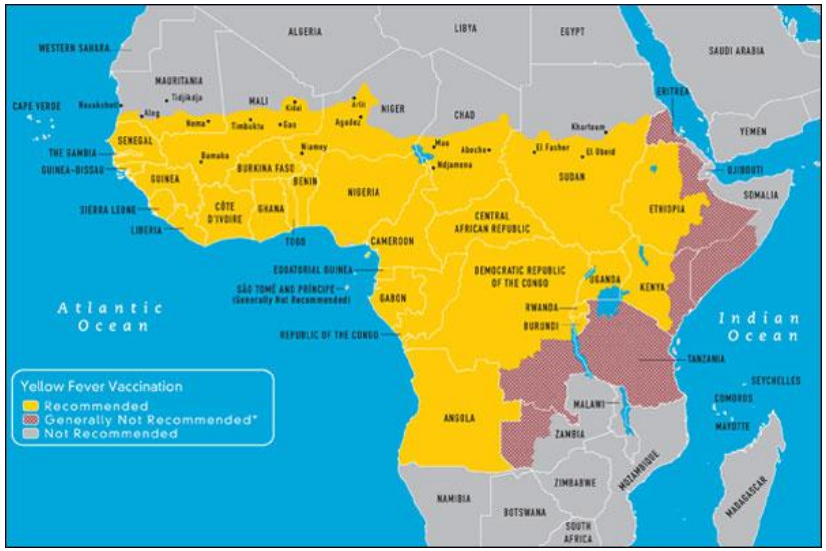
# Yellow Fever

## South America

## Infection Risk 5/100,000


## West Africa

## Infection Risk 50/100,000



# Zika Virus

- Mosquito-borne arbovirus
  - *Aedes aegypti*
- Modes of Infection
  - Mosquito bite
  - Vertical transmission
  - Sexual transmission
  - Blood transfusion

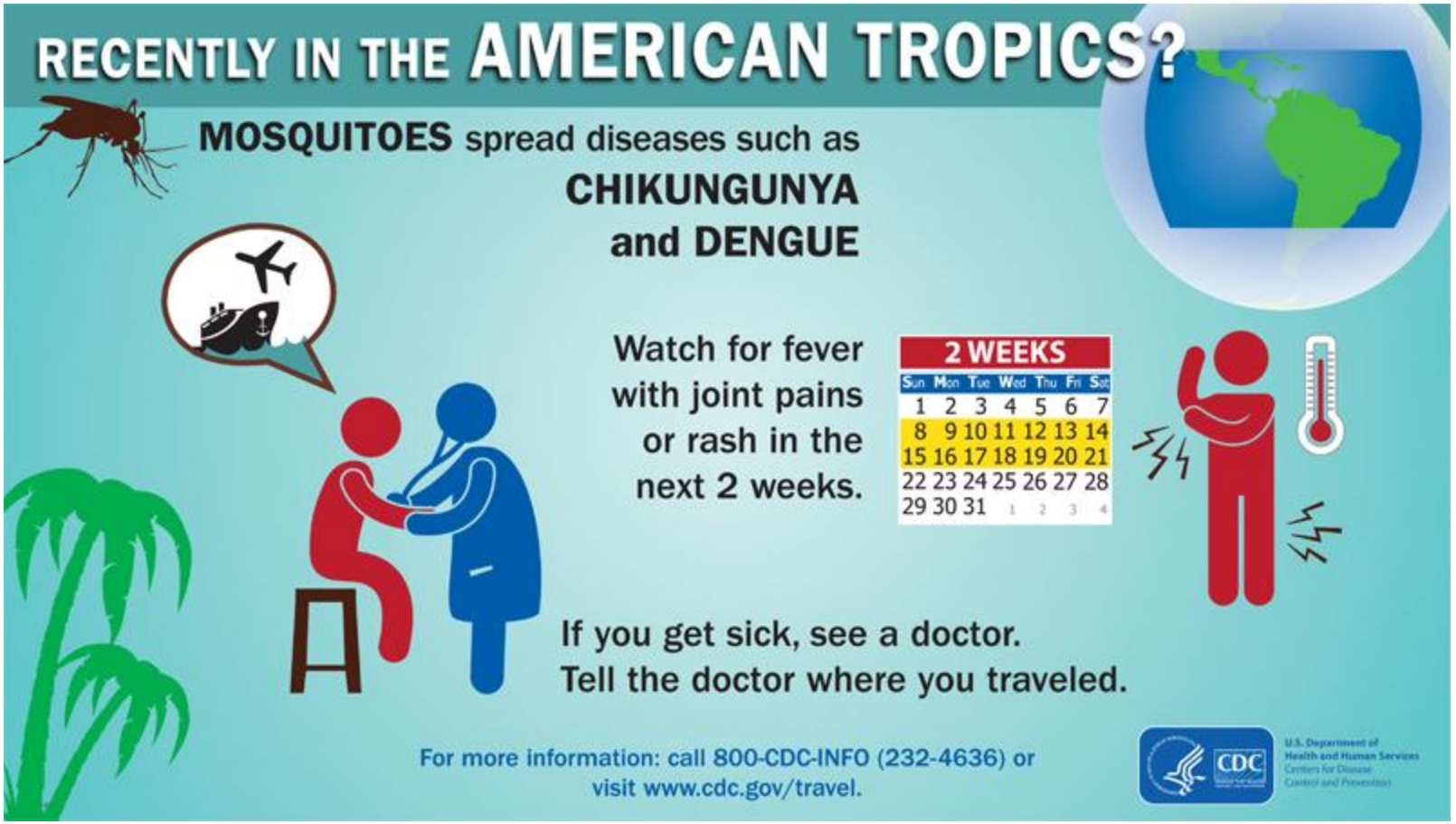
# Zika Virus

- 80% of infections are asymptomatic
- Mild Illness – 95% of symptomatic infections
  - Fever, arthralgia, conjunctivitis
  - Diffuse maculopapular rash
    - Pruritic, spares palms and soles
- Symptoms last up to one week

Treatment: Supportive Care

# Zika Virus Prevention and Safety

- DEET containing repellants
- Mosquito Control
- Zika and Pregnancy
  - Avoid travel where Zika transmission is a concern
  - Pregnancy avoidance
    - 6 months from last possible exposure for men
    - 2 months from last possible exposure for women


RECENTLY IN THE AMERICAN TROPICS?
MOSQUITOES spread diseases such as
CHIKUNGUNYA
and DENGUE
Watch for fever
with joint pains
or rash in the
next 2 weeks.
2 WEEKS
Sun Mon Tue Wed Thu Fri Sat
1 2 3 4 5 6 7
8 9 10 11 12 13 14
15 16 17 18 19 20 21
22 23 24 25 26 27 28
29 30 31
If you get sick, see a doctor.
Tell the doctor where you traveled.
For more information: call 800-CDC-INFO (232-4636) or
visit www.cdc.gov/travel.
CDC
U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention

# Dengue

- Flavivirus, spread by mosquitos
  - Most common mosquito-borne viral disease
- 4-10 days of incubation
- Symptoms: fever, rash, retro-orbital pain, neutropenia and thrombocytopenia, transaminitis
- Treatment is supportive
  - Avoidance of aspirin
- Dengue vaccine for certain populations

# Chikungunya

- Mosquito is vector
- Difficult to differentiate from Dengue
- Onset 3-7 days
- Symptoms: fevers, chills, headache, rash, back pain, joint and muscle pain
- Supportive care
  - Avoidance of aspirin

# Cutaneous Larva Migrans

- Caused by nematodes (hookworm)
- “Creeping Eruption” or “Ground itch”
  - Enters through skin
- Use of footwear is preventive
- Treatment with Albendazole 400mg po x1

# Herpes B Virus Infection

- A.K.A. Macacine Herpesvirus 1
  - Endemic among macaque monkeys
- Fatal encephalomyelitis in humans
  - 50 confirmed cases since 1932
- Transmission by bite
  - PEP within several hours
    - Valacyclovir 1g q8H x14d

# Rabies

- Acute, fatal, meningoencephalitis
- 55,000 people die annually from rabies
  - 3 human cases/year in the US
- Transmission via animal bite or scratch
- Major risk groups
  - bats, raccoons, skunks, foxes
- Pre-exposure vaccine ppx: 0, 7, 21 or 28 days

Treatment: HRIG then 4 dose vaccine schedule (Days 0,3,7,14)

# Leptospirosis

- Spirochete that survives in standing water, contaminated soil
- ~1 million cases/year, 60,000 deaths
- Early infection resembles influenza
  - Fevers, chills, nausea, calf and lower back pain
  - Elevated bilirubin, transaminitis, thrombocytopenia
- Antibody testing is available

Doxycycline 100mg po BID x7 days
Alternative: Amoxicillin PO, Ceftriaxone IV

# Hantavirus (Old World)

- Hemorrhagic fever with renal syndrome
  - Asia, Europe
- Nonspecific febrile prodrome
  - Hemorrhage, back pain, hypotension, DIC, Renal failure
  - Mortality up to 15%
- Treatment is supportive

# GOING TO THE AMERICAN TROPICS?

**MOSQUITOES** spread diseases such as **CHIKUNGUNYA and DENGUE.**

Mosquitoes bite day and night.
Prevent mosquito bites by using insect repellent.

**DON'T LET MOSQUITOES RUIN YOUR TRIP.**

For more information: call 800-CDC-INFO (232-4636) or visit www.cdc.gov/travel.

CDC

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

# Other Diseases to Consider

- *Mycobacterium tuberculosis*
- HIV Infection
- Syphilis
- Acute Infectious Hepatitis
- Influenza, COVID-19
- Measles, Polio, Meningitis
  - vaccine history, booster if needed

# Questions

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