



Virginia Mason™

Call of the wild: Zoonotic Infections

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Infectious Diseases

Disclosures

No financials

I am a hypochondriac

I do love the outdoors!

Objectives

Understand the epidemiology, clinical features, and treatments of selected outdoor infections

I hate ticks...

Case

- 20 y/o with a PMHx of traumatic splenectomy as a child has just returned from Wash U for spring break where she is a biology major. She spends her time researching the common red crested barn finch. She trapes around fields and goes in many barns. She presents with a 10 day history of subjective fever, chills, myalgias, severe HA with neck stiffness.
- In the ER she is found to have a temp of 38.6, HR 96, BP 100/70, RR 16
- She is admitted for concern for meningitis

However on her back the following is seen:



Version 2

However on her back the following is seen:



Version 3

However on her back the following is seen:





STARI: Southern Tick-associated Rash Illness

- Rash: expanding bull's-eye rash
- Fever, HA, fatigue, myalgias
- Milder illness with no known complications
- spread by lone star tick
- No bacteria identified
- Treatment unknown
- Most get abx for Lyme



Lyme



Centers for Disease Control and Prevention, <http://phil.cdc.gov/phil/>

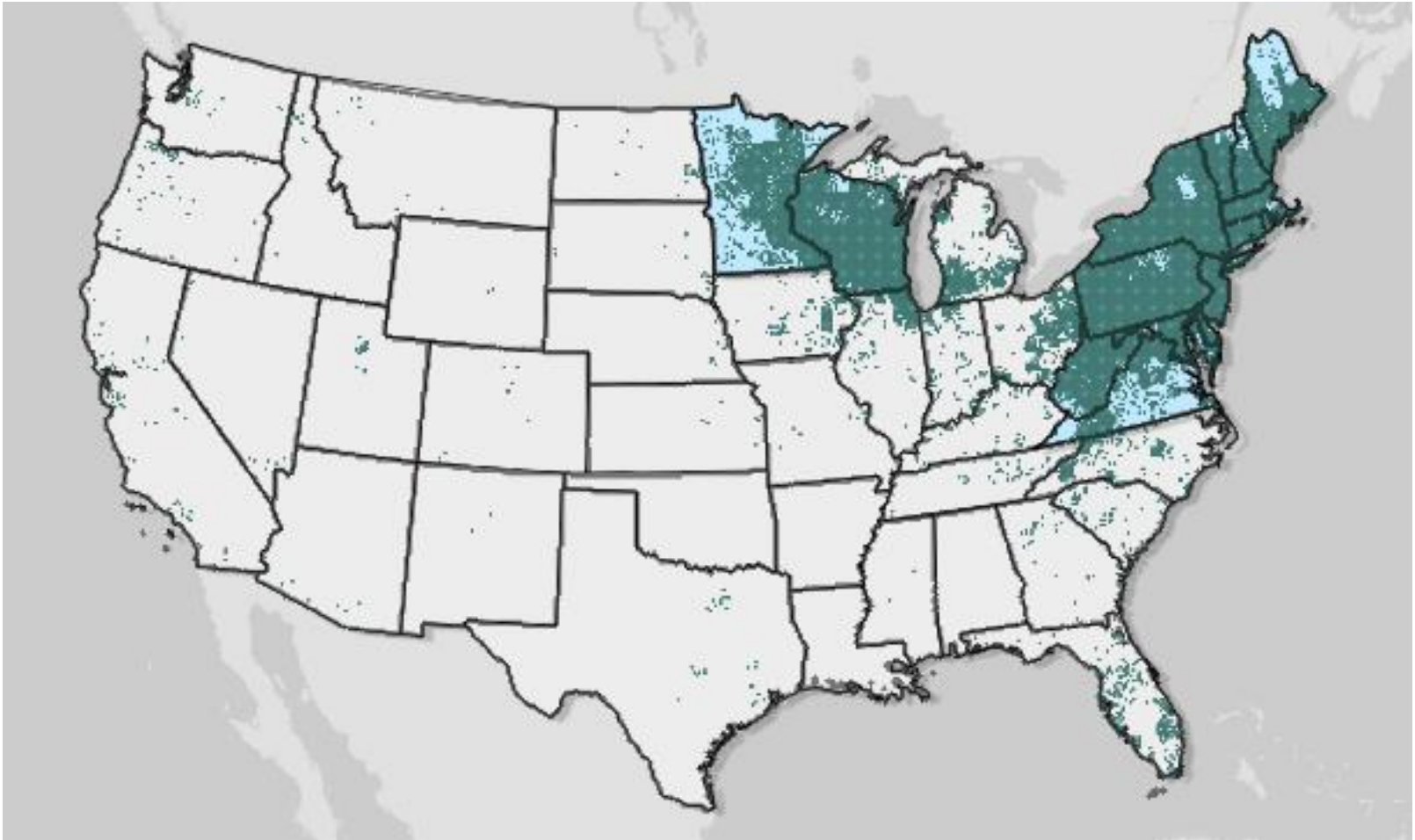
Caused typically by *Borrelia burdogradorferi* (some newer subspecies are being described)

Borrelia burgdoferi

Blacklegged Tick (*Ixodes scapularis*)



US Map



https://www.cdc.gov/lyme/datasurveillance/lyme-disease-maps.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Flyme%2Fdatasurveillance%2Fmaps-recent.html

Lyme: 3 Stages of Illness



- **Localized Infection** (3-30 days post bite): EM rash at site of tick bite, fatigue, fever, chills, HA, myalgia, arthralgia, LAN
- **Early Disseminated Infection** (days to weeks): additional EM rashes, facial or Bell's Palsy, HA with meningismus, arthralgia/arthritis, cardiac findings (heart block, myocarditis, cardiomyopathy), conjunctivitis or iritis/panophthalmitis
- **Late Disseminated** (months to years): large joint migratory polyarthrititis, neuro symptoms like shooting pain, peripheral neuropathy, short term memory loss

Lyme

Diagnosis:

- Screening ELISA with reflex to Western Blot
- Two different ELISAs
- PCRs from CSF and synovium (in setting of + serology as false positives are common when serology is negative)

Treatment:

- Early Infection: doxycycline for 10 days; amoxicillin or cefuroxime for 14 days
- Arthritis: doxy or amox for 28 days
- CNS: ceftriaxone 14-28 days, doxy 14-21 days
- Cardiac: first degree AV block: po regimens, high degree AV block: iv 14-21 days

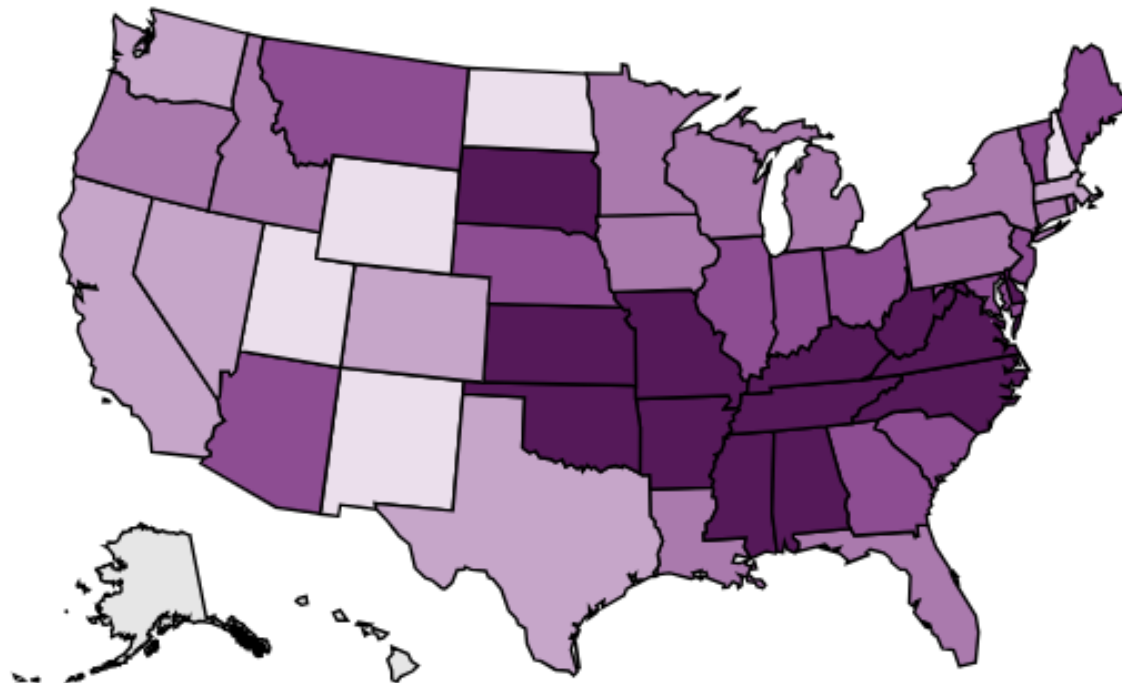
Rocky Mountain Spotted Fever



- RMSF is a severe vasculitic disease caused by the *Rickettsia rickettsii*
- When infection does occur, symptoms usually start 7 days (1-14 days) after the bite
- Two thirds of victims are children

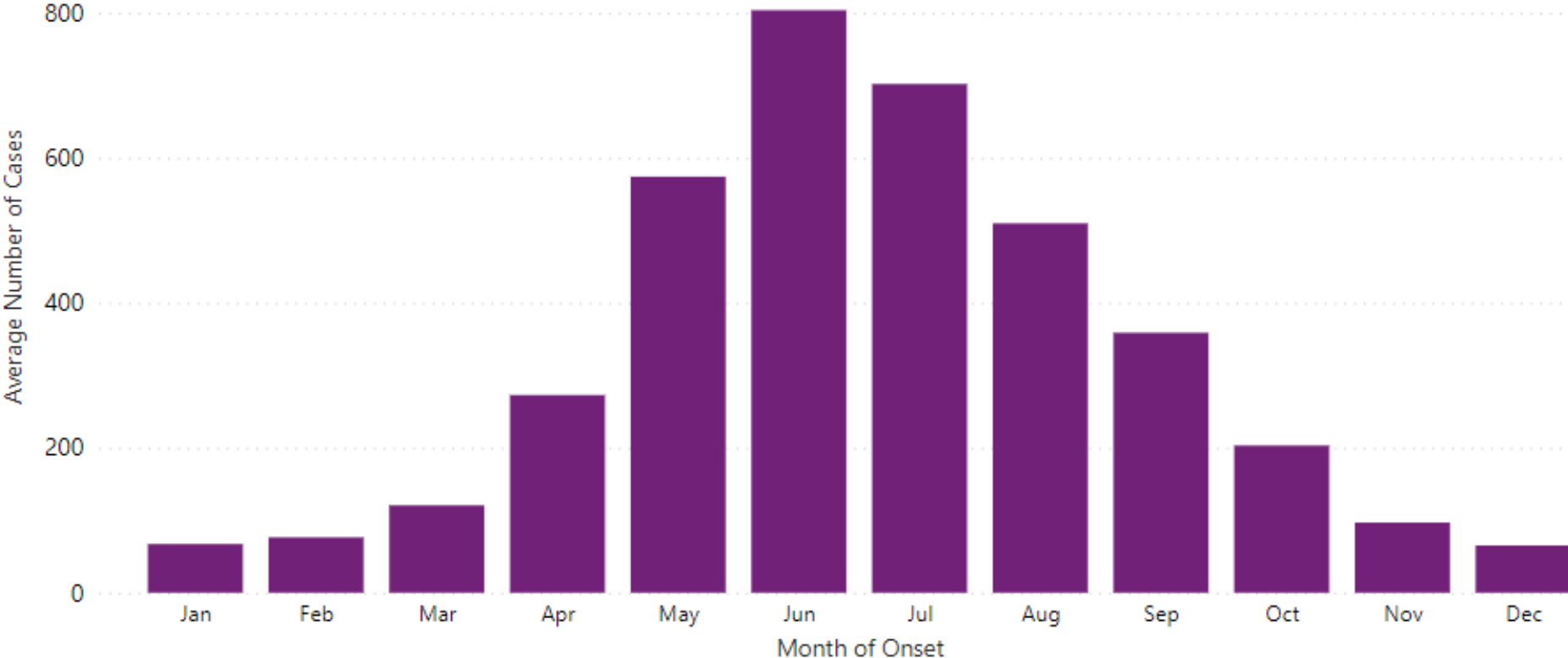
Annual incidence (per million population) of reported spotted fever rickettsiosis—United States for 2021

● 0 ● 0 to < 0.41 ● 0.41 to < 1.48 ● 1.48 to < 4.77 ● 4.77+ ● Not Notifiable

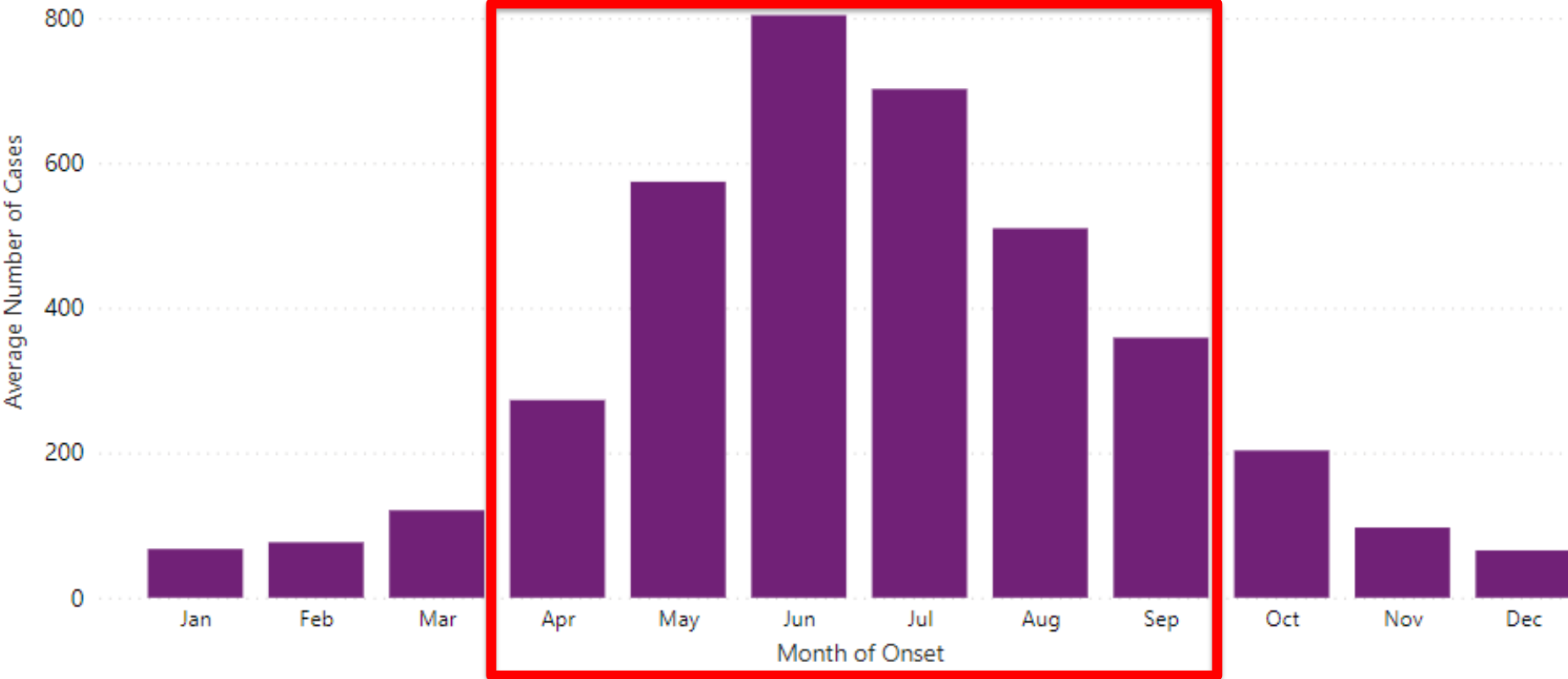


<https://www.cdc.gov/rmsf/stats/index.html>

Average number of reported cases of spotted fever rickettsiosis, by month of onset—United States, 2017–2021



Average number of reported cases of spotted fever rickettsiosis, by month of onset–United States, 2017–2021



RMSF Clinical Features

High fever

Chills

Severe headache

Muscle aches

Nausea and vomiting

Abdominal pain (may mimic acute abdomen/appendicitis)

Restlessness and insomnia

Conjunctival injection

Rash is distinctive

- Red macules appear 2 to 3 days after the fever starts and turn into petechial lesions

Centripetal spreading pattern rash starts on extremities and later spread to the central body or trunk

Shock, multisystem organ failure

RMSF



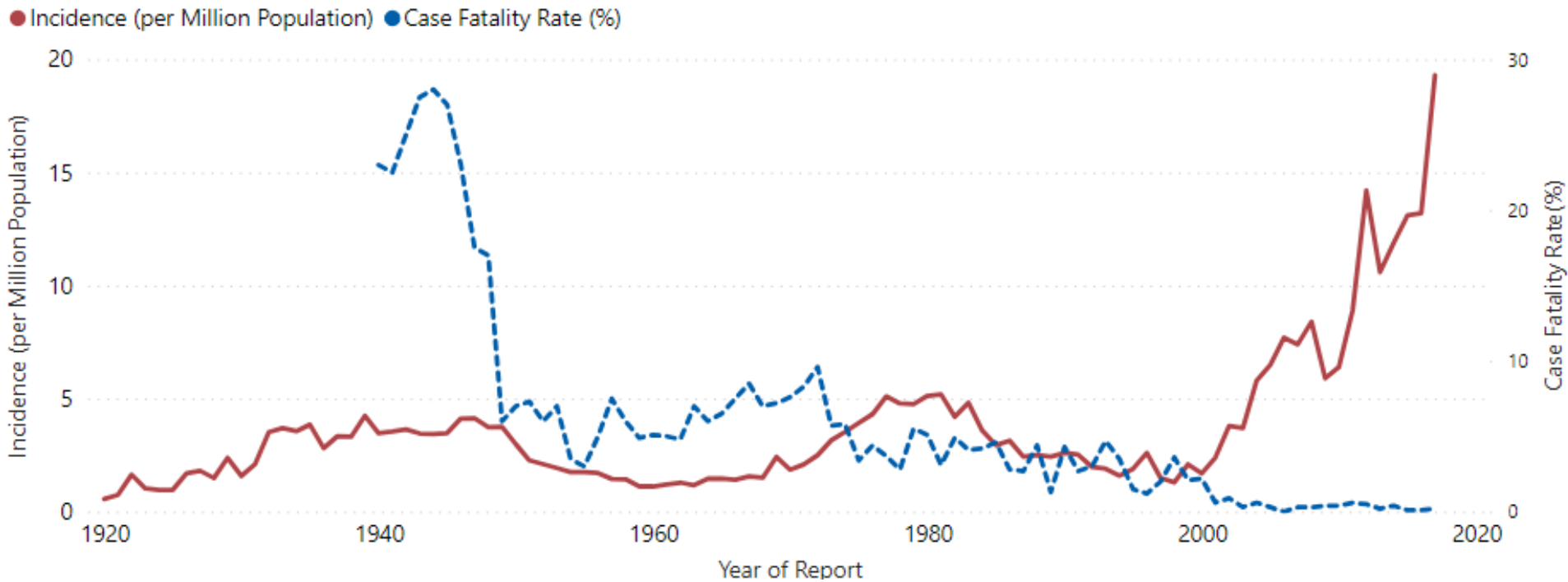
Rocky Mountain Spotted Fever

- Thrombocytopenia
- Rash in 90% but may appear days into illness
- Serology and PCR available, but send outs. *No quick diagnostic test*
- Real diagnosis requires rising titers or + PCR
- Treat with doxycycline 7-14 days (even in kids or pregnant women)
- If can't give doxy: chloramphenicol (if you have it)
- Treat first, ask questions later.

RMSF complications

- Untreated RMSF has a 20 to 75% mortality rate, which falls to 5% with appropriate treatment (before 5th day of illness)
- Children under 10 years old, American Indians, people with a compromised immune system, and people with delayed treatment are at an increased risk of fatal outcome from RMSF.

Reported incidence and case fatality of SFR in the United States, 1920–2017



<https://www.cdc.gov/rmsf/stats/index.html>

Case

- 42 y/o homeless alcoholic presents to ER with non-healing ulcer on leg and regional lymphadenopathy
- 42 y/o diabetic groundskeeper at Chambers Bay Golf Course admitted with high fever, cough, shortness of breath. Thinks he may have run over a bunny....

Tularemia

- Caused by *Francisella tularensis*
- Tick bite or deer fly bite; skin contact; ingestion of infected/uncooked meat; inhalation
- Highly infectious
- Incubation period is only 3 to 4 days (1-21 day range)
- Rapid diagnostic testing for tularemia is not widely available. The diagnosis should be suspected clinically and antibiotics started prior to laboratory confirmation.

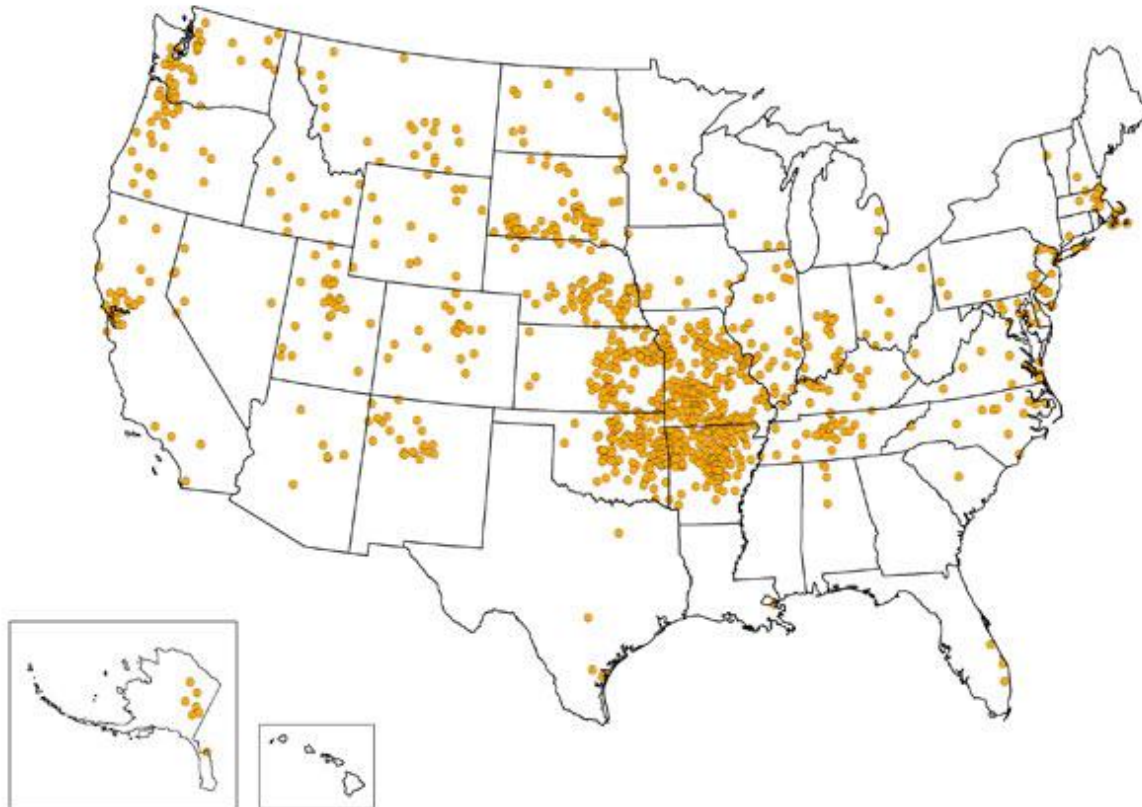
Clinical Presentation of Tularemia

| Clinical presentation | |
|---|-----|
| Ulceroglandular (Skin ulcer with adenopathy) -painful papule at the tick bite site ulcerates and is followed by regional lymphadenitis | 50% |
| Glandular (adenopathy without skin lesion) | 9% |
| Oculoglandular (conjunctival nodules with adenopathy) -eye entry | 1% |
| Oropharyngeal (sore throat with adenopathy) -oral exposure | 2% |
| Typhoidal (septicemia with possible meningitis) -acute septicemia from various exposure including oral | 8% |
| Pneumonic -inhalation of contaminated aerosols or agricultural dusts | 15% |
| unclassified | 15% |

Rx:

- Streptomycin (gentamicin ok)
- Doxycycline iv
- Chloramphenicol
- Tetracyclines (but higher failure rates)
- Ciprofloxacin

Tularemia



1 dot placed randomly within county of residence for each reported case

Case

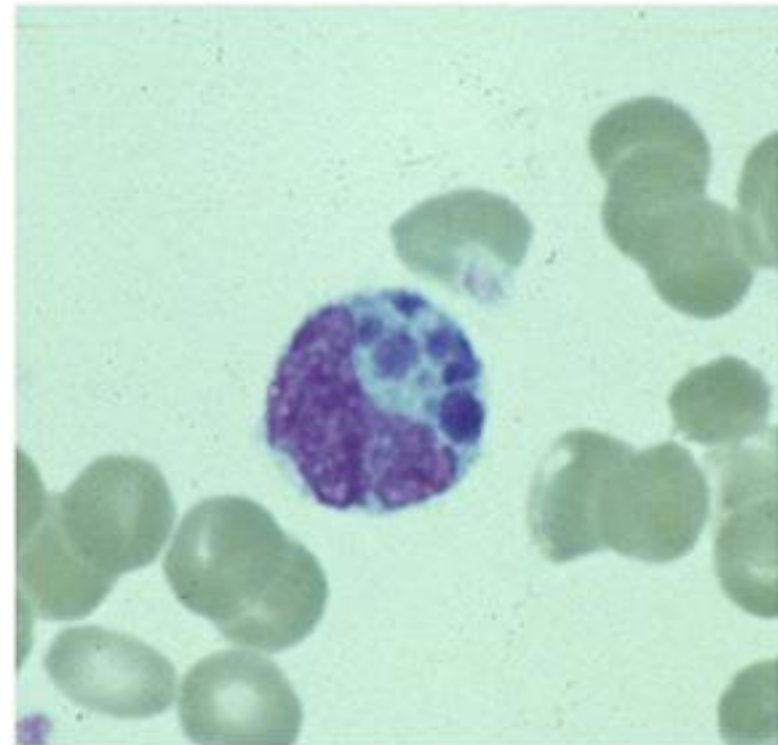
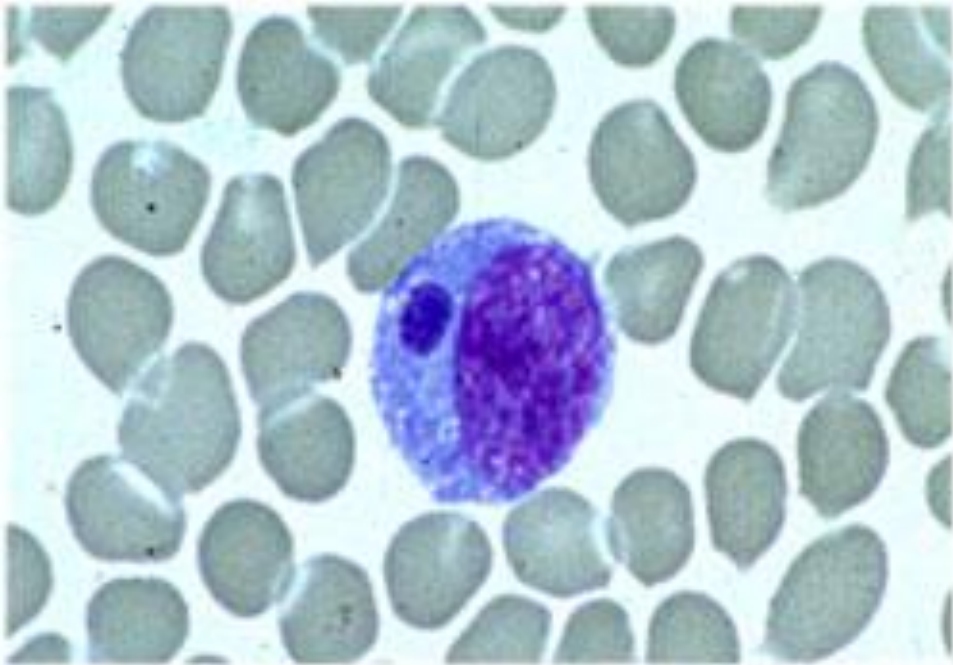
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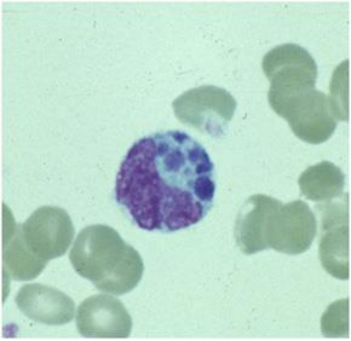
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Hematology calls you saying, you got to see what is on her peripheral smear!

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Human Granulocytic Anaplasmosis

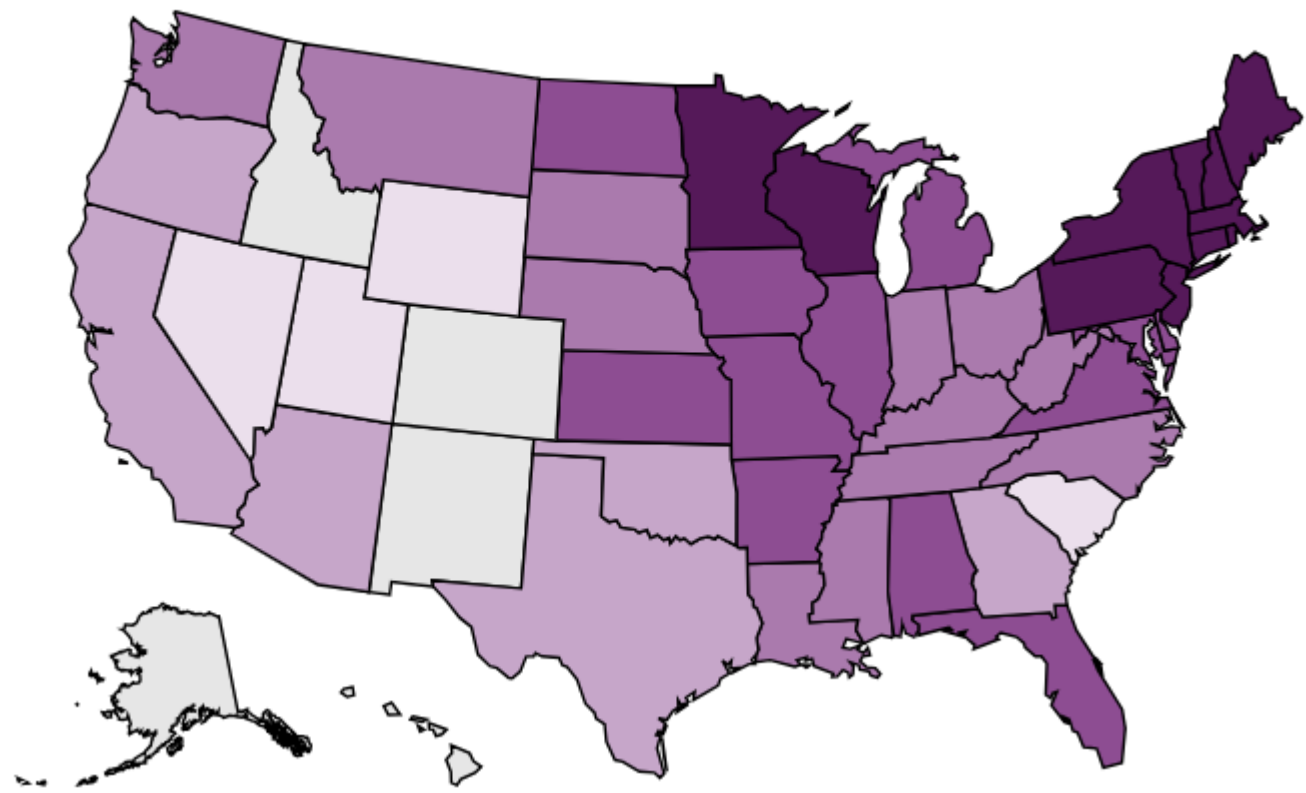


- Small Gram-negatives that cluster in inclusion vacuoles in neutrophils: morula
- Often seen on peripheral smear

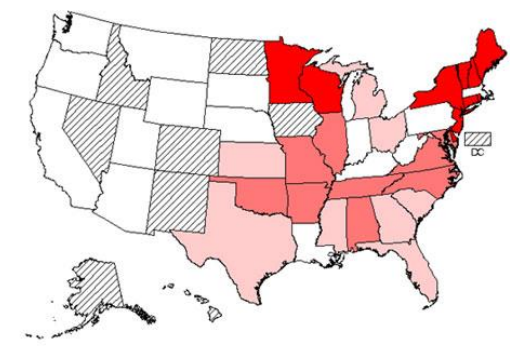
Annual incidence (per million population) of reported anaplasmosis—United States for 2021

2021

● 0 ● 0 to < 0.34 ● 0.34 to < 1.31 ● 1.31 to < 11.76 ● 11.76+ ● Not Notifiable

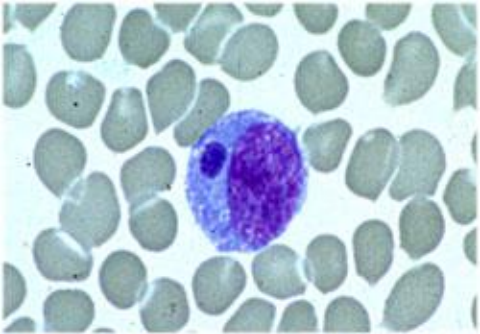


Anaplasmosis Incidence, 2010



Cases per million
■ NN ■ 0
■ 0.1-0.7 ■ 0.7-3.1
■ 3.1-136

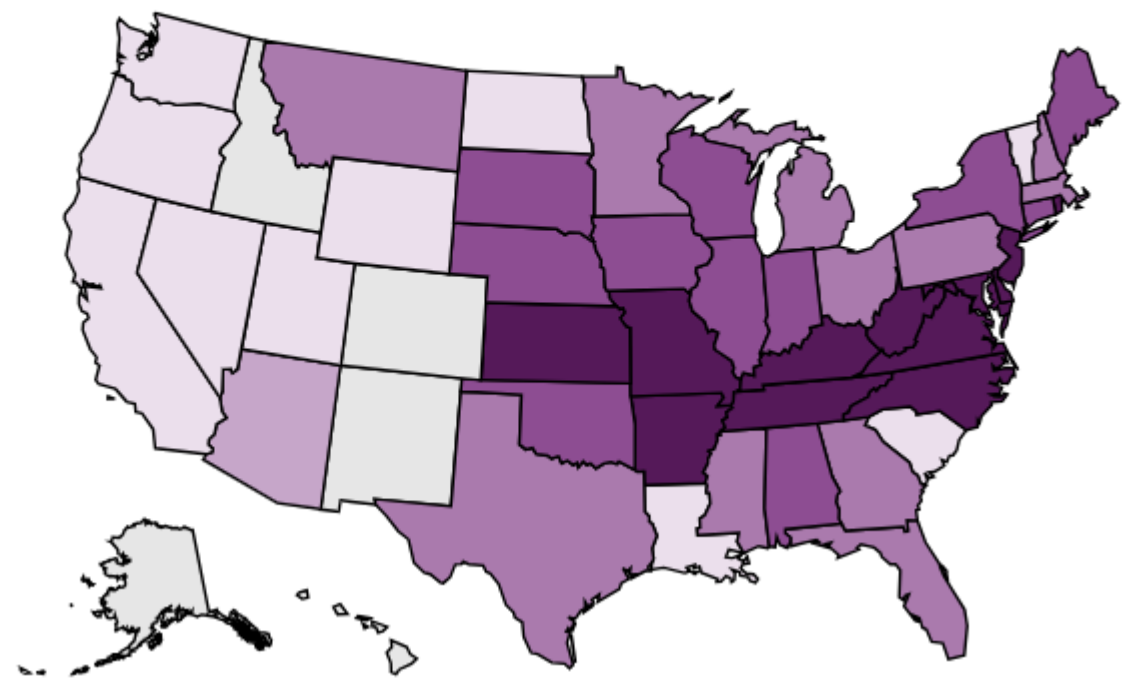
Human Monocytic Ehrlichiosis



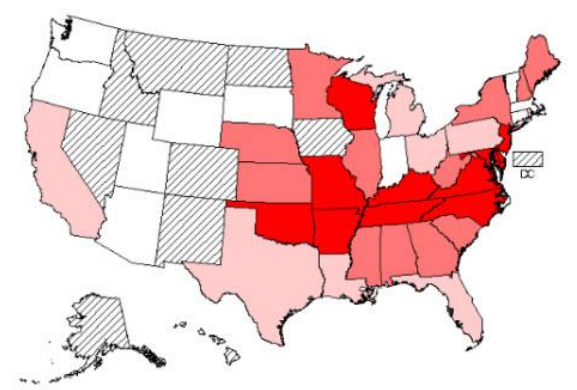
- Small Gram-negative bacteria
- Cluster inside inclusion vacuoles in monocytes best seen on a buffy coat exam: morula

Annual incidence (per million population) of reported *Ehrlichia chaffeensis* ehrlichiosis—United States for 2021

0 0 to < 0.2 0.2 to < 2.2 2.2 to < 8.4 8.4+ Not Notifiable



Ehrlichiosis Incidence, 2010



Cases per million
 NN 0
 0.03-1.0 1.0-3.3
 3.3-26

HGA and HME

- Fever, HA, myalgias, malaise, rash (less common than RMSF), n/v, cough, confusion
- Platelets often low, transaminases up, leukopenia, neutropenia
- More fulminant course in immunocompromised and those with splenectomies
- Treatment doxycycline

Comparisson

| Agent (disease) | Primary vector(s) | Approximate distribution [¶] | Incubation period (days) | Common initial signs and symptoms | Common laboratory abnormalities | Rash | Case-fatality rate |
|---|--|--|--------------------------|--|--|--|--------------------------|
| <i>Rickettsia rickettsii</i> (Rocky Mountain spotted fever) | <i>Dermacentor variabilis</i> (American dog tick), <i>Dermacentor andersoni</i> (Rocky Mountain wood tick), and <i>Rhipicephalus sanguineus</i> (brown dog tick) in Arizona ^[3] | Widespread in the United States, especially South-Atlantic and South-Central states | 2 to 14 | Fever, nausea, vomiting, myalgia, anorexia, and headache | Thrombocytopenia, mild hyponatremia, and mildly elevated hepatic transaminase levels | Maculopapular rash approximately 2 to 4 days after fever onset in about 90 percent ^Δ of patients; might involve palms and soles | 5 to 10 percent |
| <i>Ehrlichia chaffeensis</i> (human monocytotropic ehrlichiosis) | <i>Amblyomma americanum</i> (lone star tick) | South and Mid-Atlantic, North/South-Central United States, and isolated areas of New England | 5 to 14 | Fever, headache, malaise, and myalgia | Leukopenia, thrombocytopenia, and elevated serum transaminase levels | Rash in <30 percent of adults and approximately 60 percent of children | 2 to 3 percent |
| <i>Anaplasma phagocytophilum</i> (human granulocytotropic anaplasmosis) | <i>Ixodes scapularis</i> and <i>Ixodes pacificus</i> (blacklegged tick) in the United States | New England, North-Central and Pacific states | 5 to 21 | Fever, headache, malaise, myalgia, and vomiting | Leukopenia, thrombocytopenia, elevated serum transaminase levels | Rare | <1 percent |
| <i>Ehrlichia ewingii</i> infection | <i>Amblyomma americanum</i> (lone star tick) | South-Atlantic and South-Central United States to isolated areas of New England | 5 to 14 | Fever, headache, myalgia, nausea, and vomiting | Leukopenia, thrombocytopenia, and elevated serum transaminase levels | Rare | No documented fatalities |

Prevention of tick borne diseases

- Spraying clothing with permethrin 0.5% spray is the most effective.
- Tucking pants into socks before hiking and performing a careful tick check after disrobing
- Exposed skin can be protected with DEET (preferably in the 20 to 35% range)

Prevention of tick borne diseases

- If an attached tick is discovered, it should be grasped with forceps or a tick removal device, as close to the skin as possible, and traction applied slowly, without twisting, until it releases.
- Note that the fluids released are infective too: don't squash it. Wash up afterward.
- Using alcohol, heat, nail polish removal, or petroleum jelly on the tick may actually increase the risk of disease transmission

I hate lice too

- Louse-borne relapsing fever: *Borrelia recurrentis*
- Epidemic louse-borne typhus: *Rickettsia prowazekii*; outbreaks with flying squirrels
- Trench fever: *Bartonella quintana*
- All treated with doxycycline

**Did I tell you about that time
I got bit by a rat?**

Rat bite fever

- *Streptobacillus moniliformis*, *Streptobacillus notomytis*, and *Spirillum minus*
- Normal colonizers of rat nasopharynx
- Infection risk 10% post bite
- Incubation period of 2-10 days
- Abrupt onset irregularly relapsing fever, rigors, vomiting, headaches, arthralgia, myalgia, regional lymphadenopathy
- 2-4 days after fever onset, maculopapular rash
- Dx: culture from blood, synovial fluid; PCR
- Rx: Penicillin G, ceftriaxone, tetracycline

Case

26 y/o radiology resident just returned from an Eco-trek in the jungles of Hawai'i. She presents with fevers, malaise, arthralgia, n/v, diarrhea, and a dry cough. She gets better....

She gets admitted with conjunctival suffusion, renal and liver failure.

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Leptospirosis

- Spirochete
- Shed in urine and feces of many animals. Can live in environment for weeks
- We are infected via contact with mucous membranes, skin, cuts, ingestion

Signs and Symptoms of Leptospirosis

The clinical manifestations are highly variable. Typically, the disease presents in four broad clinical categories:

- (i) a mild, influenza-like illness (ILI);
- (ii) Weil's syndrome characterized by jaundice, renal failure, hemorrhage and myocarditis with arrhythmias;
- (iii) meningitis / meningoencephalitis;
- (iv) pulmonary hemorrhage with respiratory failure.

Presentations may also overlap as the infection progresses.

Leptospirosis

- Incubation period is usually 7-12 days
- Illness usually begins abruptly with fever and other symptoms. Leptospirosis may occur in two phases:
 - After the first phase (with fever, chills, headache, muscle aches, vomiting, or diarrhea) the patient may recover for a time but become ill again.
 - If a second phase occurs, it is more severe; the person may have kidney or liver failure or meningitis. This phase is also called Weil's disease.
- The illness lasts from a few days to 3 weeks or longer. Without treatment, recovery may take several months.

High Risk Groups

- Workers in the agricultural sectors
- Sewerage workers
- Livestock handlers
- Pet shops workers
- Military personnel
- Search and rescue workers in high-risk environment
- Disaster relief workers (*e.g.* during floods)
- People involved with outdoor/recreational activities such as water recreational activities, trekking, *etc.*
- Travelers who are not previously exposed to the bacteria in their environment especially those travelers and/or participants in jungle adventure trips or outdoor sport activities
- People with chronic disease and open skin wounds.

Leptospirosis Diagnosis

- Serology (IgM, IgG) – appear after first week
- Culturing the organism from clinical specimens (blood, cerebrospinal fluid or urine) – lab should know you are looking for this as it requires special media and may take up to 3 months to grow
- PCR from blood, urine, CSF – positive in the first week

Leptospirosis treatments

- Severe cases are usually treated with IV penicillin, doxycycline, or ceftriaxone
- Less severe cases treated orally with antibiotics such as doxycycline, azithromycin, or amoxicillin.
- Jarisch-Herxheimer reactions may occur after the start of antimicrobial therapy.

PROPHYLAXIS

- Pre-exposure Prophylaxis
 - May be considered for people at high risk of exposure to potentially contaminated
 - sources e.g. soldiers going into jungles, rescue team, persons involved in activities in possible high risk areas e.g. adventurous sports.
- Doxycycline 200mg weekly or Azithromycin 500mg weekly throughout the stay (*For pregnant women and those who are allergic to Doxycycline*)

Case

1. 28 y/o surgery resident returns from a week of vacation in Colorado. Has high fevers, HA, and swelling under his arm. He buried a dead squirrel at his camp site.
2. 28 y/o surgery resident returns from a week of vacation in CO. He presents to the ER with high fever, prostration, and shock. He buried a dead squirrel at his camp site.
3. 28 y/o surgery resident returns from a week of vacation in CO. He presents to the ER with high fever, bloody sputum, and rapidly develops ARDS. He buried a dead squirrel at his camp site.

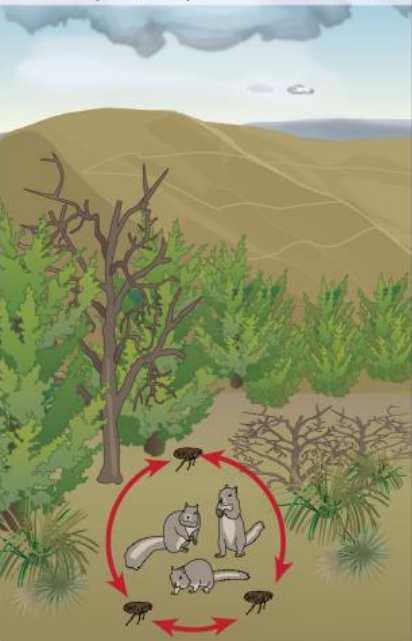
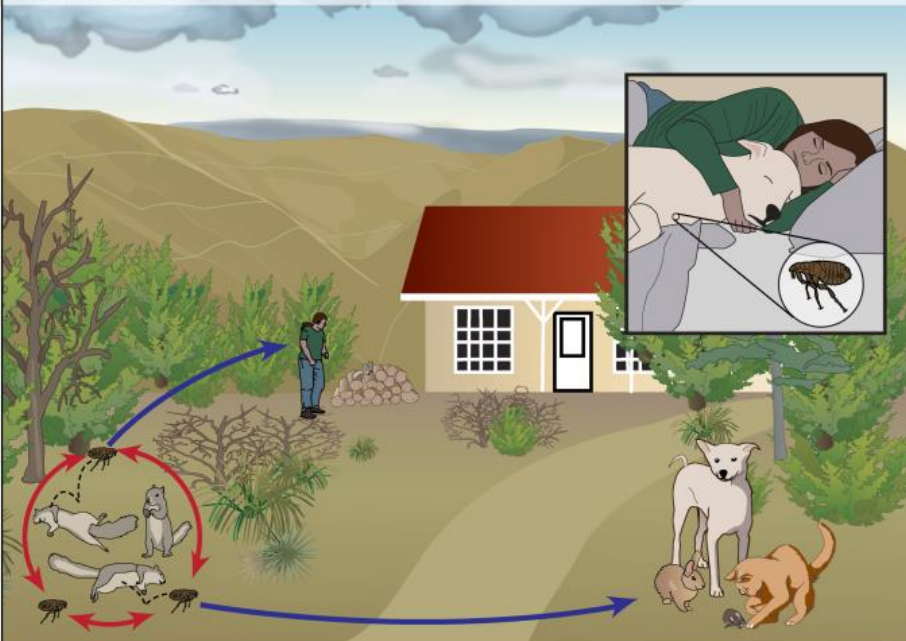
Yersinia pestis

- Murine zoonosis
- Infected from bites from fleas, scratches or bites from domestic cats, handling of infected tissues, inhalation of respiratory secretions
- 3 major presentations: Bubonic plague, Septicemic plague, Pneumonic plague

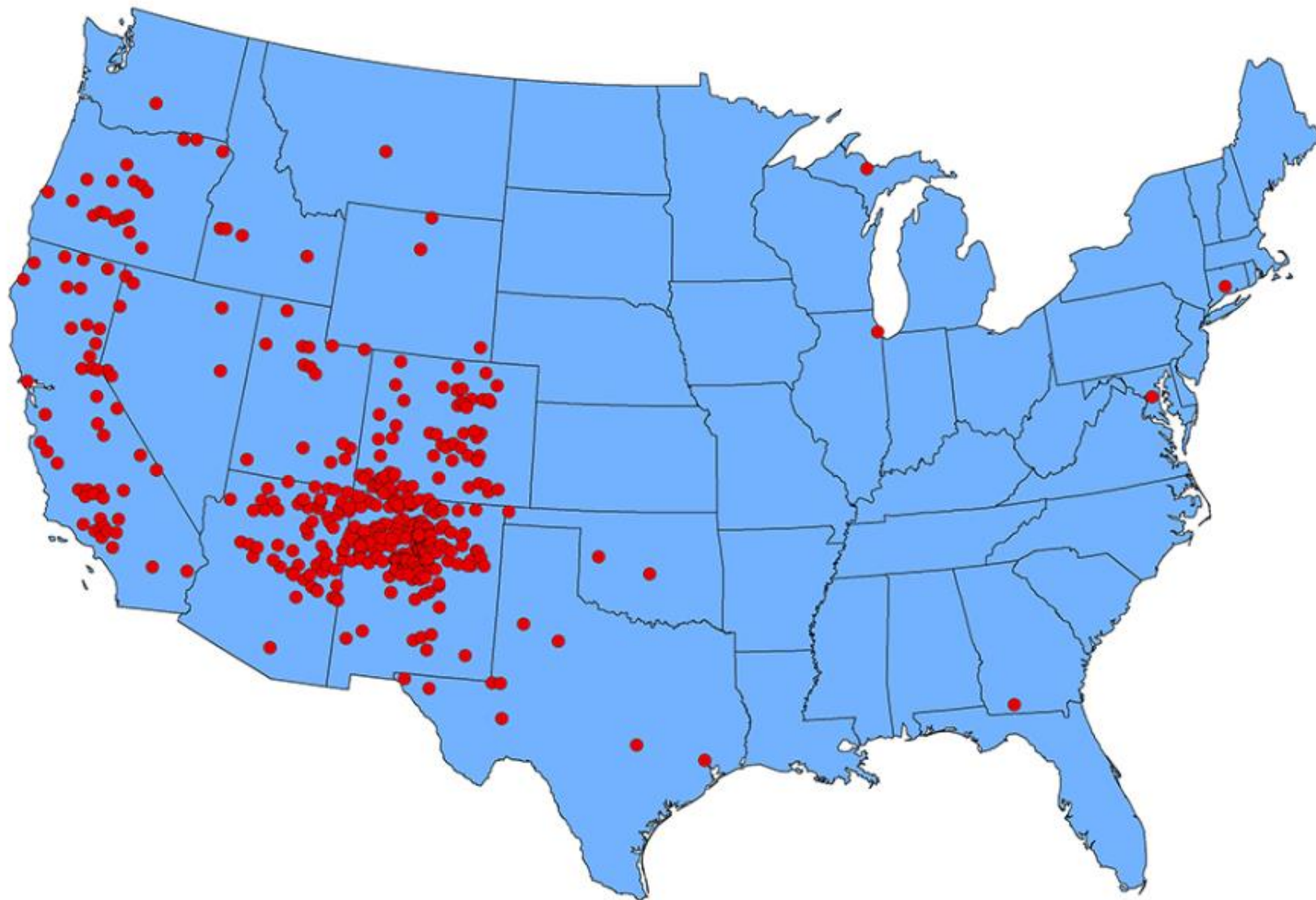
- Present throughout Southwestern United States (Arizona, Colorado, New Mexico, Utah)

Plague Ecology in the United States



| Plague in Nature | Plague in Humans |
|---|---|
| <p>Plague occurs naturally in the western U.S., especially in the semi-arid grasslands and scrub woodlands of the southwestern states of Arizona, Colorado, New Mexico and Utah.</p> | <p>Occasionally, infections among rodents increase dramatically, causing an outbreak, or epizootic. During plague epizootics, many rodents die, causing hungry fleas to seek other sources of blood. Studies suggest that epizootics in the southwestern U.S. are more likely during cooler summers that follow wet winters.</p> |
|  |  |
| <p>The plague bacterium (<i>Yersinia pestis</i>) is transmitted by fleas and cycles naturally among wild rodents, including rock squirrels, ground squirrels, prairie dogs and wood rats.</p> | <p>Humans and domestic animals that are bitten by fleas from dead animals are at risk for contracting plague, especially during an epizootic. Cats usually become very ill from plague and can directly infect humans when they cough infectious droplets into the air. Dogs are less likely to be ill, but they can still bring plague-infected fleas into the home. In addition to flea bites, people can be exposed while handling skins or flesh of infected animals.</p> |

Reported Cases of Human Plague - United States, 1970-2020



1 dot placed in state of residence for each reported plague case

Bubonic Plague

- Most common form, 80-95% of cases
- Often no apparent bite mark, but sometimes can find eschar
- Sudden onset f/c. HA, prostration
- Lymphadenopathy (bubo), nonfluctuant but large and tender with overlying edema
- DIC in 50%
- Mortality 50-90% if untreated, 10-20 if treated

Plague



Septicemic plague

- 10-20% of cases
- No preceding bubo
- Hypotension, multisystem organ failure

Plague



Pneumonic Plague

- Primary: inhalation
- Secondary: spread from septicemic
- Primary: short incubation of hours to days with dyspnea, fevers, pleuritic CP, cough with bloody sputum. Rapidly fatal unless abx started within first day of illness
- 100% mortality if untreated (50% if treated)

Labs:

- WBC >20K and thrombocytopenia present in 50%
- Sputum with GNRs (esp in those with pneumonia, hemoptysis, and potential exposures)
- Can be cultured from blood, sputum, CSF, LN aspirate – notify lab of concern as risk to lab staff

Treatment

- Drug of choice is an aminoglycoside, classically streptomycin but gent is fine
- Doxy or tetracycline second line but may be as good.
- Levo may work as well but limited human data (cures monkeys just fine!)
- Chloramphenicol
- TMP-SMX works but poorer outcomes

- Droplet precautions and post-exposure prophylaxis with doxy or levo or TMP-SMX (if pregnant) for pneumonic plague and within 48 hrs of treatment

Case

- 20 y/o with a PMHx of traumatic splenectomy as a child has just returned from Wash U for spring break where she is a biology major. She spends her time researching the common red crested barn finch. She trapes around fields and goes in many barns. She presents with a 10 day history of subjective fever, chills, myalgias, severe HA with neck stiffness.
- In the ER she is found to have a temp of 38.6, HR 96, BP 100/70, RR 16
- She is admitted for concern for meningitis

- LP shows mild lymphocytoc pleocytosis
- She rapidly develops respiratory failure, is intubated
- CXR shows:

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Hantavirus



- Sin Nombre virus spread by rodents (classically the deer mouse)
- Found in rodent urine, feces, saliva
- Disturbing fresh droppings can aerosolize the virus leading to airborne transmission
- watch for this when spring cleaning
- Buzzwords: hoarder, house cleaning, rural cabins with mice,

Hantavirus Cardiopulmonary Syndrome

- Prodrome phase of 2-8 days followed by a cardiopulmonary phase for 2-7 days
- Prodrome/febrile phase: acute onset fever, chills, myalgias, nausea, vomiting, weakness, diarrhea. HA, abdominal pain, cough
- Cardiopulmonary phase: rapid onset shock and non-cardiogenic pulmonary edema
- 38% mortality

Hantavirus

- Lab findings: thrombocytopenia, increased LDH, transaminitis, lactic acidosis. Can get leukocytosis (even to 90K!), marked immunoblasts
- Diagnostic triad: sudden appearance of thrombocytopenia, left shift, and immunoblasts >10%
- Hantavirus ELISA for IgM and IgG with confirmatory WB
- Immunostaining on path tissue (post-mortem) available
- PCR in research settings

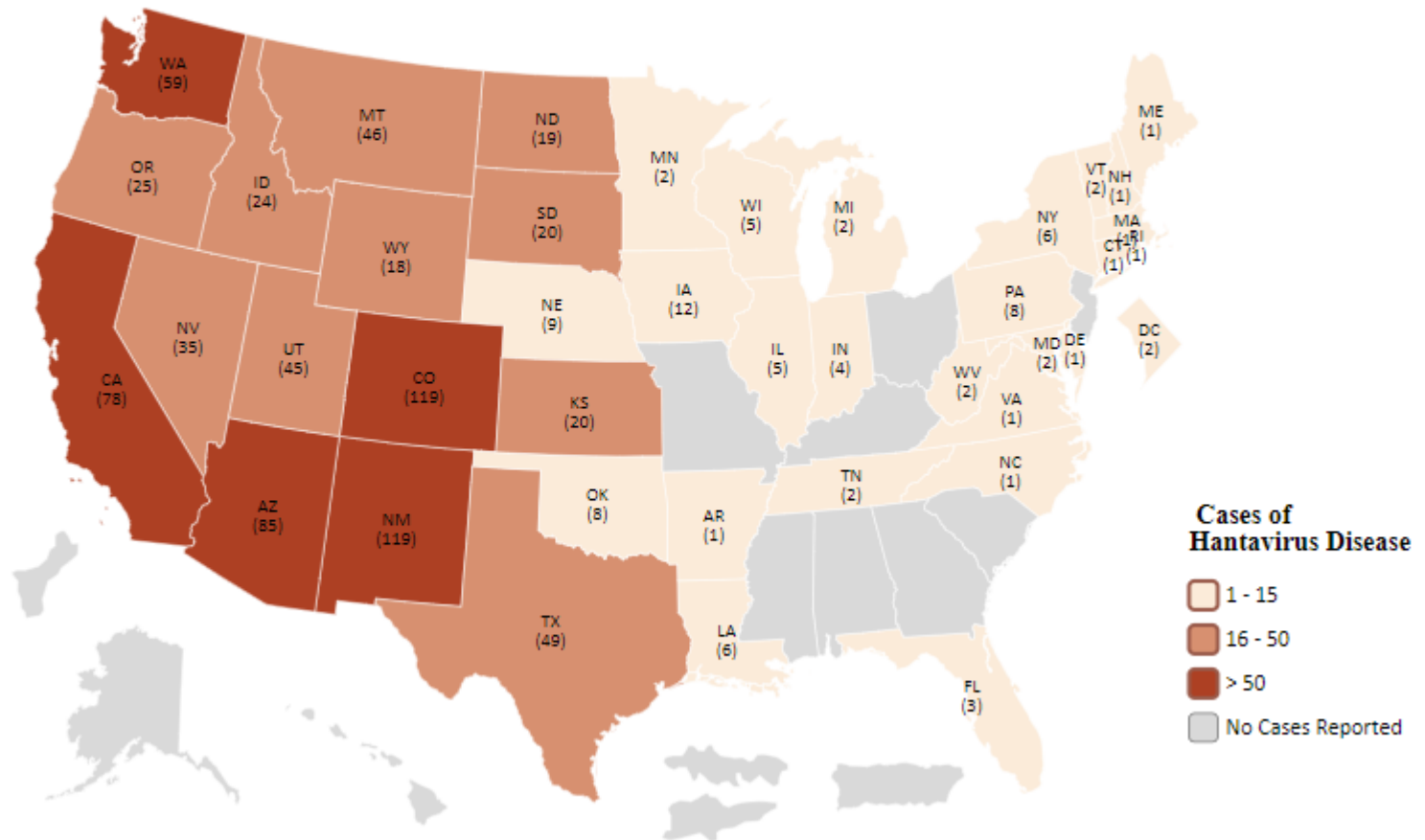
Treatment

- ECMO
- Ribavirin? For Hantaan virus 7-fold decrease in mortality. For Sin Nombre virus no clear benefit
- Supportive care
- Prevention:
Vaccine is available to Hantaan and Seoul viruses in Korea and China (killed virus vaccines)
- Fatality rate 10-50%

Map of US Cumulative Cases of Hantavirus by State through 2021



All cases through 2021 Single year cases, by month and cumulative





Virginia Mason™

Each Person.
Every Moment.
Better Never Stops.