


# Tick-Talk

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## Disclosures

- No disclosures relevant to this talk
  - Will not be discussing off-label use of medications
- Small honorarium from AAP for writing questions for PrepID
- Small honorarium from NBME for writing questions for the USMLE steps

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## Objectives

- At the end of the session, the attendee will be able to:
  - Recognize the epidemiology of tick-borne diseases
  - Identify common presentations of tick-borne diseases
  - Plan the appropriate management of a child with suspected tick-borne disease
  - Interpret diagnostic studies of common tick-borne diseases

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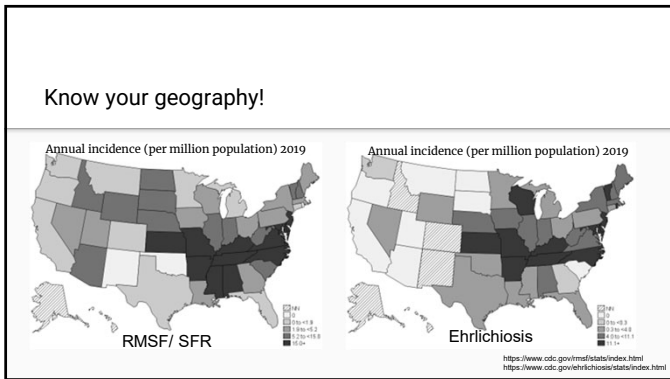
## There are many human tick-borne diseases in the US

In the United States, some ticks carry pathogens that can cause human illness, including:

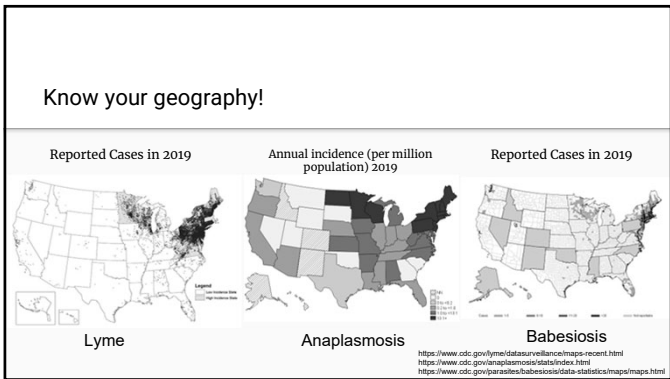
- Anaplasmosis** is transmitted to humans by tick bites primarily from the blacklegged tick (*Ixodes scapularis*) in the northeastern and upper midwestern U.S. and the western blacklegged tick (*Ixodes pacificus*) along the Pacific coast.
- Babesiosis** is caused by microscopic parasites the white blood cells. Most human cases of babesiosis in the U.S. are caused by *Babesia microti*. *Babesia microti* is transmitted by the blacklegged tick (*Ixodes scapularis*) and is found primarily in the northeast and upper midwest.
- Borrelia burgdorferi** infection has recently been described as a cause of illness in the upper midwestern United States. It has been found in blacklegged ticks (*Ixodes scapularis*) in Minnesota and Wisconsin. *Borrelia burgdorferi* is a new species and is the only species besides *B. burgdorferi* known to cause Lyme disease in North America.
- Brexitia septempunctata** infection has recently been described as a cause of illness in the U.S. It is transmitted by the blacklegged tick (*Ixodes scapularis*) and has a range similar to that of Lyme disease.
- Burkholderia** infection has been identified in a limited number patients in the Midwest and southern United States. At this time, we do not know if the virus might be found in other areas of the United States.
- California tick fever** is caused by a virus transmitted by the Rocky Mountain wood tick (*Dermacentor andersoni*). It occurs in the the Rocky Mountain states at elevations of 4000 to 10,500 feet.
- Ehrlichiosis** is transmitted to humans by the lone star tick (*Amblyomma americanum*). Found primarily in the southeastern and eastern U.S.
- Haemolytic uremic syndrome** have been identified in the Midwestern and southern United States. Studies suggest that Lone Star ticks can transmit the virus. It is unknown if the virus may be found in other areas of the U.S.
- Lyme disease** is transmitted by the blacklegged tick (*Ixodes scapularis*) in the northeastern U.S. and upper midwestern U.S. and the western blacklegged tick (*Ixodes pacificus*) along the Pacific coast.
- Powassan disease** is transmitted by the blacklegged tick (*Ixodes scapularis*) and the groundhog tick (*Ixodes coheni*). Cases have been reported primarily from northeastern states and the Great Lakes region.
- Rocky Mountain spotted fever (RMSF)** is transmitted by the American dog tick (*Dermacentor variabilis*), Rocky Mountain wood tick (*Dermacentor andersoni*), and the brown dog tick (*Phiphatulus sanguineus*) in the U.S. The brown dog tick and other tick species are associated with RMSF in Central and South America.
- STARI (Stellaris tick-associated rash illness)** is transmitted via bites from the lone star tick (*Amblyomma americanum*), found in the southeastern and eastern U.S.
- Tularemia (rabbit-skin fever) (TSSF)** is transmitted to humans through the bite of infested ticks. TSSF has been reported in 11 states: Arizona, California, Colorado, Idaho, Kansas, Minnesota, Nevada, New Mexico, Ohio, Oklahoma, Oregon, Texas, Utah, Washington, and Wyoming and is associated with sleeping in mass cabins and vacation homes.
- Tuberculosis** is transmitted to humans by the dog tick (*Dermacentor variabilis*), the wood tick (*Dermacentor andersoni*), and the lone star tick (*Amblyomma americanum*). Tuberculosis occurs throughout the U.S.
- Yersinia enterocolitica** (Yersinia pseudotuberculosis) is transmitted to humans by the Pacific Coast tick (*Dermacentor occidentalis* ticks). This is a new disease that has been found in California.

<https://www.cdc.gov/ticks/diseases/index.html>

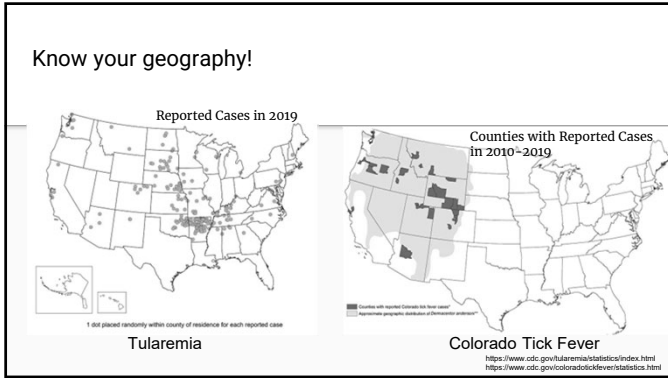
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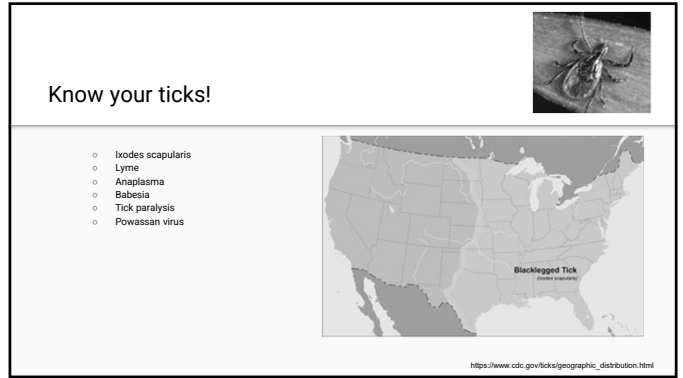
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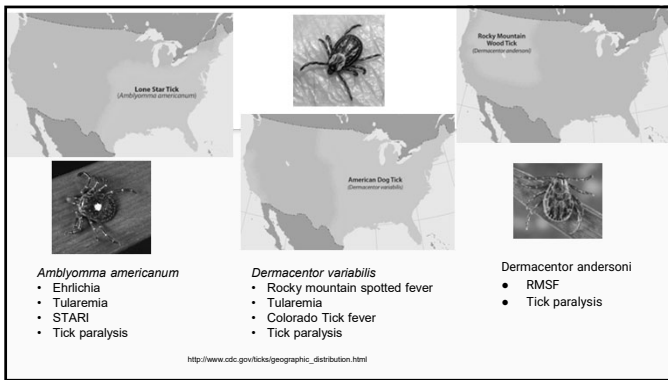
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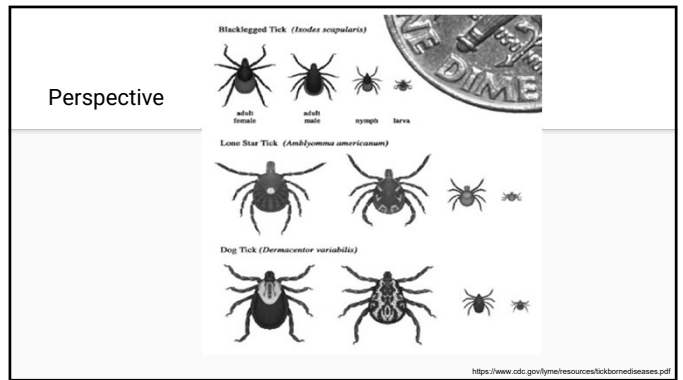
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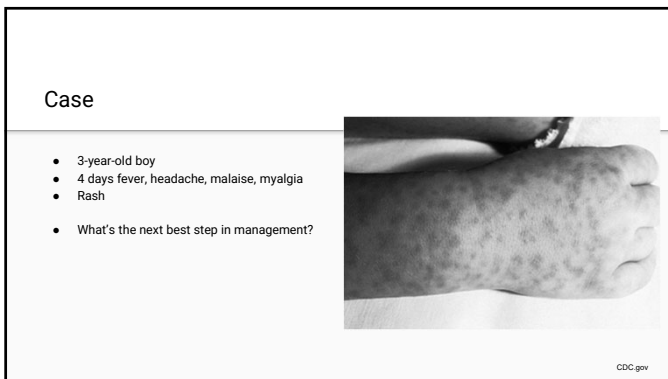
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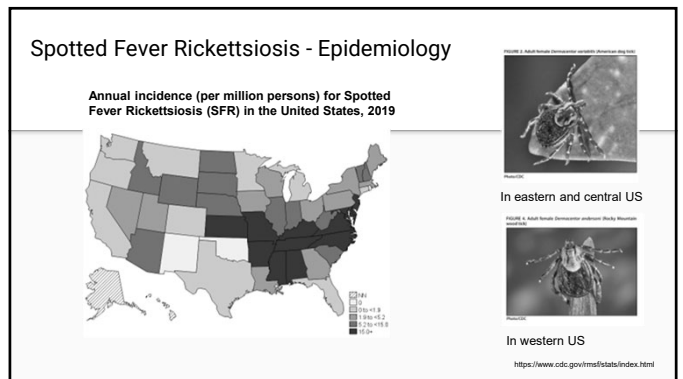
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### RMSF Clinical Presentation

- Incubation period: 2-14 days
- Sudden onset of fever, headache
  - Nausea, vomiting, anorexia, photophobia, myalgia
  - Rash (2-5 days after fever)
    - Starts as maculopapular petechial (late)
    - Centripetal; ankles and wrists spreads to torso palms and soles
    - Absent in 5% of children and 20% of adults
    - Atypical in 10%
  - Meningeal signs
  - Hepatomegaly, splenomegaly (10-20%)
  - Peripheral or periorbital edema in children




<https://www.cdc.gov/rmsf/symptoms/index.html>  
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<http://phill.cdc.gov>

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### RMSF Laboratory Evaluation

- Thrombocytopenia
  - WBC elevated or normal
  - Leukopenia and anemia can occur
- Hyponatremia (Na<130 mg/dL in 20-50%)
- Elevated liver transaminases (worsen with disease progression)
- Lymphocytic pleocytosis if LP done

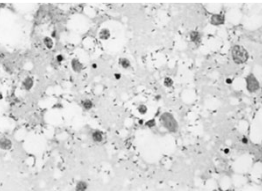


<https://www.cdc.gov/rmsf/symptoms/index.html>  
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<https://phill.cdc.gov>

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### RMSF Diagnosis

- Made on clinical basis and confirmed later
  - Never delay treatment!!!
- IgM, IgG testing (IFA)
  - Start increasing 7-10 days after onset of symptoms
  - Low positive common in certain areas
  - IgM Ab may remain elevated for months
  - + Diagnosis requires >= 4-fold increase in IgG 2-4 weeks later
  - Cross reacts with other Spotted Fever Rickettsia group
- Serum or blood PCR
  - Positive within first 7 days, prior to doxycycline therapy
  - NOT sensitive – a negative PCR does not rule out disease



Giemza stain – not routinely done.  
<https://phill.cdc.gov>

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### RMSF Treatment

- If you suspect RMSF Start Doxycycline immediately
  - Works best if given within 1st 5 days of symptoms
  - Fever subsides within 24-48h
  - Doxycycline = treatment of choice regardless of age
    - Given for 7-10 days (at least 3 days after fever resolves)
    - Use of sulfa containing drugs may worsen clinical course
- Case fatality 20-80% if untreated. Median time to death 8d
  - In the pre-antibiotic era, case fatality rate was ~ 25%
  - Present-day case-fatality rates, estimated at 5-10% overall

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### Doxycycline in Young Children

- 1960s, tetracycline - permanent teeth discoloration advice against all tetracyclines use in children <8yo
- Affinity to bind to calcium is lower with doxycycline (19%) compared to tetracycline (40 – 75%)
- No risk of tooth discoloration when doxycycline is administered at standard doses and durations in children

Gaillard Tet al. Malar J 2017;16:148; Todd SR, et al. J Pediatr 2015;166:1246-51.  
Biggs et al. MMWR Recomm Rep 2016;65:1-44.  
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### Case

- A 13-year-old girl who spends a lot of time outdoors in MO, hiking and hunting, is admitted with fevers, headaches and myalgias. She has no rash or lymph node swelling
- Her labs show leukopenia and hyponatremia
- You suspect a tick-borne illness other than RMSF

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Disease	Causal Agent	Major Target Cell	Tick Vector	Geographic - Distribution
Ehrlichiosis caused by <i>Ehrlichia chaffeensis</i> (human monocytic ehrlichiosis)	<i>E chaffeensis</i>	Usually monocytes	Lone star tick ( <i>Amblyomma americanum</i> )	Predominantly SE, south-central, from the East Coast extending westward to Texas; has been reported outside USA
Anaplasmosis (human granulocytic anaplasmosis)	<i>Anaplasma phagocytophilum</i>	Usually granulocytes	Blacklegged tick ( <i>Ixodes scapularis</i> ) or Western blacklegged tick ( <i>I pacificus</i> )	USA: NE and upper MW states and northern California; Europe and Asia
Ehrlichiosis caused by <i>Ehrlichia ewingii</i>	<i>E ewingii</i>	Usually granulocytes	Lone star tick ( <i>A americanum</i> )	USA: SE, south central and MW states; Africa, Asia
Ehrlichiosis caused by <i>Ehrlichia muris euclairensis</i>	<i>E muris euclairensis</i>	Unknown, suspected in monocytes	Blacklegged tick ( <i>Ixodes scapularis</i> )	USA: Minnesota, Wisconsin

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### Ehrlichiosis/Anaplasmosis

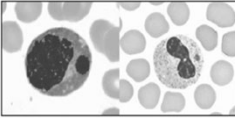
- Fever, headache, chills, malaise, myalgia, nausea
  - More arable: arthralgia, vomiting, diarrhea, cough, confusion
- Rash in a minority of adults
  - More common in Ehrlichia than Anaplasma infections
  - More common in children with Ehrlichia (up to 60%)
- Severe manifestations: ARDS, encephalopathy, meningitis, DIC, hemorrhage, renal failure
  - May be more severe in patients on sulfa drugs
  - Can trigger HLH

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### Ehrlichiosis / Anaplasmosis

- Significant laboratory findings:
  - Leukopenia, lymphopenia, thrombocytopenia
  - Hyponatremia, elevated serum hepatic transaminases
  - CSF: lymphocytic pleocytosis and increased proteins
- Diagnosis:
  - PCR (sensitive)
  - 4-fold increase in titers
  - Morulae on peripheral smear – not sensitive
- Treatment: Doxycycline x 5-7d (at least 3d from defervescence)
  - 10-14d for anaplasmosis to cover possible concurrent *Borrelia burgdorferi*




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<https://www.cdc.gov/mmwr/volumes/68/mr6802a1.htm>

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### Case

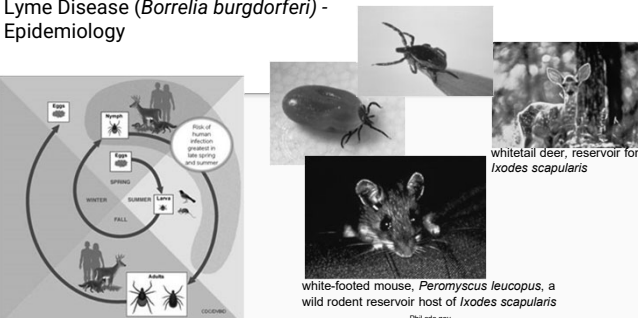
- A 12-year-old girl who lives in upstate NY and spends a lot of time hiking, presents with this rash in July
- How do you make the diagnosis?



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

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### Lyme Disease (*Borrelia burgdorferi*) - Epidemiology



white-footed mouse, *Peromyscus leucopus*, a wild rodent reservoir host of *Ixodes scapularis*

whitetail deer, reservoir for *Ixodes scapularis*


Phl.cdc.gov

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### Lyme Disease - Epidemiology

Reported Cases of Lyme Disease — United States, 2019




- Also endemic in eastern Canada, Europe, China, and Japan
- Ticks:
  - I scapularis* in the East and MW US
- Cases occur April- October
  - Most June-July
- Co-infection with *Anaplasma* and/or *Babesia* common

<https://www.cdc.gov/lyme/datasurveillance/index.html#>

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### Lyme Disease Clinical Presentation

- Incubation period: 1-32 d, median 11d
  - Late manifestations can occur months after the tick bite
- Early Localized:
  - Erythema migrans: MOST common manifestation in children
    - Red macule/papule  $\Rightarrow$  expands over days to weeks to a
      - large, annular, erythematous lesion up to > 5 cm in diameter
      - Usually painless, non pruritic
      - Classic "bull's-eye" appearance rare

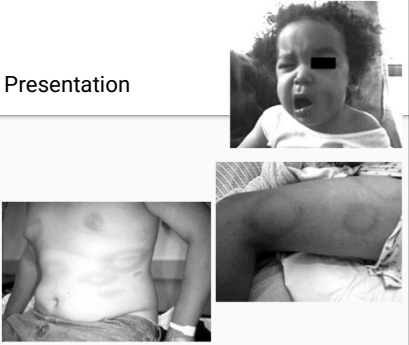


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[https://www.cdc.gov/lyme/igms\\_symptoms/ashes.html](https://www.cdc.gov/lyme/igms_symptoms/ashes.html)

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### Lyme Disease Clinical Presentation

- Early Disseminated
  - Multiple erythema migrans lesions (smaller)
  - Neuro: CN palsies (especially CN VII), lymphocytic meningitis, polyradiculitis
  - Ophthalmic: conjunctivitis, optic neuritis, keratitis, uveitis
  - Constitutional: low-grade fever, arthralgia, myalgia, headache, fatigue
  - Carditis – usually heart block, less common in children



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### Lyme Disease Clinical Presentation

- Late disease
  - In patients not treated at an earlier stage of illness
  - Most common: Lyme arthritis in children
  - Polyneuropathy, encephalopathy, and encephalitis extremely rare
- European Lyme disease: borrelial lymphocytoma and acrodermatitis chronica atrophicans
  - More likely to produce neurologic disease, whereas arthritis is uncommon

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### Lyme Disease Diagnosis

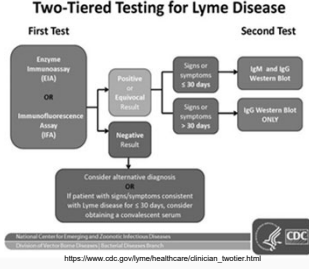
- Available tests are not perfect – very low specificity (especially IgM FALSE POSITIVES)
  - If not in endemic area – DO NOT TEST
  - If atypical symptoms, constitutional symptoms without objective signs of infection: DO NOT TEST
- Early localized – clinical diagnosis (erythema migrans in endemic in appropriate season are diagnostic)
  - DO NOT TEST (Ab not sensitive early)

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### Lyme Disease Diagnosis

- Early Disseminated and late:
  - Borrelia burgdorferi Ab EIA or IFA first: if negative STOP
  - If positive Western Blot
    - 2/3 IgM bands/5/10 IgG bands
      - IgM - 30d from symptom onset ONLY
    - Cross-reactivity +++
    - Ab stay positive for years  $\Rightarrow$  do not repeat



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Disease Category	Drug(s) and Dose
Erythema migrans (single or multiple) (any age)	Doxycycline x 10 days OR Amoxicillin x14 days OR Cefuroxime x14 days OR, for a patient unable to take a beta-lactam or doxycycline, Azithromycin x7 days
Isolated facial palsy	Doxycycline x 14 days
Arthritis	Same as early but x 28 days
Persistent arthritis after first course of therapy	Retreat using an oral agent as for first-episode arthritis for 28 days OR Ceftriaxone x 14–28 days
Atrioventricular heart block or carditis	Same as early localized x 14 days (range 14–21 days) OR Ceftriaxone x14 days (range 14–21 days for a hospitalized patient) can transition to po to complete the 14- to 21-day course
Meningitis	Doxycycline x 14 days OR Ceftriaxone x 14 days

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### Lyme Disease - Prophylaxis

- In areas of high endemicity (the coastal northeast), where 30% to 50% of I scapularis ticks harbor B burgdorferi, the overall risk of Lyme disease following a recognized tick bite is < 3%
  - After a high-risk deer tick bite, the risk of infection may be 25% in hyperendemic areas
- 1 prophylactic 200-mg dose (or 4.4 mg/kg for children <45 kg) of doxycycline can be used
  - Especially if I scapularis tick that is engorged (has fed for >36 hours) and prophylaxis can be started w/in 72 hours of tick removal

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### Chronic Lyme dilemma...

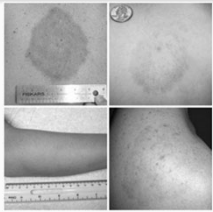
- Tests not specific
  - Should not be performed for people without symptoms or signs suggestive of Lyme disease and plausible geographic exposure
- Some patients have prolonged, persistent symptoms following standard treatment for Lyme disease
  - Phenomenon not unique to Lyme disease
- Persistent, treatment-refractory infection with B burgdorferi not substantiated scientifically
- Double-blinded, randomized, placebo-controlled trials: retreatment with additional antimicrobial agents for patients with residual post-treatment Lyme disease subjective symptoms may be associated with harm and does not offer benefit

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### STARI (Southern Tick Associated Rash Illness)

- S central and SE states
- Lone Star tick (Amblyomma americanum)
- Red rash similar to Lyme
  - The rash usually appears within 7 days of tick bite
  - expands to a diameter of >=8 cm
  - +/- fatigue, headache, fever, and muscle pains
  - No disseminated complications!
- Diagnosis: clinical
- Treatment: unknown if antibiotics necessary
  - Doxycycline often used



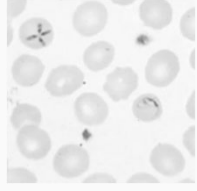
https://www.cdc.gov/stari/index.html

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### Case

- A 12-year-old boy presents with fever x 1 week and fatigue
- Lives in Connecticut
- On laboratory work-up, he has a significant hemolytic anemia
- Peripheral smear shows this

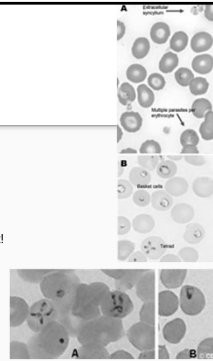


https://www.cdc.gov/tgdx/babesiosis/index.html

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### Babesiosis

- Tick: Ixodes scapularis
- NE and upper Midwest
- Often asymptomatic or mild, nonspecific symptoms
  - Severe and life threatening in asplenic, immunocompromised, or elderly
- Labs: hemolytic anemia ++, thrombocytopenia
- Blood smear: Maltese cross pathognomonic but not always present!
- Treatment:
  - Clindamycin + oral quinine for 7 to 10 days
  - OR atovaquone + azithromycin for 7 to 10 days




https://www.cdc.gov/tgdx/babesiosis/index.html

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### Case

- 8-year-old from Missouri coming with fever, malaise, fatigue, and neck swelling
- Multiple tick bites



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### Tularemia

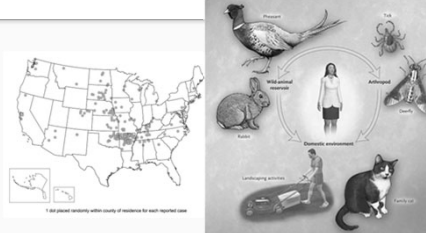
- Rabbit Fever = Deer Fly Fever
  - Mortality rates 5-15% (up to 60% with pneumonic)
    - Down to 2% with antibiotics
- Francisella tularensis
  - Highly infectious (10-50 organisms)
    - F. tularensis subsp tularensis (N. America, virulent)
    - F. tularensis subsp holarctica (Eurasia, less virulent)
  - Can survive for weeks in water, soil, moist hay and decaying animal carcasses

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### Tularemia - Transmission

- Reservoirs: rabbits, squirrels, muskrats and other rodents
  - hunting or skinning infected animals!
  - Ingestion, inhalation, inoculation
- No human-to-human transmission
- Vectors:
  - Deer flies
  - Mosquitoes
  - Ticks!!




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### Tularemia - Clinical

- Range: asymptomatic illness to septic shock and death
- Incubation period: 3-5 d (range 1-21d)
- Abrupt onset of nonspecific systemic symptoms (fever, chills, anorexia, malaise)
- Ulceroglandular
  - Most common in adults
  - Erythematous papulo-ulcerative lesion with a central eschar
  - Tender regional lymphadenopathy
    - Cervical/occipital in children/ inguinal in adults
- Glandular
  - Most common in children
  - Usually from tick bite
  - Tender regional lymphadenopathy
    - Multiple lymph nodes may be affected
    - May suppurate



<https://www.centerforhealthsecurity.org/>  
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### Tularemia - Clinical

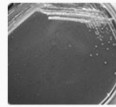
- Pharyngeal (oropharyngeal) – ingestion
  - Fever, sore throat, exudative pharyngitis, cervical ladd +/- pharyngeal or tonsillar ulcers/ pseudomembranes
- Oculoglandular (Parinaud's Sd)
  - painful conjunctivitis, ulcerations, ipsilateral pre-auricular ladd
- Typhoidal - ingestion
  - Fever, chills, myalgia, HSMG
- Pneumonic – aerosol or hematogenous
  - CXR: peribronchial infiltrates, lobar consolidation, pleural effusion, hilar adenopathy ARDS
- Intestinal - ingestion- abdominal pain, vomiting, diarrhea

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### Tularemia- Diagnosis

- High index of suspicion!!
- F. tularensis titers:
  - 1 Ab titer >= 1:128 by MA or of >=1:160 TA
  - >>=4x rise in titer between acute and convalescent specimens
    - Cross-reactions with Brucella, Legionella, and other GNB
- Immunohistochemical staining on tissue
- Culture (blood, pleural fluid, skin lesions, lymph nodes, sputum, or pharynx)
  - !!!Notify micro lab of suspicion!!!
    - Contagious!!
    - Needs cysteine enriched media



cysteine heart agar with 9% chocolateized blood agar  
PHIL.cdc.gov  
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### Tularemia- Treatment

- Drug of choice = Gentamicin IV x 10 days
- Ciprofloxacin x10-14 days: 86% cure rate, low relapse rate – not FDA approved for Tularemia
- Doxycycline = higher relapse rate

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### Colorado Tick Fever



- Tick: *Dermacentor andersoni*
- Western US and Canada
- Clinical presentation
  - Self-limited: sudden onset of fever, chills, headache, myalgia, malaise
  - Sore throat, vomiting, abdominal pain, maculopapular or petechial rash
  - 50% patients experience a biphasic illness
  - Adults >30 years of age may have prolonged weakness and fatigue
  - Labs: Leukopenia common, WBC with relative lymphocytosis and atypical lymphocytes. Moderate thrombocytopenia common
- Diagnosis:
  - Viral RNA or IgM and neutralizing Ab
- Treatment: supportive

<https://www.cdc.gov/coloradotickfever/hc-treatment-prevention.html>

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### Tick Paralysis

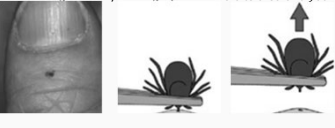
- Epidemiology
  - Most cases reported in NW US (BC and WA), and Australia
  - More common in children <10 years
  - April- June
- Caused by a toxin secreted in tick saliva during feeding that reduces motor neuron action potentials and the action of acetylcholine
- Symptoms develop 4-7 days after tick attachment
- Paresthesia, fatigue and weakness, +/- muscular pain
  - NO Fever
  - Unsteady gait ascending complete paralysis
  - Absent DTR
- Fatality rate 6-12% if undiagnosed
- Treatment: tick removal!

<https://www.updatdate.com/contents/tick-paralysis>  
<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5534a1.htm>

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### How do you remove the tick?



- Use fine-tipped tweezers to grasp the tick as close to the skin's surface as possible
  - Avoid folklore remedies such as nail polish, petroleum jelly, or heat to make the tick detach from the skin
- Pull upward with steady, even pressure
  - Don't twist or jerk the tick; this can cause the mouth-parts to break off and remain in the skin
- After removing the tick, thoroughly clean the bite area and your hands



[https://www.cdc.gov/ticks/removing\\_a\\_tick.html](https://www.cdc.gov/ticks/removing_a_tick.html)

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### Prevention

- 1 Tick zone: Avoid areas with forest and brush where deer, rodents, and ticks are common.
- 2 Wood chip barrier: Use a 3 ft. barrier of wood chips or rock to separate the "tick zone" and rock walks from the lawn.
- 3 Wood pile: Keep wood piles on the wood chip barrier, away from the home.
- 4 Tick migration zone: Maintain a 9 ft. barrier of lawn between the wood chips and areas such as patios, gardens, and play sets.
- 5 Tick safe: Enjoy daily living activities such as gardening and outdoor play inside this perimeter.
- 6 Gardens: Plant deer resistant crops. If desired, an 8-ft. fence can keep deer out of the yard.
- 7 Play sets: Keep play sets in the "tick safe zone" in sunny areas where ticks have difficulty surviving.

Based on a diagram by K. Stafford, Connecticut Agricultural Experiment Station

<https://www.cdc.gov/ticks/avoid/index.html>

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### References

- <https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6502.pdf>
- <https://www.cdc.gov/ticks/tickbornediseases/index.html>
- <https://www.cdc.gov/ticks/diseases/index.html>
  - Respective tickborne illness with links to resources for Health Professionals
- American Academy of Pediatrics 2021-2024 Report of the Committee on Infectious Disease (Redbook 2021)
  - Chapters for Lyme disease, Rickettsial diseases, Rocky Mountain Spotted Fever, Ehrlichiosis, Tularemia

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### Questions?

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