

TICK TALK – UPDATE ON TICKBORNE ILLNESSES: EPIDEMIOLOGY AND MANAGEMENT UPDATE ON LYME AND RICKETTSIAL DISEASES

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Disclosures

- ⦿ None

Acknowledgements

- Paul Lantos, MD
- Ross McKinney, MD

‘Show and Tell’

- ⦿ What is the name of this tick?
 - Adult tick or Nymph?
- ⦿ What diseases can it transmit?



Objectives

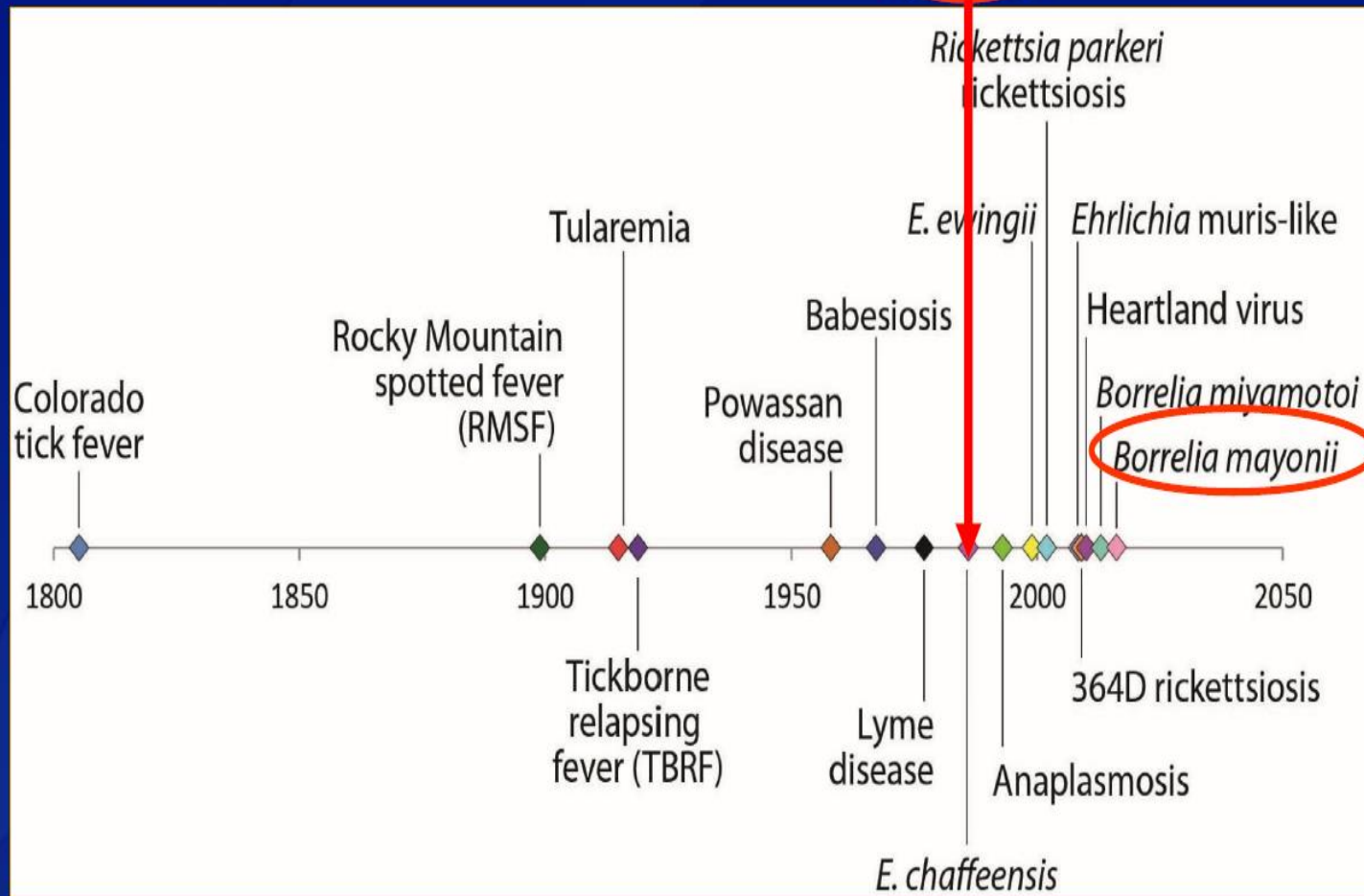
1. Discuss ticks as vectors
2. Describe the common “tick-borne diseases” seen in the US
3. Describe acute febrile (rickettsial) tick-borne illnesses
4. Review management of more common febrile tick-borne diseases
5. Delineate the presentations & potential sequelae of Lyme Disease

Ticks

- Most important arthropod vector in temperate regions
- Arachnids: ticks and mites
 - Ixodid ticks = hard bodied (most human biters)
 - Argasid ticks = soft bodied, *Ornithodoros spp*
- Three stages: larvae, nymph and adult

Emerging Tickborne Diseases

STARI



USA

- RMSF
- Human monocytic ehrlichiosis
- Lyme Disease
- STARI
- R. parkeri spotted fever
- Babesiosis
- Human granulocytic anaplasmosis
- Colorado Tick Fever
- Powassan virus encephalitis
- Q fever
- Tularemia
- Tick paralysis
- **Borrellia mayonii**

Global

- African tick bite fever
- Mediterranean spotted fever
- Tick-borne encephalitis
- Tick-borne relapsing fever

- Crimean-Congo hemorrhagic fever
- Kyasanur forest disease
- European Lyme disease
- Omsk Hemorrhagic Fever (OHF)
- Tickborne encephalitis (TBE)
- Anaplasmosis, babesiosis, ehrlichiosis, tularemia, tickborne relapsing fever, RMSF, Powassan disease can acquire internationally also

To name a few!

Common Ticks in United States

1 inch

Blacklegged Tick (*Ixodes scapularis*)



Lone Star Tick (*Amblyomma americanum*)



Dog Tick (*Dermacentor variabilis*)



2

The Southeastern Tick Milieu

- *A. americanum* - *by far* the dominant human-biting tick in the southeastern US
- *D. variabilis* - second most common
- *I. scapularis* rare
- *A. maculatum* emerging

Merten, H.A. and L.A. Durden, *J Vector Ecol*, 2000. **25**(1): p. 102-13.

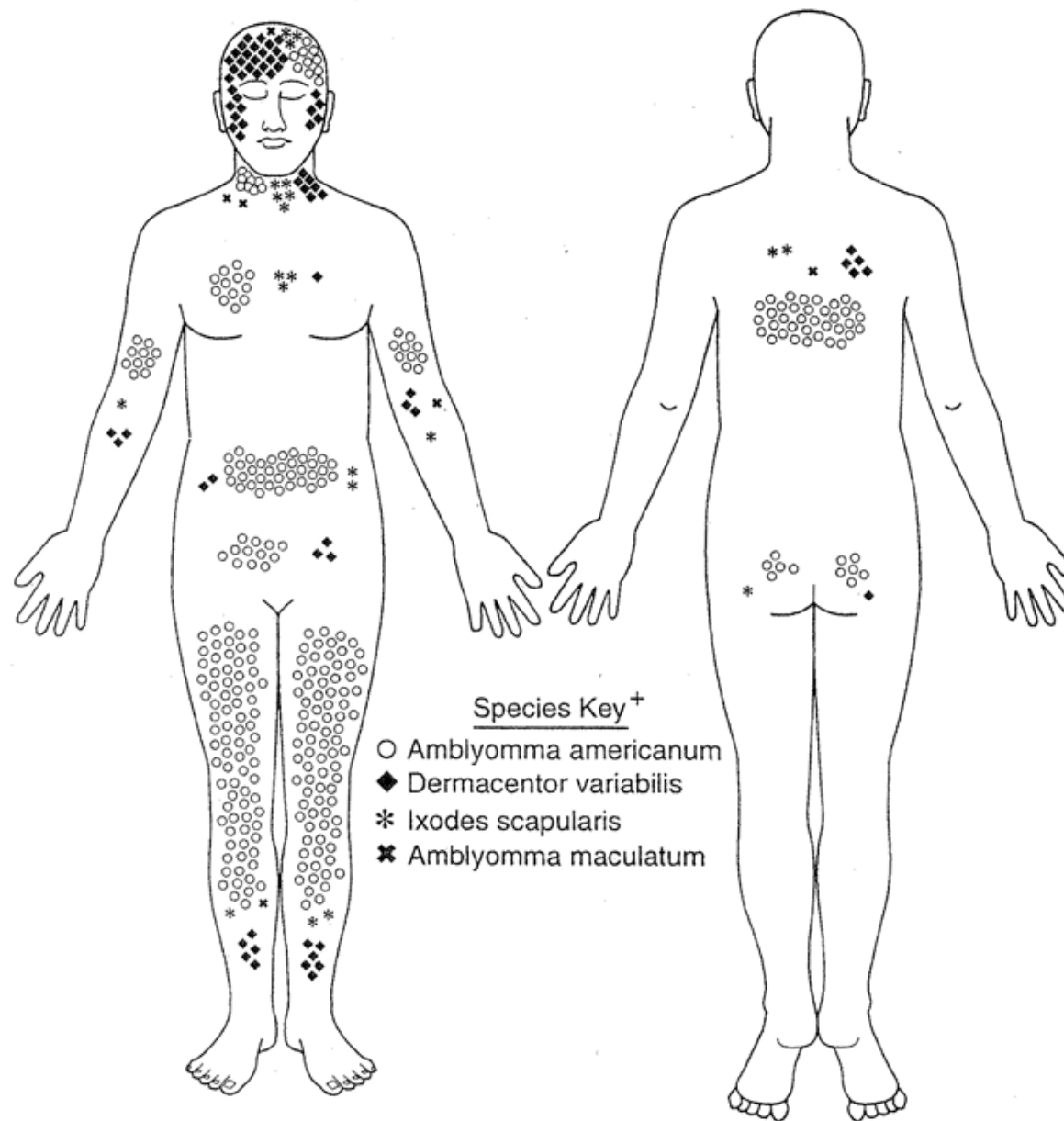
Felz, M.W. and L.A. Durden, *J Med Entomol*, 1999. **36**(3): p. 361-4.

Felz, M.W., L.A. Durden, and J.H. Oliver, Jr., *J Parasitol*, 1996. **82**(3): p. 505-8.

Anigstein, L. and D. Anigstein, *Tex Rep Biol Med*, 1975. **33**(1): p. 201-11.

Campbell, B.S. and D.E. Bowles, *Journal of Wilderness Medicine*, 1994. **5**: p. 405-412.

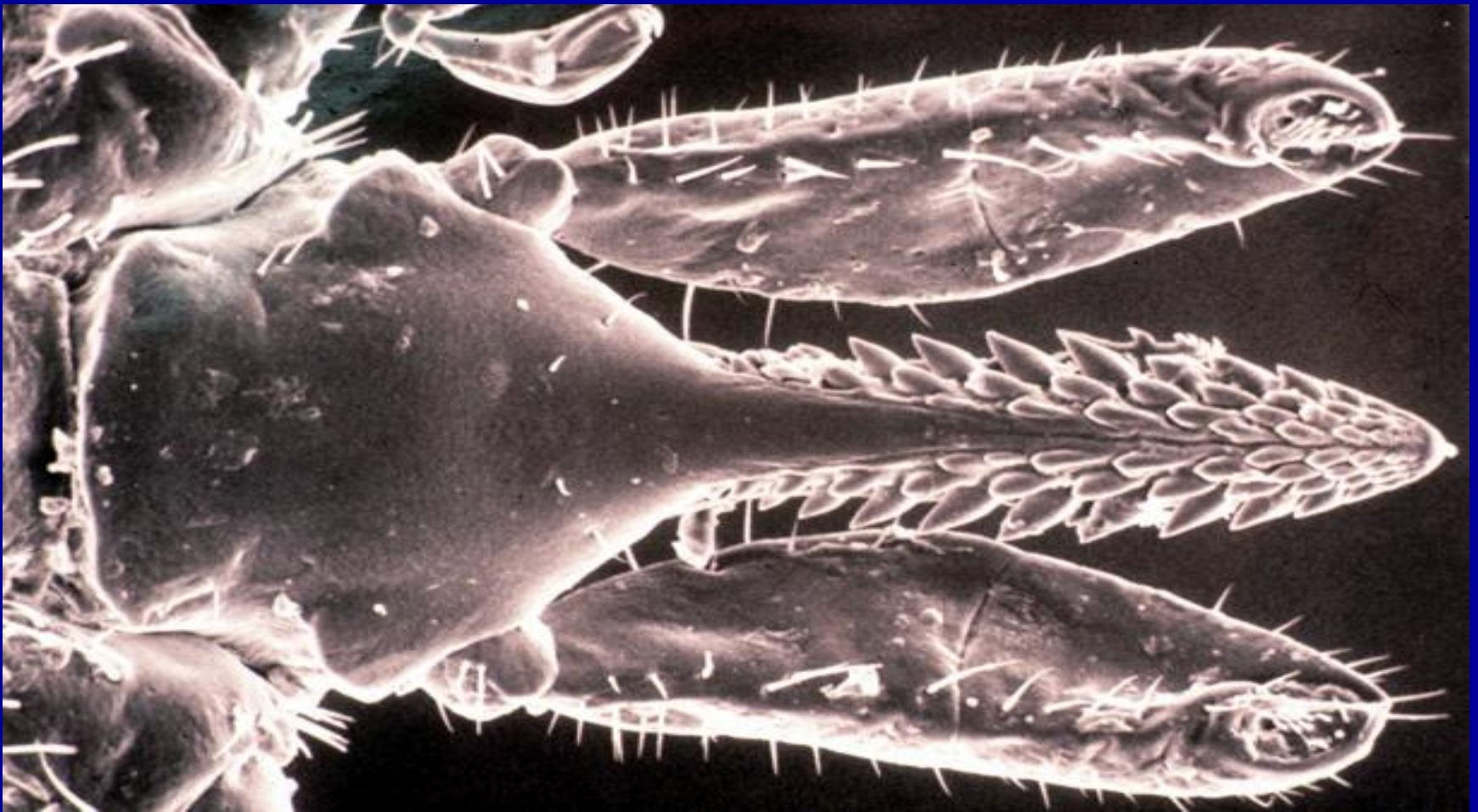
Goddard, J. and C.P. McHugh, *Mil Med*, 1990. **155**(6): p. 277-80.



⁺Each symbol represents 1 attached tick.

Fig. 1. Tick attachment sites by species for humans in Georgia and South Carolina, 1995–1998.

Business End of a Tick



- extension.unh.edu/News/graphics/tickhead.jpg



Case Presentation

- 15yo M previously well with 4 days of fever (Tmax 39 C) and headaches
- Presents to ED with persistent fever and chills, fatigue, arthralgias, worsening headaches
- Also with abdominal pain and vomiting
- No recent travel, +tick bite ~2 weeks ago

Emergency Department



- Gen: awake, lying in bed, shielding eyes from light
- T 38.4 HR 112 RR 24 BP 142/63 sat 100% on RA
- Wt 118kg (99%) Ht 189cm (98%) BMI 33 (98%)
- HEENT: PERRL, oropharynx clear, conjunctival injection
- Neck supple, no LAD
- Lungs: Clear to A
- CV: tachycardic, nl S1, S2, pulses 2+, cap refill <2sec
- Abd: soft, hepatosplenomegaly – both ~2cm below costal margin
- Skin: scattered petechiae throughout. Macular erythematous rash with irregular borders on arms. No rash on palms or soles.

PE cont



- MSK: tender knees, ankles, wrists bilaterally. PIP joints tender
- Neuro: A&O x3, reflexes and strength intact, CN III-XII grossly intact. Sensation intact. No dysmetria, - Romberg



Laboratory Values

134	104	6	< 129
3.9	24	0.7	

Uric acid 4.3
LDH 384

2.0	12	66K
	37	

Tot prot 6.3, alb 3.6
AST 75, ALT 98
Alk Phos 216

Diff: 55% seg0s, 1% bands, 20%
lymphs, 10% monos, 5% variant lymphs

ALC=500

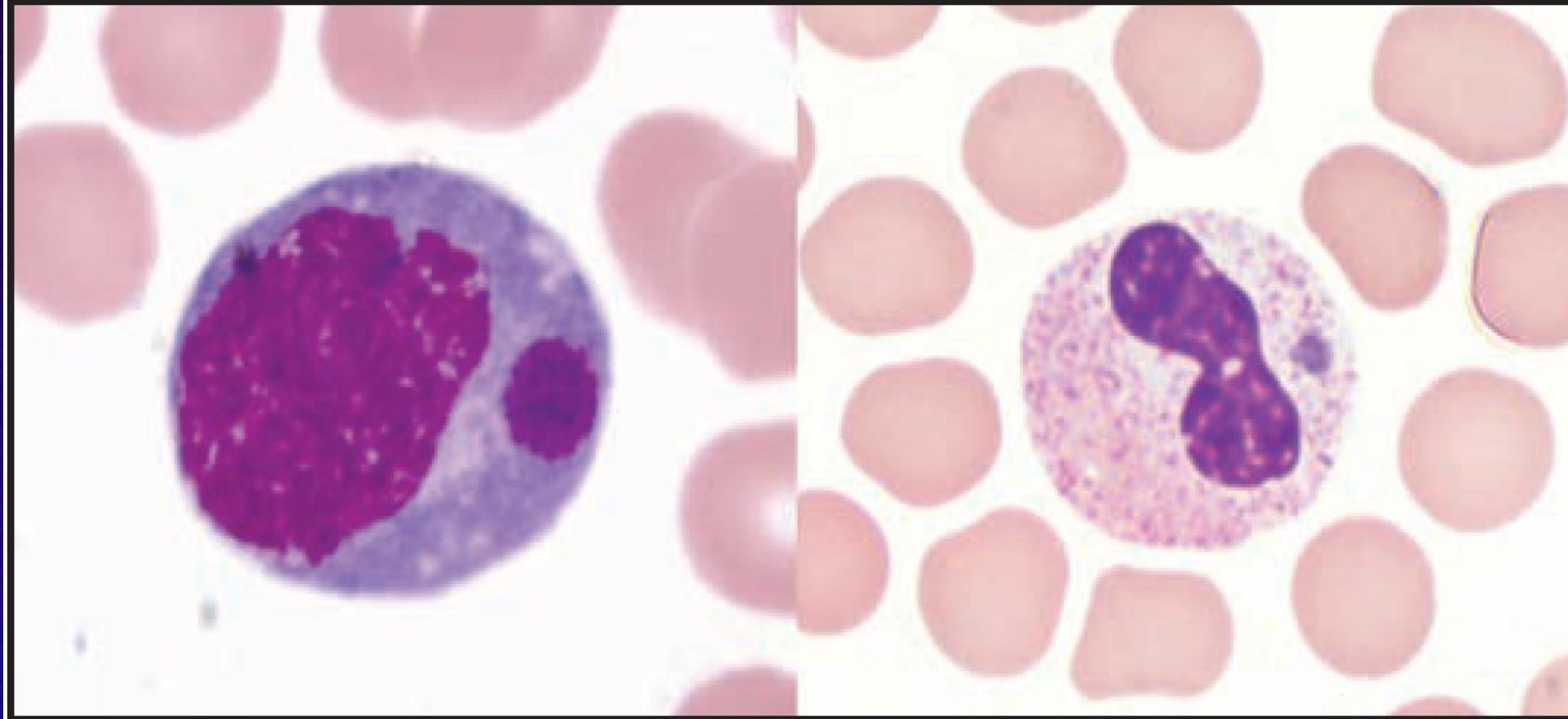


Differential Diagnosis?



- Sepsis
 - Meningitis
 - EBV / CMV
 - Ehrlichiosis
 - RMSF
 - Non-infectious etiologies, eg Leukemia
 - Others?
- Any guesses as to etiology for his illness?
 - *Additional clue needed?*

Hematology laboratory calls you re: abnormality on blood smear



Photos/J. Stephen Dumler, University of Maryland (left); Bobbi S. Pritt, Mayo Clinic (right)

Acute Febrile Tick-borne Diseases

- Rickettsial illnesses
 - Spotted fever group, including Rocky Mtn Spotted Fever
 - Ehrlichiosis
 - Anaplasmosis
- Babesiosis
- Lyme disease does not cause acute febrile syndrome

Human Monocytic Ehrlichiosis

- *Ehrlichia chaffeensis*
 - Transmitted by lone star tick (*A. americanum*)
 - Rickettsial organism
 - Infects monocytes
- First recognized in 1987
- 40-60% hospitalized, 2-4% mortality

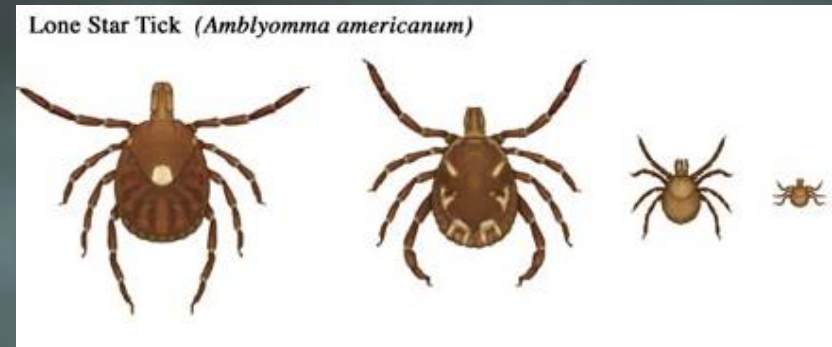
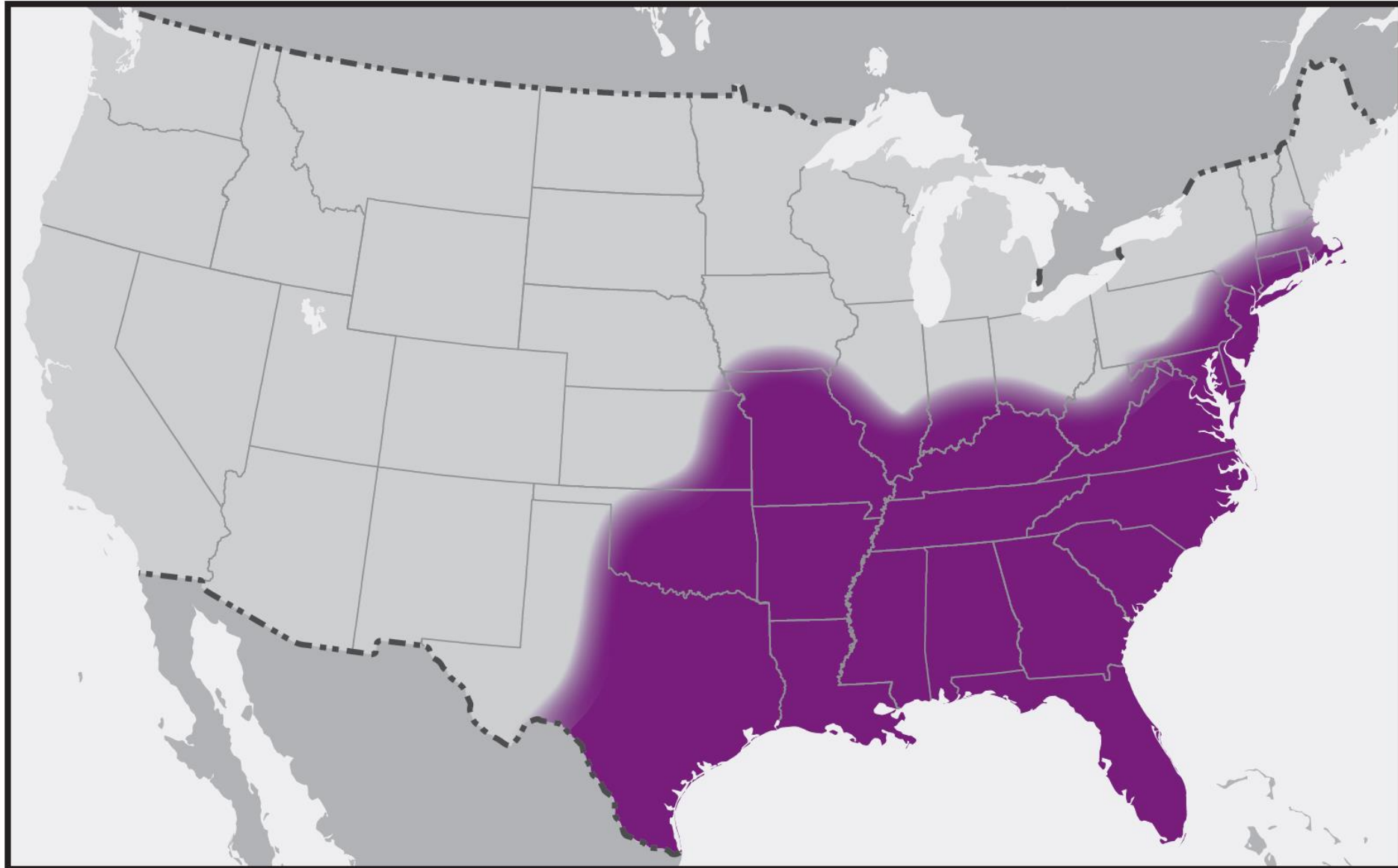
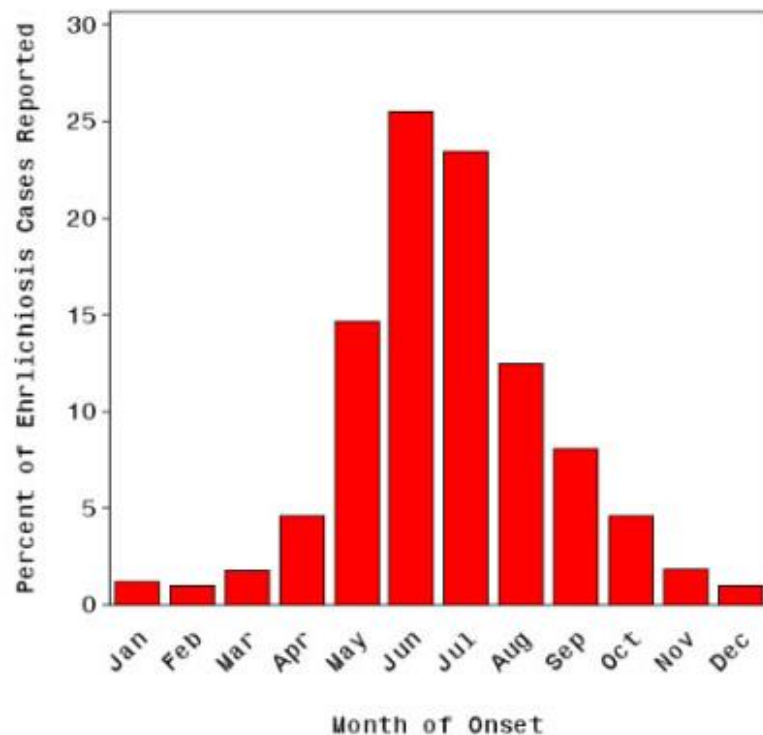


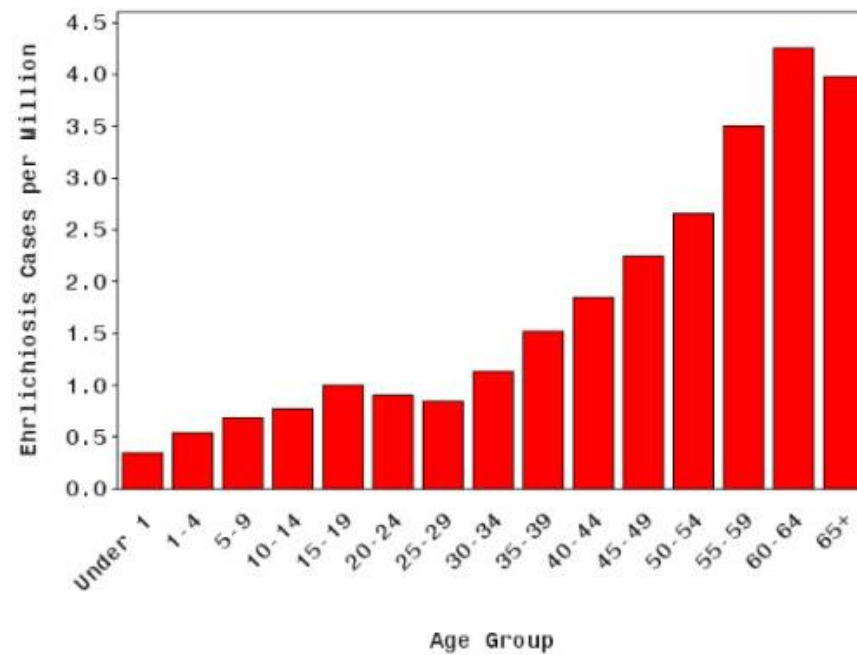
FIGURE 13. Approximate U.S. distribution of *Amblyomma americanum* (lone star tick)



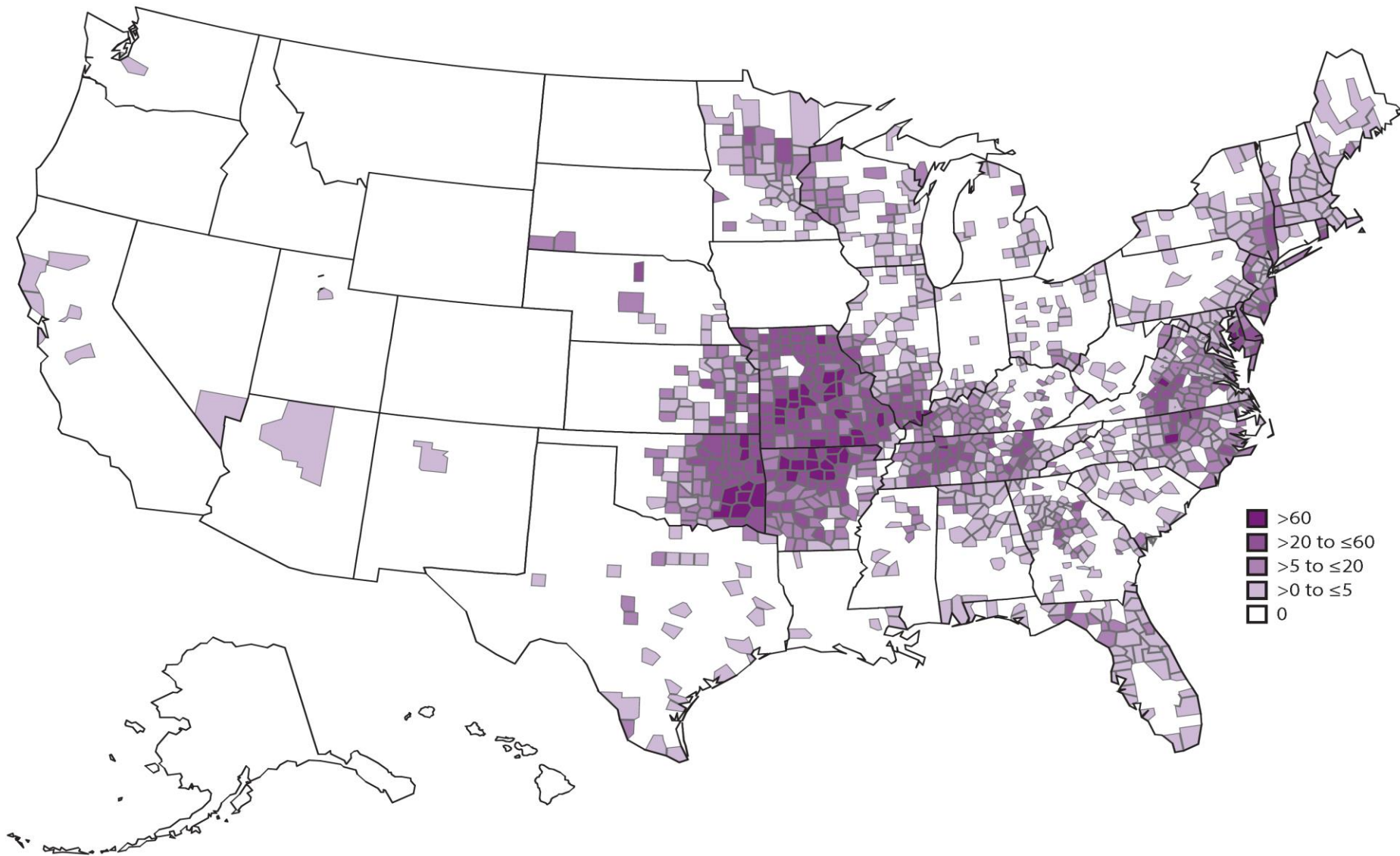
Percent of Ehrlichiosis Cases Reported each Month, 1994-2010



Ehrlichiosis Incidence by Age Group, 2000-2010



Reported Ehrlichia Incidence in US, 2000-2013



Adults with Ehrlichiosis

Symptom or sign

Patients, % (no. evaluated)

Fever	97
Myalgia	57
Headache	80
Malaise	82
Nausea	64
Vomiting	33
Diarrhea	23
Cough	26
Arthralgias	41
Rash	31
Stiff neck	3
Confusion	19

Laboratory finding

Leukopenia	62
Thrombocytopenia	71
Elevated serum AST or ALT level	83

“Rocky Mountain Spotless Fever”

Symptom, sign, or finding	Patients, % (no. evaluated)	
	HME	HGA
Symptom or sign		
Fever	97 (633)	93 (521)
Myalgia	57 (250)	77 (516)
Headache	80 (240)	76 (385)
Malaise	82 (234)	94 (288)
Nausea	64 (143)	38 (258)
Vomiting	33 (192)	26 (90)
Diarrhea	23 (197)	16 (95)
Cough	26 (155)	19 (260)
Arthralgias	41 (211)	46 (504)
Rash	31 (286)	6 (357)
Stiff neck	3 (240)	21 (24)
Confusion	19 (279)	17 (211)
Laboratory finding		
Leukopenia	62 (276)	49 (336)
Thrombocytopenia	71 (247)	71 (336)
Elevated serum AST or ALT level	83 (276)	71 (177)

NOTE. Data are from [1]. ALT, alanine aminotransferase; AST, aspartate aminotransferase.

From: Ehrlichioses in Humans: Epidemiology, Clinical Presentation, Diagnosis, and Treatment. Clin Infect Dis. 2007;45(Supplement_1):S45-S51

TABLE 2. Clinical Signs/Symptoms of Children With Human Monocytic Ehrlichiosis (n = 32)

Characteristic	Percent of Patients	
	Confirmed	Probable
Fever (>101°F)	100	100
Headache*	77	63
Myalgia*	77	63
Rash (any)	57	72
Abdominal pain*	62	69
Nausea/vomiting	57	56
Fever/rash/tick bite	43	56
Altered mental status	36	61
Fever/rash/headache*	54	44
Lymphadenopathy	50	44
Diarrhea	36	28
Conjunctivitis	14	22

*Only obtained from patients >2 years of age.

$P > 0.05$ for all comparisons.

Laboratory Findings in Children with Ehrlichiosis on Admission

Findings	Percent of Patients	
	Confirmed	Probable
Thrombocytopenia $<150,000/\text{mm}^3$	93	94
Aspartate aminotransferase $>55 \text{ U/L}$	92	89
Alanine aminotransferase $>55 \text{ U/L}$	85	67
Albumin $<3.0 \text{ mg/dL}$	56	73
Lymphopenia $<1500/\text{mm}^3$	58	56
Leukopenia $<4000/\text{mm}^3$	57	56
Hyponatremia		
$<135 \text{ mEq/L}$	54	56
$<130 \text{ mEq/L}$	8	17
Hemoglobin $<10 \text{ mg/dL}^*$	46	6
Bilirubin $>1.5 \text{ mg/dL}$	38	43

* $P = 0.025$; $P > 0.05$ for all other comparisons.

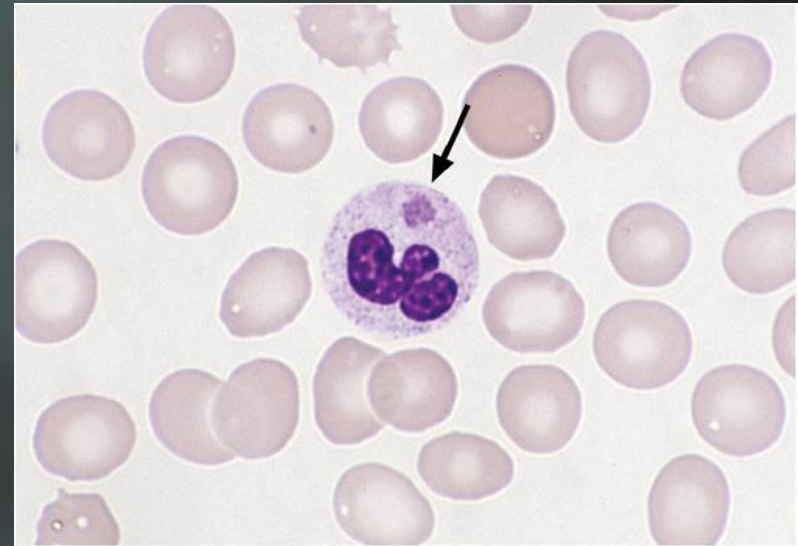
Severe Disease due to Ehrlichiosis

Less common:

- “Septic” shock-like picture
- Multiple organ failure
- Respiratory failure
- Severe CNS disease in immunocompromised pts

Diagnostic Techniques for *Ehrlichia*

- Peripheral blood smear
 - Variable sensitivity, 2-38%
- Serology (IFA) – retrospective Dx
 - Paired sera required
 - 4-fold rise in titer to 1:80
- PCR highly sensitive (60-85+%)



Name this finding?





Rocky Mountain Spotted Fever (RMSF)

- Caused by *Rickettsia rickettsii*
 - Mortality 13-25% in pre-antibiotic era
 - Still 20% in untreated
- Transmitted throughout Americas
- ~2000 annual cases in US (MMWR 2010)
- Cases reported throughout most of contiguous US
 - 5 states (NC, OK, AK, TN, MO) account for >60% cases
 - increasing reports in Arizona
- *Dermacentor variabilis* primary vector
 - < 1 per 1000 ticks carry *R rickettsii*



H T Ricketts



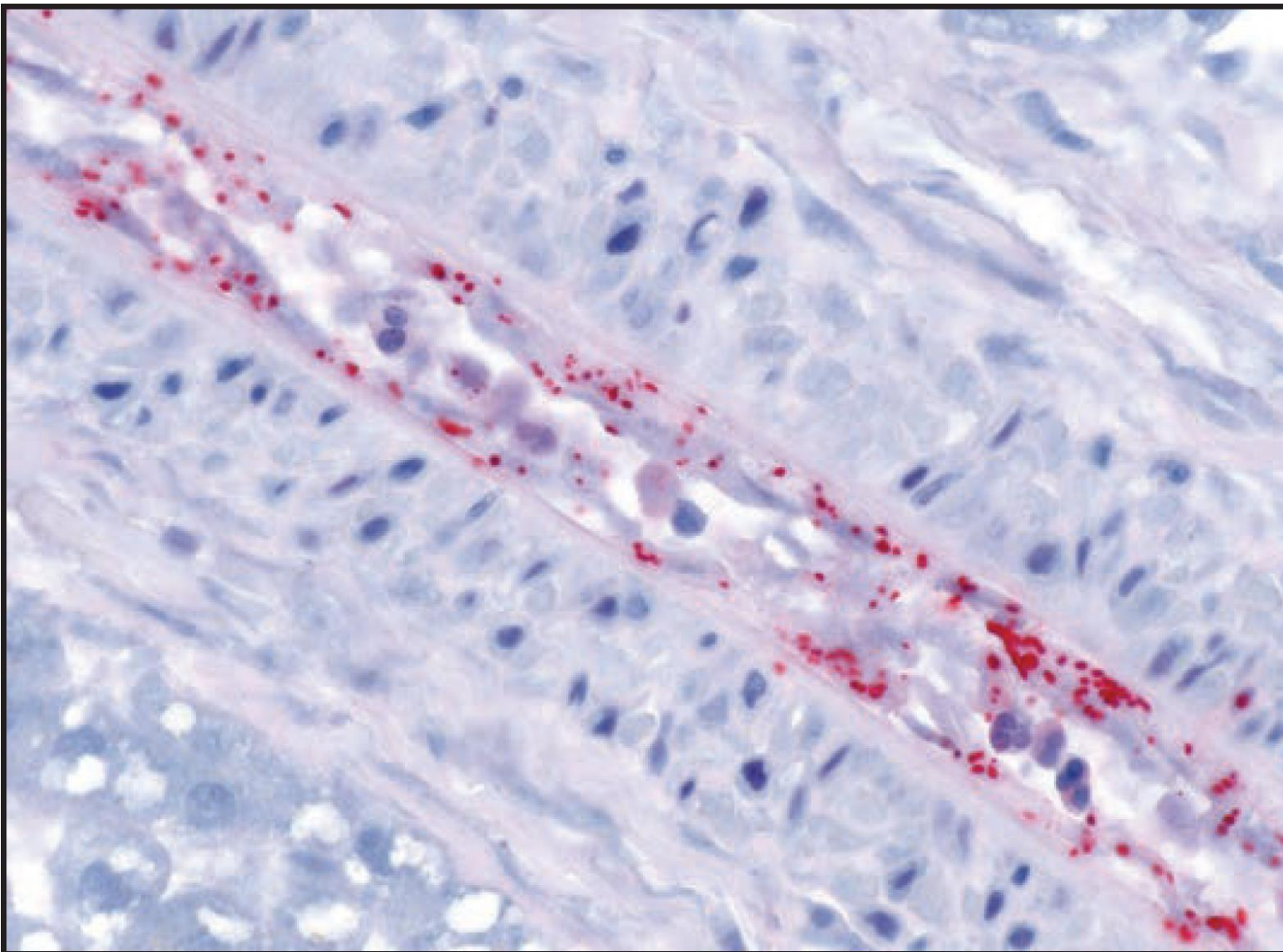
RMSF

- Conveyed to human through tick's saliva
- Requires several hours of attachment
(at least 4-6, perhaps 24 hrs)
Rickettsiae activated by warm blood meal
- Incubation period 2 - 14 dys (range 1-21)
- Most severe Rickettsial disease in US

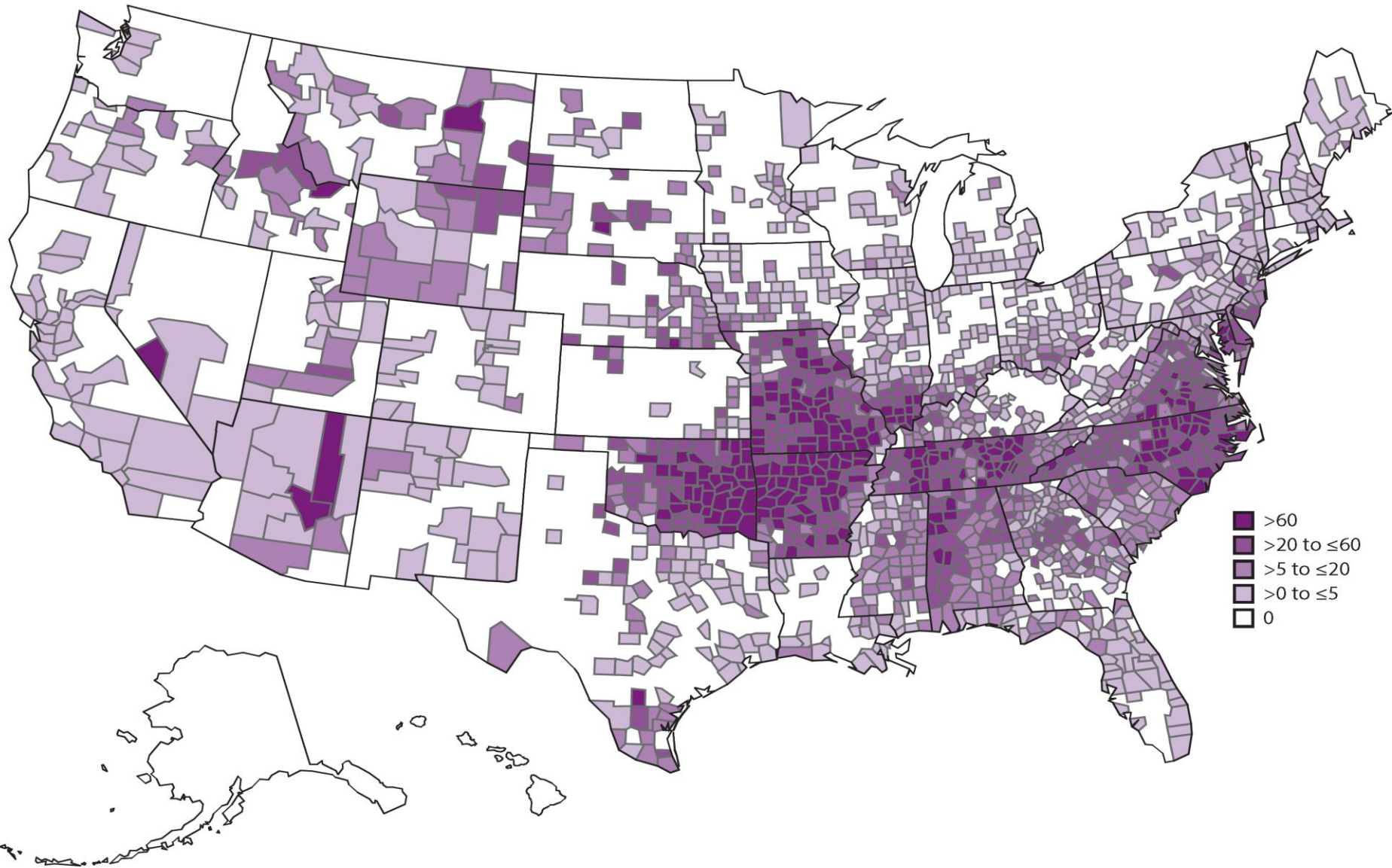
Pathogenesis

- *R. rickettsiae* infect endothelium of blood vessels
- Immune reaction causes vasculitis with leaky vessels
 - petechiae, edema, inflammation

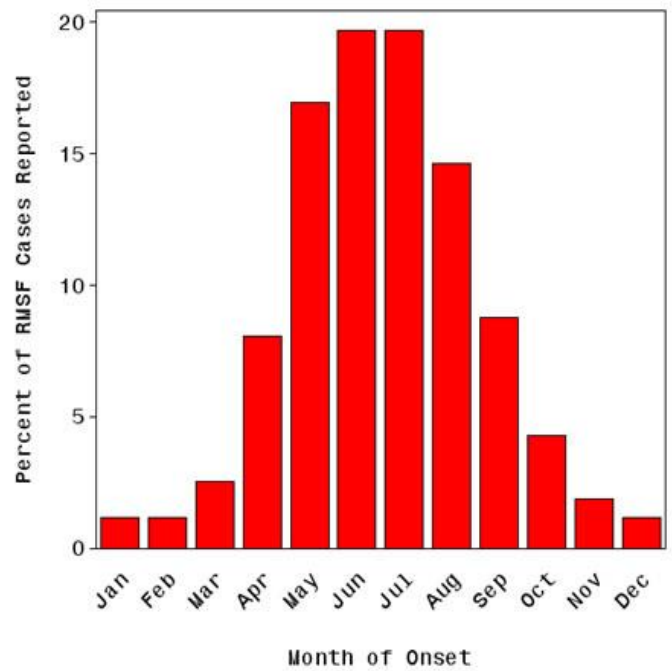
FIGURE 20. Immunohistochemical stain demonstrating *Rickettsia rickettsii* (red) in blood vessel endothelial cells



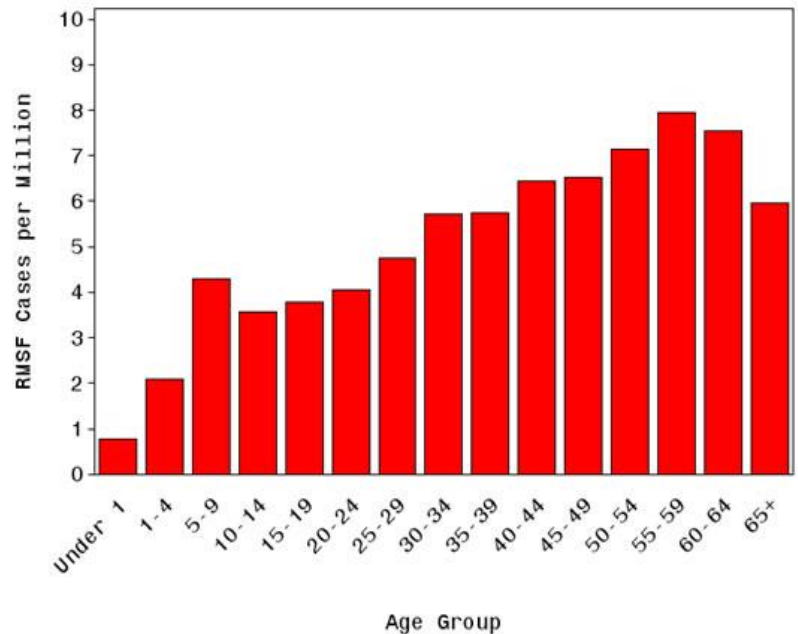
Reported RMSF Incidence by County, 2000-2013



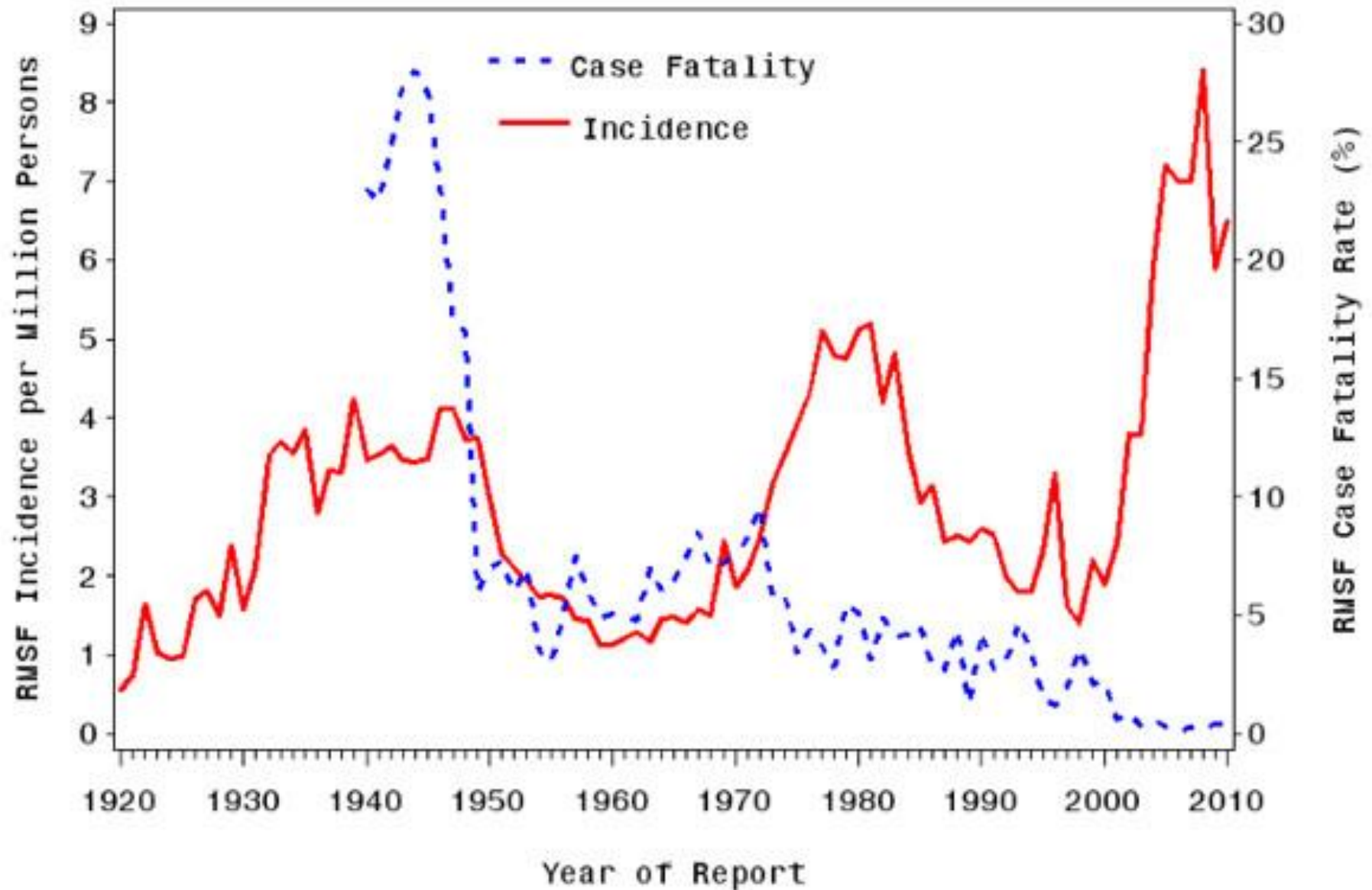
Percent of RMSF Cases Reported each Month, 1993-2008



RMSF Incidence by Age Group, 2000-2008



RMSF Case Fatality over Time



RMSF Clinical Manifestations

	J Pediatrics	J Inf Dzs
# subjects (n)	92	262
Median age (years)	5.8	15
Fever	98	99
Rash	97	88
Palms / Soles	65	74
Headache	61	91
Nausea / Vomiting	73	60
Myalgia	45	83
Abdominal pain	36	52
Conjunctival redness	30	30
Altered mental status	33	26
History of a tick bite	49	84

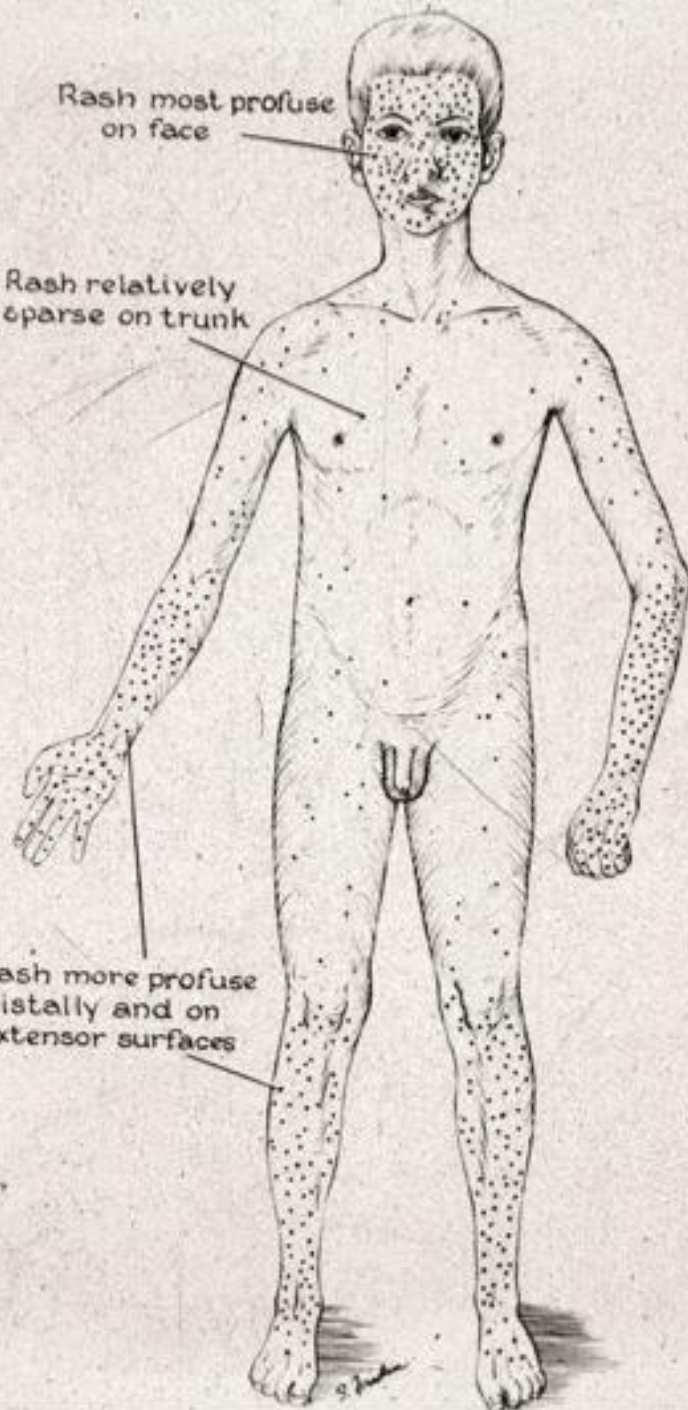
1. *J Pediatr.* Feb 2007;150(2):180-4, 184.e1

2. *J Inf Dis.* Vol. 150, No. 4 (Oct., 1984), pp. 480-488

Rash most profuse
on face

Rash relatively
sparse on trunk

Rash more profuse
distally and on
extensor surfaces





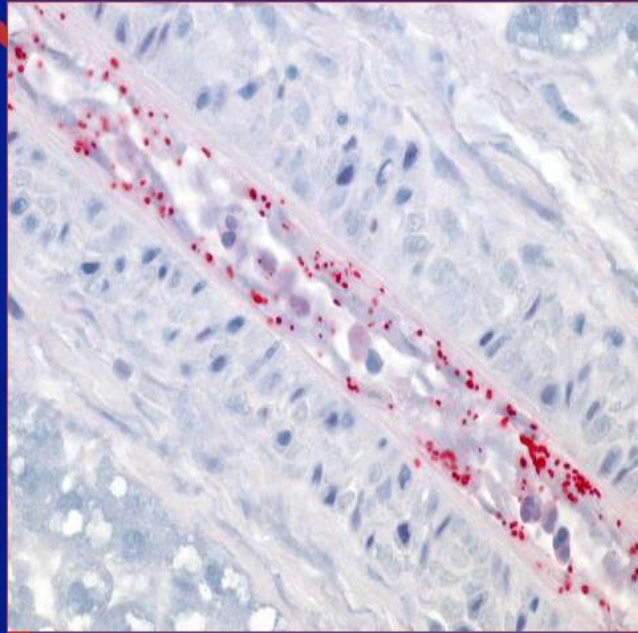


Severe RMSF

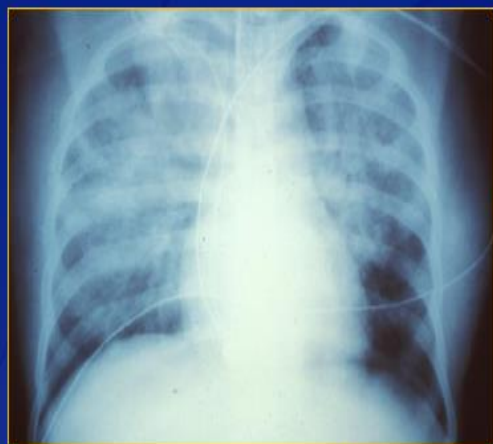
- Hypotension, coma, severe thrombocytopenia, acute renal failure, gangrene, digit / limb loss
- 73% of patients sought medical care within 3 days
 - 90% of patients within 5 days
- Only 28% received effective antibiotics within 5 days
- 39% had rash at first MD visit
- Only 51% had history of tick contact
- Mortality if treated within 5 days = 6.5%; after 5 days = 22.9%



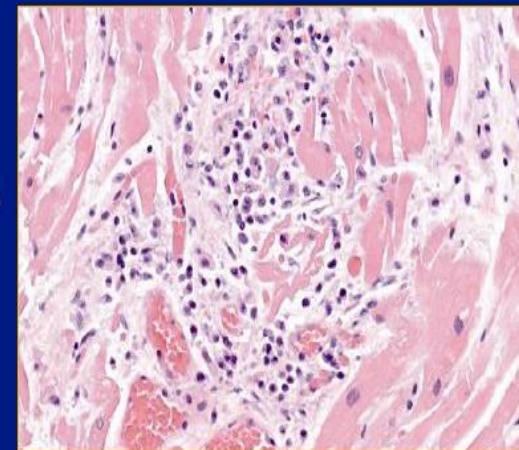
Gangrene



Cerebral edema



Pulmonary edema



Myocarditis

Photos courtesy of Dr. Chris Paddock and Dr. Gerardo Alvarez Hernandez

Risk Factors for Fatal Outcome

- ❑ Delayed onset or absence of rash
- ❑ Age <10 years or ≥60 years
- ❑ Chronic conditions with signs/symptoms that overlap with RMSF (i.e. alcoholism, chronic lung disease)
- ❑ Glucose-6-phosphate dehydrogenase deficiency
- ❑ Off-season onset (colder months, first and last cases of the year)
- ❑ **Delay in administration of effective therapy (doxycycline)**

Laboratory Manifestations

- Laboratory abnormalities *nonspecific* and *occasional*
 - Hyponatremia – usually mild, seen in $\leq 50\%$
 - Mild AST, ALT, and BUN elevations
 - Thrombocytopenia
 - No characteristic change in WBC

Diagnosis

- Serology – *retrospective Dx*
 - **IgG IFA gold standard serologic test**
 - Titers rise 7-10 days after infection
 - EIA less reliable
 - **Paired convalescent sample required by State Lab**
- Blood PCR - poor sensitivity for RMSF
- Skin Bx & Immunostaining (70% sens)
- PCR or Culture skin lesions

Treatment – Ehrlichiosis and RMSF

- Doxycycline drug of choice
 - 4.4 mg/kg/day divided BID for children
 - 100 mg twice daily, max
 - Duration = 3 days beyond defervescence for RMSF
 - Duration = 7-14 days for HME
- Alternatives for MILD cases (esp in pregnancy)
 - Chloramphenicol (for RMSF)
 - Rifampin (for HME)
- If no defervescence in ~48hrs, consider other diagnoses

Doxycycline Tooth Staining Study

- ❑ Short term doxycycline use does not:
 - Darken shade of teeth
 - Cause visible staining of teeth
 - Increase risk of enamel hypoplasia
- ❑ Doxycycline can be safely administered to children without fear of tooth staining at dose and duration recommended for rickettsial diseases

Todd SR, Dahlgren FS, Traeger MS, et al. No visible dental staining in children treated with doxycycline for suspected rocky mountain spotted Fever. The Journal of pediatrics 2015; 166(5): 1246-51.

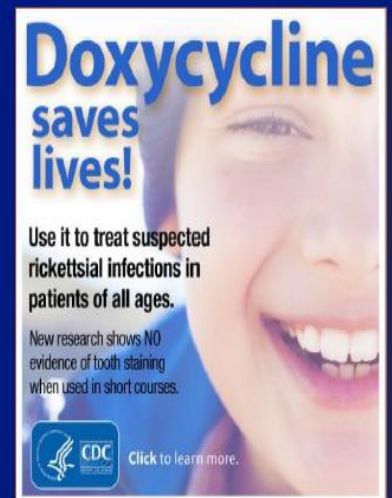


TABLE 1. Selected clinical features of tickborne rickettsial diseases — United States

Disease	Incubation period	Common initial signs and symptoms	Cutaneous signs	Common laboratory findings	Estimated case-fatality rate
Rocky Mountain spotted fever	3–12 days	Fever, headache, chills, malaise, myalgia, nausea, vomiting, abdominal pain, photophobia, anorexia	Maculopapular rash approximately 2–4 days after fever onset in most, might become petechial and involve palms and soles	Thrombocytopenia, slightly increased hepatic transaminase levels, normal or slightly increased white blood cell count with increased immature neutrophils, hyponatremia	5%–10%
<i>Rickettsia parkeri</i> rickettsiosis	2–10 days	Fever, myalgia, headache	Eschar, sparse maculopapular or vesiculopapular rash that might involve palms and soles	Mild thrombocytopenia, mild leukopenia, increased hepatic transaminase levels	—*
<i>Rickettsia</i> species 364D rickettsiosis	—†	Fever, headache, myalgia, fatigue	Eschar or ulcerative lesion with regional lymphadenopathy	—†	—*
<i>Ehrlichia chaffeensis</i> ehrlichiosis (human monocytic ehrlichiosis)	5–14 days	Fever, headache, malaise, myalgia, nausea, diarrhea, vomiting	Rash in approximately 30% of adults and 60% of children, variable rash pattern that might involve palms and soles, appears a median of 5 days after illness onset	Leukopenia, thrombocytopenia, increased hepatic transaminase levels, hyponatremia, anemia	3%
<i>Ehrlichia ewingii</i> ehrlichiosis	—†	Fever, headache, malaise, myalgia	Rash rare	Leukopenia, thrombocytopenia, increased hepatic transaminase levels	—*
<i>Ehrlichia muris</i> -like agent ehrlichiosis	—†	Fever, headache, malaise, myalgia	Rash in approximately 12%	Thrombocytopenia, lymphopenia, leukopenia, increased hepatic transaminase levels, anemia	—*
Human anaplasmosis (human granulocytic anaplasmosis)	5–14 days	Fever, headache, malaise, myalgia, chills	Rash rare, in <10%	Thrombocytopenia, leukopenia, mild anemia, increased hepatic transaminase levels, increased numbers of immature neutrophils	<1%

Can you name this disease?

www.idimages.org

cdc.gov

Considerations:

Lyme Dz

STARI

Hypersensitivity reaction to bite

Cellulitis

Bacterial superinfection of bite

Nummular eczema

Tinea

Spider bite



Lyme Disease



Lyme Disease: Background

- Bacterial agent:
 - *Borrelia burgdorferi*
 - Spirochete
- Transmitted by Ixodes spp. ticks
 - *I. scapularis* in eastern US
 - *I. pacificus*, *I. ricinus*, *I. persulcatus* elsewhere
- Wild rodents - natural reservoir
 - White footed mouse



Spring

Summer

Fall



US Vector-Borne Diseases

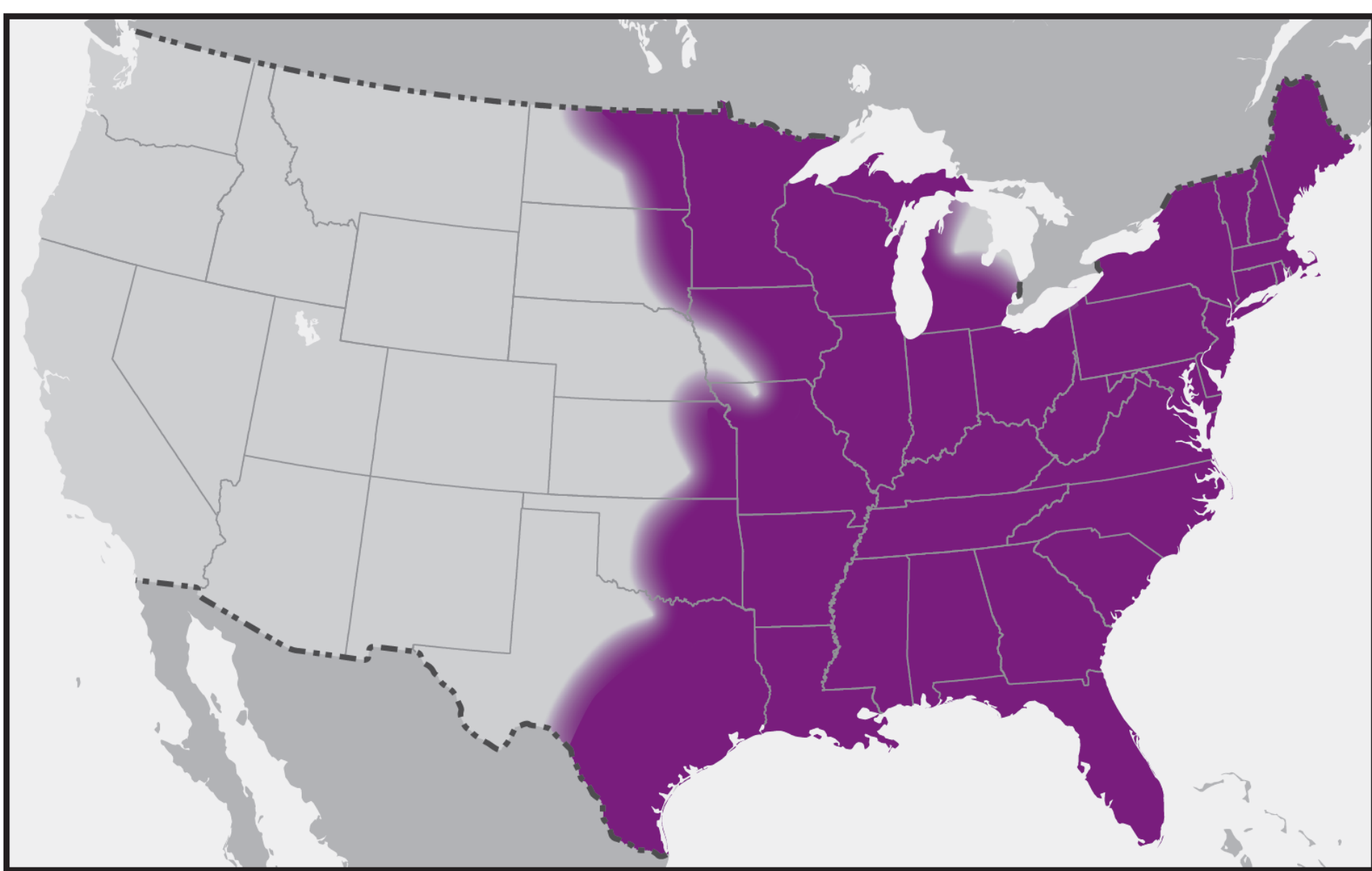
Tick-borne

- Lyme – **38,486**
- RMSF – ~ 2500
- HME – 951 (underreported)
- HGA – 1161
- Babesiosis – < 100 ?
- Colorado tick fever – < 100 ?
- Powassan virus – 6

Mosquito-transmitted

- West Nile – 720
- *LaCrosse* – 70
- EEE – 4
- WEE – ~ 10
- SLV – 12
- California serogroup – 55
- Malaria – 1451
- Dengue – ? **Prob hundreds**

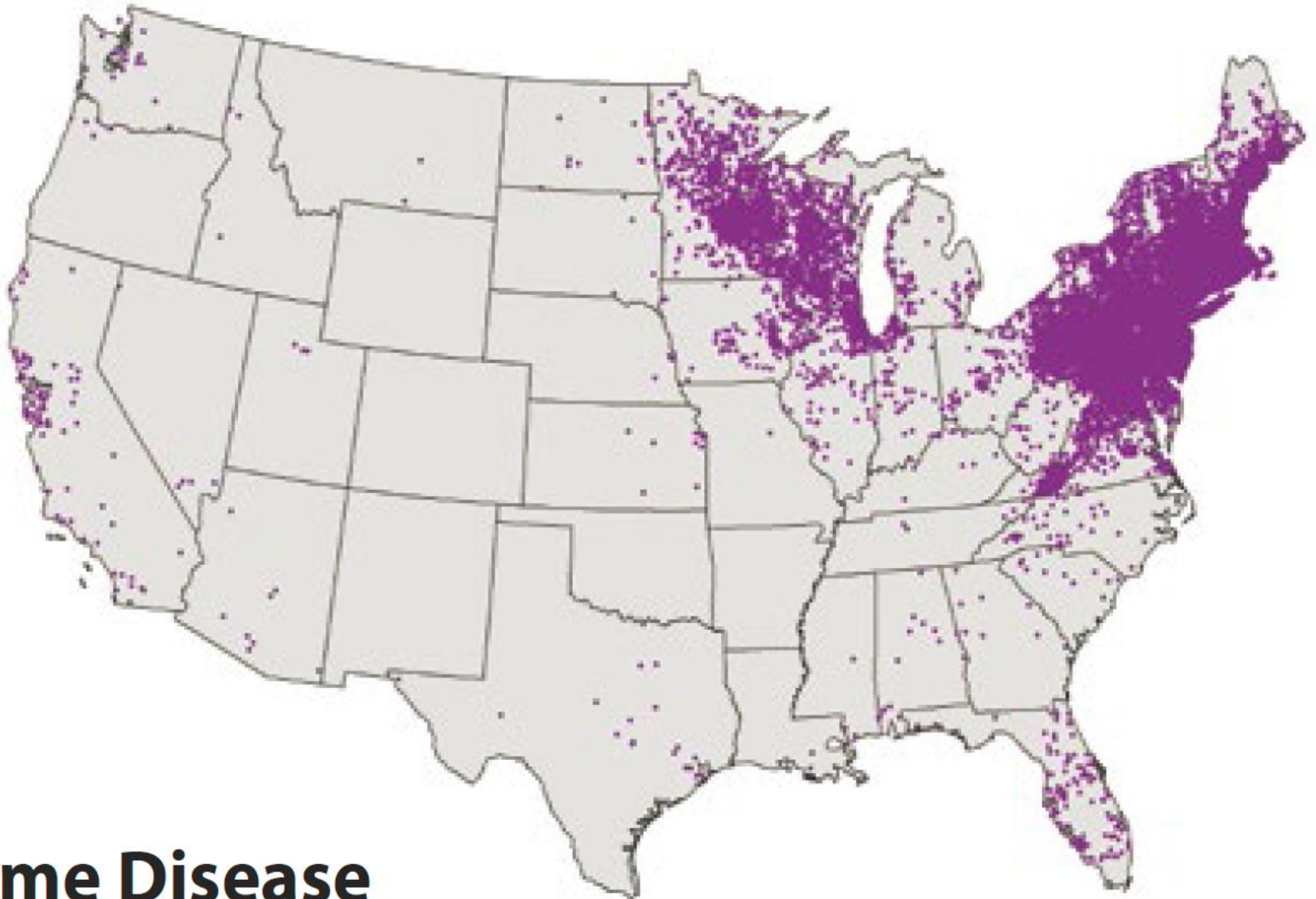
FIGURE 16. Approximate U.S. distribution of *Ixodes scapularis* (blacklegged tick)



Public Health Impact: Lyme Disease

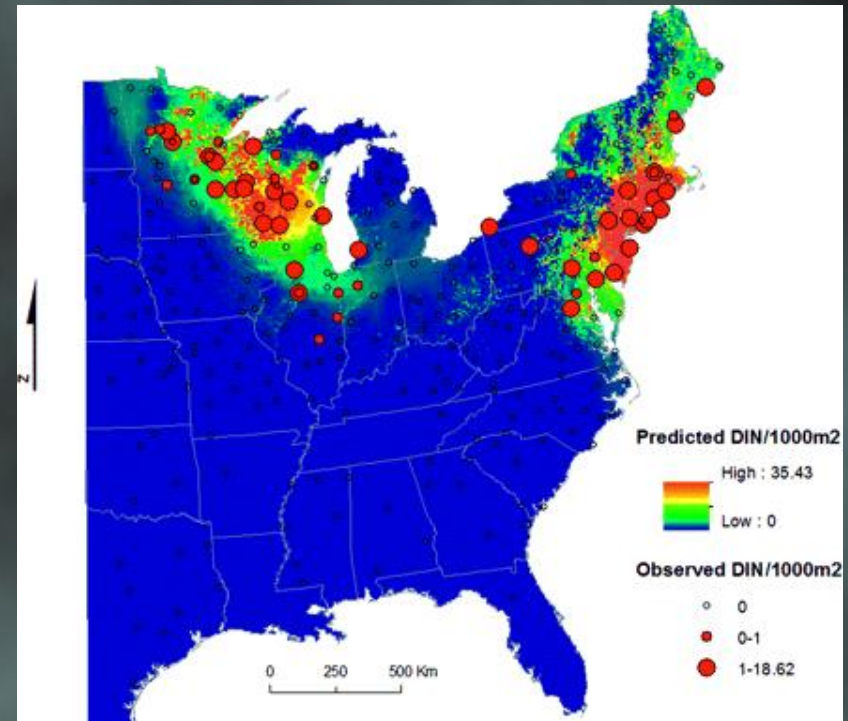
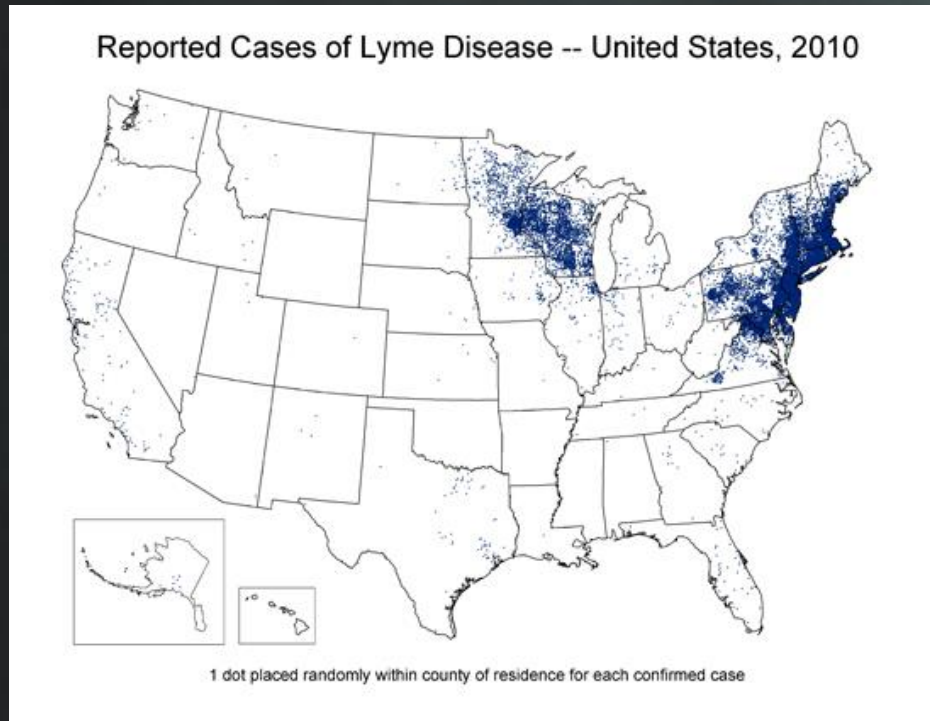
- 5th most common reportable disease in US
 - Chlamydia, gonorrhea, salmonella, syphilis
 - Incidence slightly higher than new dx of HIV
 - Underreported
- Concentrated geographically
 - Very high disease burden in NE and Midwest US

Lyme Disease Cases reported to CDC, 2015



Lyme Disease

“Acaralogical” Risk of Lyme



Abrupt N-S gradient of clinical Lyme risk – correlates with tick sampling data
N of 39th parallel – 207,600 km of sampling at **36 sites produced 1384 nymphs**
S of 39th parallel – 223,400 km of sampling at **60 sites produced 21 nymphs** (5 in NC)

Lyme disease cases reported by state, 2005-2015													*confirmed cases per 100,000 population
State	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015 Confirmed	2015 Incidence*	
Alabama	3	11	13	6	3	1	9	13	11	28	14	0.3	
Alaska	4	3	10	6	7	7	9	4	14	5	1	0.1	
Georgia	6	8	11	35	40	10	32	31	8	4	8	0.1	
Kansas	3	4	8	16	18	7	11	9	18	12	11	0.4	
Kentucky	5	7	6	5	1	5	3	8	17	11	12	0.3	
Maine	247	338	529	780	791	559	801	885	1127	1169	993	74.7	
Maryland	1235	1248	2576	1746	1466	1163	938	1113	801	957	1249	20.8	
Massachusetts	2336	1432	2988	3960	4019	2380	1801	3396	3816	3646	2922	43.0	
Michigan	62	55	51	76	81	76	89	80	114	93	125	1.3	
Minnesota	917	914	1238	1046	1063	1293	1185	911	1431	896	1174	21.4	
New York	5565	4460	4165	5741	4134	2385	3118	2044	3512	2853	3252	16.4	
North Carolina	49	31	53	16	21	21	18	27	39	27	38	0.4	
Pennsylvania	4287	3242	3994	3818	4950	3298	4739	4146	4981	6470	7351	57.4	
South Carolina	15	20	31	14	25	19	24	35	33	20	13	0.3	
Tennessee	8	15	31	7	10	6	5	2	11	7	6	0.1	
Texas	69	29	87	105	88	55	28	33	48	20	18	0.1	
Virginia	274	357	959	886	698	911	756	805	925	976	1102	13.1	
Wisconsin	1459	1466	1814	1493	1952	2505	2408	1368	1447	991	1309	12.7	
U.S. TOTAL	23,305	19,931	27,444	28,921	29,959	22,561	24,364	22,014	27,203	25,359	28,453	8.9	

Is Lyme Moving South?

Virginia: increasing cases in southern counties over last 5 years

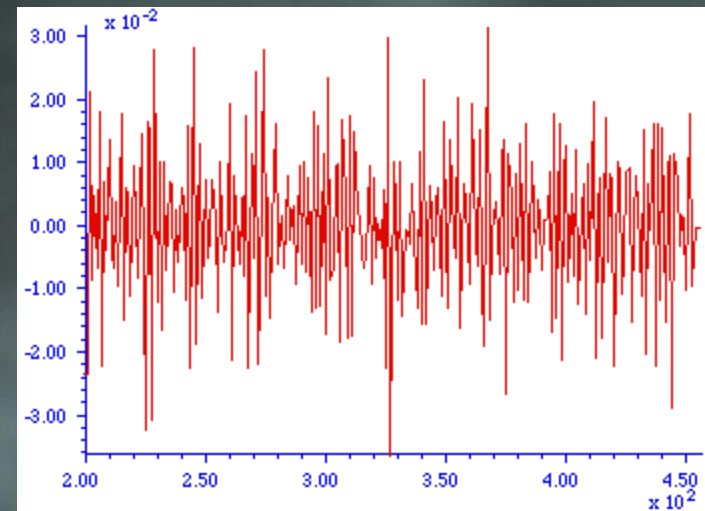
North Carolina: Small # confirmed (local) cases annually
No marked increase – yet?

Human Lyme in Southeast

- Low # local Lyme cases per year (NC DPH)
- Incidence without marked change in South, to date
- Human incidence small fraction of northeast (CDC data)
 - NE States – incidence 10 – 100 per 100,000; gross underreporting
 - NC, SC, GA – incidence 0.1-0.4 per 100,000
- Canine serosurveillance (C6 peptide)
 - ~ 6% of dogs positive in VA
 - ~ 1% of dogs positive in NC and SC

Signal to Noise Problem?

- Most cases are of “cutaneous Lyme”
 - No laboratory proof of diagnosis
 - No clinical verification
 - Indistinguishable from STARI
- False positive serologies
 - Testing in low prob. illnesses
- Travel histories not always available
 - “Local” cases may be imported
- There are “endemic” counties but infected vectors not found
- Case-based surveillance *insufficient* for vector-borne zoonoses
- *Ixodes* tick surveillance best surrogate measure of human risk



Antibiotic prophylaxis for patients with a tick bite

Single dose of doxycycline for prevention of Lyme disease when all of the following conditions are met:

- Highly endemic area
- Attached tick identified as an adult or nymphal *I. scapularis*
- Tick attached for > 36 hours based on engorgement or history
- Prophylaxis can be started within 72 hrs. of tick removal
- Doxycycline treatment is not contraindicated

Dose = 200 mg po x 1 for adults

From: The Clinical Assessment, Treatment and Prevention of Lyme disease, human granulocytic anaplasmosis and babesiosis: Clinical practice guidelines from the Infectious Diseases Society of America; CID; 2006

Clinical review of Lyme

- Lyme has well-described manifestations
- Pretest probability of Lyme is extremely low if one lacks specific objective findings

Clinical review of Lyme

- Early localized disease: erythema migrans rash
- Early disseminated disease:
 - Meningitis and / or neuropathy (usually CN VII)
 - Carditis (AV block)
- Late disseminated disease:
 - Arthritis (large joints with inflammatory effusions)
 - Chronic encephalopathy (very rare, poorly defined)

Lyme Disease: Clinical Manifestations in Children

- Prospective study: 201 Connecticut children with Lyme disease enrolled between April 1992 & November 1993
- Median age 7yo (range 1 to 21 yo)
- Presenting manifestations:
 - Erythema migrans in 89 %
 - Single EM lesion in 66%
 - Multiple lesions 23%
- Arthritis – 7 %
- Facial palsy – 3 %
- Aseptic meningitis – 1 %
- Carditis – 0.5 %

Erythema Migrans

- 70-80% of patients
- Typically 7-14 days after bite
- Expanding, round, erythematous
 - 5 – 30cm (up to 61cm reported)
 - Single lesion in ~80%
- Up to 2/3rds without “bullseye” appearance
- Diagnostic testing NOT USEFUL in erythema migrans



cdc.gov



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Treatment of Erythema Migrans



- 14 dys (range 10-21 dys) of oral antibiotics (Doxy, Amox, Cefurox, Azithro)
- Doxycycline is preferred drug (4mg/kg/dy)
- Azithromycin results in more treatment failures
 - Cure rates ~80%
- 10 – 21 days
 - No advantage to longer courses



**Awaiting new Guidelines, out
end of 2017 or early 2018**

Stupica et al. Clin Infect Dis. 2012 May 21. [Epub ahead of print]

Wormser et al. Ann Intern Med. 2003 May 6;138(9):697-704

Shapiro E. Lyme Disease. NEJM 2014;370:1724



DDx includes STARI

- “Southern Tick-Associated Rash Illness”
- Associated with Lone Star ticks
 - Biologically incapable of transmitting *B. burgdorferi*
- Clinically indistinguishable from Lyme EM
- No evidence of *B. burgdorferi* in STARI lesions
- No known long term “Lyme” sequelae (e.g. arthritis)
- Cause remains unknown (not necessarily an infection)
- No controlled evidence that antibiotics are necessary
 - Some Rx with oral Abx because resembles early Lyme Dz
- MOST EM-rashes in NC & Southeast probably STARI

Southern Tick-associated Rash Illness (STARI)



Life stages of lone star tick
(*Amblyomma americanum*)

Early Disseminated Lyme: Acute Neuroborreliosis

- 15% of untreated patients
- Presentation: weeks - months after infection
- **Meningitis**
 - Headache, mild meningeal symptoms
 - Lymphocytic pleocytosis
- **Cranial and peripheral neuropathies**
 - May coexist with meningitis
 - 6th and 7th cranial nerve palsies common
 - Polyradiculopathy, mononeuritis multiplex

Early Disseminated Lyme: Lyme Carditis

- 5% of untreated patients
- Several weeks after infection
- **AV block** - any degree, including complete
 - Usually self-ltd and responds to therapy
- **Myocarditis / pericarditis** (less common)



Treatment of Early Disseminated Lyme

- Meningitis
 - IV Ceftriaxone for 14 days - standard of care
 - Oral doxycycline for 14 days **may** be equivalent
- Isolated CN palsies (without meningitis)
 - Oral therapy (preferably doxycycline 4mg/kg/dy) for 14 days
 - Beta lactams or macrolides *may be* effective if no meningitis
 - Amox 50/kg/dy or Cefuroxime axetil 30/kg/dy
- Carditis
 - Oral antibiotics for 14 days; initially IV if hospitalized
 - Consult cardiologist if symptomatic or high degree AV block

Later Onset: Lyme Arthritis

- Most common manifestation in US
- 60% of untreated patients
- Months after onset of illness
- Intermittent attacks of true arthritis
 - Typically one or two large joints, esp knee
 - Swelling out of proportion to pain
 - Seldom red
 - Generally less than $<100,000$ WBC, mostly PMNs
- Treatment = 28 days of oral antibiotics

Lyme Arthritis: Antibiotic-refractory

- ~10% of treated patients
- Persistent inflammation for months to years
 - Histopathology of chronic inflammatory arthritis
- Nearly always PCR and culture negative
 - Both synovial tissue and joint fluid
- HLA-DRB1-associated
- Should be regarded as **autoimmune** phenomenon
 - Anti-inflammatory drugs (NSAIDs, methotrexate)
 - Arthroscopic synovectomy

Lyme Disease: Diagnostic Testing

- Two-step serologic test
 - ELISA
 - Whole cell *B. burgdorferi* lysate
 - Confirmatory Western Blot
 - IgG 10 bands – $\geq 5/10$ = positive
 - IgM 3 bands – $\geq 2/3$ = positive
 - only useful in first 4-6 weeks
 - Less sensitive when have Erythema migrans (~38% sens)
 - Neuroborreliosis ~87% sensitivity
 - Lyme arthritis 97-100% sensitivity



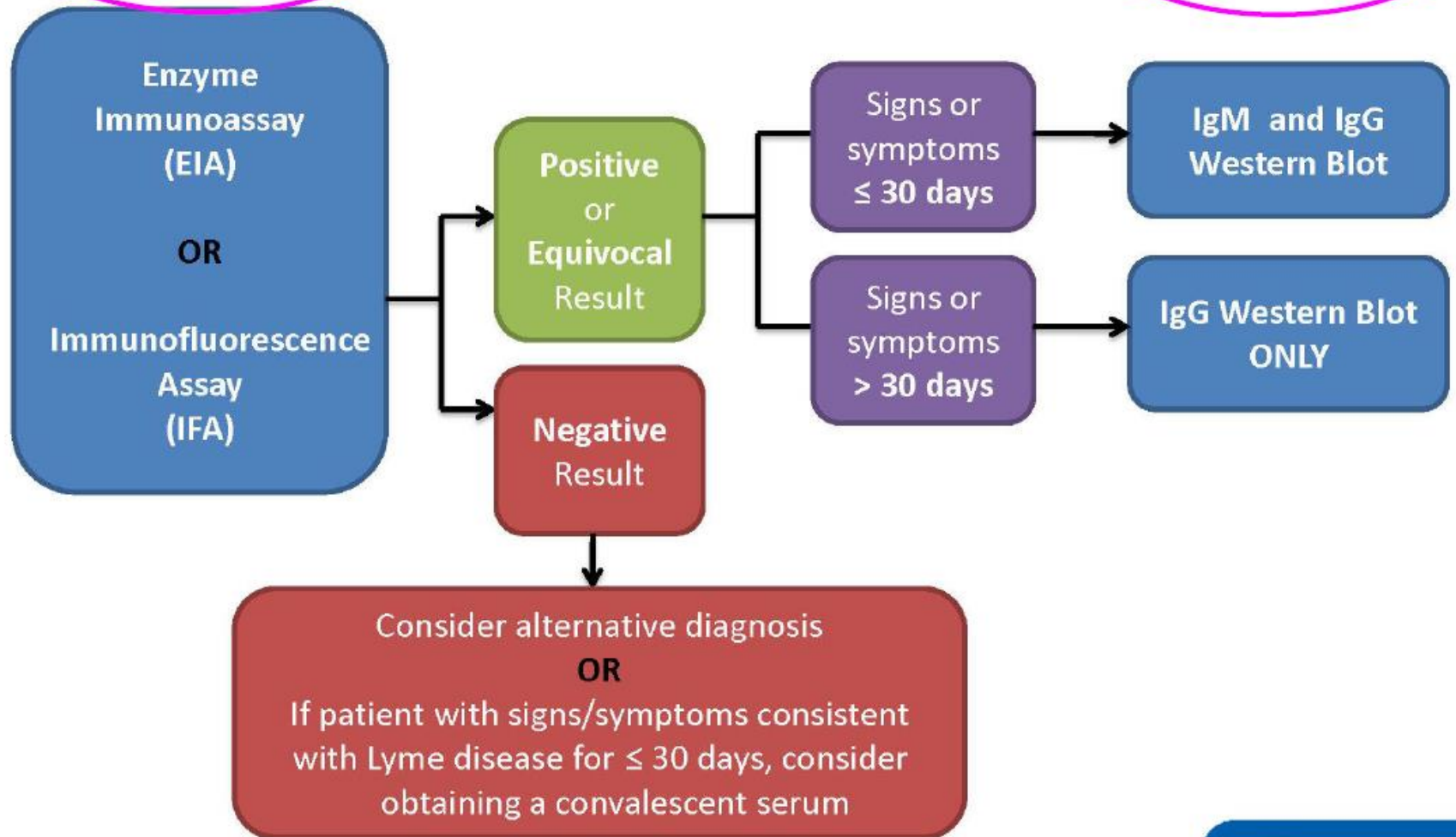
Best Practices when Testing for Lyme

1. Order tests correctly:
 - First step = ELISA (aka EIA, aka “total Lyme antibody” or Lyme IgG/IgM)
 - Second step = Western blot (aka immunoblot)
 - WB not interpretable unless ELISA was positive or equivocal!
 - Order “Lyme ELISA with reflex to Western blot”
2. A positive test is insufficient to diagnose Lyme
 - Pt must have a compatible clinical illness
 - Only order a test when pretest probability is reasonably high
 - Pt request alone is not enough to justify testing
3. Use established criteria to interpret a Lyme test
 - eg, 4 positive IgG bands is a **NEGATIVE Western blot**

Two-Tiered Testing for Lyme Disease

First Test

Second Test



Outcomes of Lyme disease

- At 1-2 year follow-up people treated with 'standard' therapy for confirmed Lyme have good outcomes
- Incidence of chronic symptoms not clearly different in patients with a history of treated Lyme disease
- Several trials of prolonged IV antibiotics for "post-Lyme" patients: virtually no evidence of benefit, abundant evidence of harm

Prognosis

- Most patients treated with antibiotics recover completely
- In patients with persistent or recurrent joint swelling, re-treatment with a second 4-week course may be needed
- Some patients – particularly those diagnosed with later stages of disease – may have persistent symptoms of fatigue, muscle aches, reduced concentration
 - Preferred term for this is Post-treatment Lyme Disease Syndrome (PTLDS)
 - Placebo-controlled trials have not shown a sustained benefit of extended antibiotic treatment

Chronic Lyme Disease

- Controversial; diagnosis mainly given to persons with syndromes of chronic pain or chronic fatigue, or alternative medical diagnoses
- **No pathologic, microbiologic, or clinical definition**
- Background rate of these symptoms very high
- In endemic areas >2/3 of patients referred for Lyme disease are without evidence of active or past infection
- Inappropriate testing responsible for some diagnoses

Borrelia mayonii: Emerging Tickborne Pathogen



Clinical Features of Patients (n=6)

- Ages ranged from 10 to 67 years; 4 male, 2 female
- 2 patients had a known tick bite, but all reported exposure to ticks or tick habitat in Minnesota or Wisconsin
- 5 presented with an acute febrile illness
- 3 had potential neurologic involvement (confused speech, profound somnolence, visual difficulties)
- 4 had rash – only 1 was suggestive of an EM
- 1 had arthralgia

Borrelia mayonii: Emerging tickborne pathogen

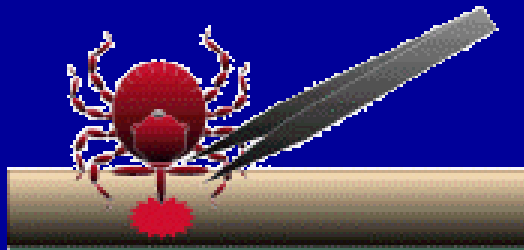
Patient Outcomes

- 2 of 6 patients were hospitalized
- All were treated with antibiotics recommended for treatment of Lyme disease
- 5 patients recovered completely, while 1 reported residual joint pain

Tick Removal

- Hot match
- Petroleum Jelly
- Nail Polish
- Which one works best?
- None of the Above!!!!

Tick Removal



- Use fine tipped tweezers
- Fasten to mouth parts
- Gently pull
- Don't crush or squeeze tick after removal!

Show and Tell

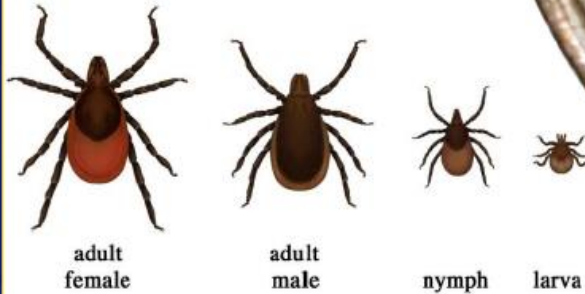
- What is the name of this tick?
- What diseases can it transmit?



- Amblyomma americanum*
 - STARI
 - Human monocytic ehrlichiosis (*Ehrlichia chaffeensis*)
 - Tularemia

Selected Tick Vectors

Blacklegged Tick (*Ixodes scapularis*)



Lone Star Tick (*Amblyomma americanum*)



Dog Tick (*Dermacentor variabilis*)



Transmit pathogens that cause the following diseases:

- Lyme disease
- Anaplasmosis
- Babesiosis
- Powassan virus disease
- Borrelia miyamotoi* disease
- Ehrlichiosis
- STARI
- Tularemia
- Rocky Mtn. Spotted Fever
- Tularemia

Conclusions

— RMSF and HME:

- Cause acute febrile illnesses
- Can be life threatening, common
- Clinical manifestations protean
- Standard of care is empiric treatment (Dx delayed)
- Clinical suspicion is primary guide to care

— Lyme disease

- Not life threatening, subacute
- Manifestations are rather specific
- Always think about geographic risk and clinical probability

Questions?

