

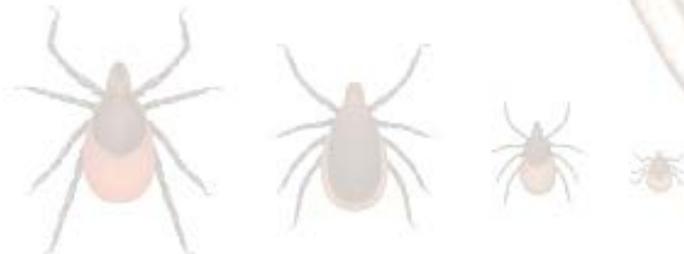


WRAIR

Walter Reed Army
Institute of Research
Soldier Health • World Health



Blacklegged Tick (*Ixodes scapularis*)



adult
female

adult
male

nymph

larva

Rickettsial Diseases

and friends....

MAJ Jason M. Blaylock, MD

21 Nov 2014

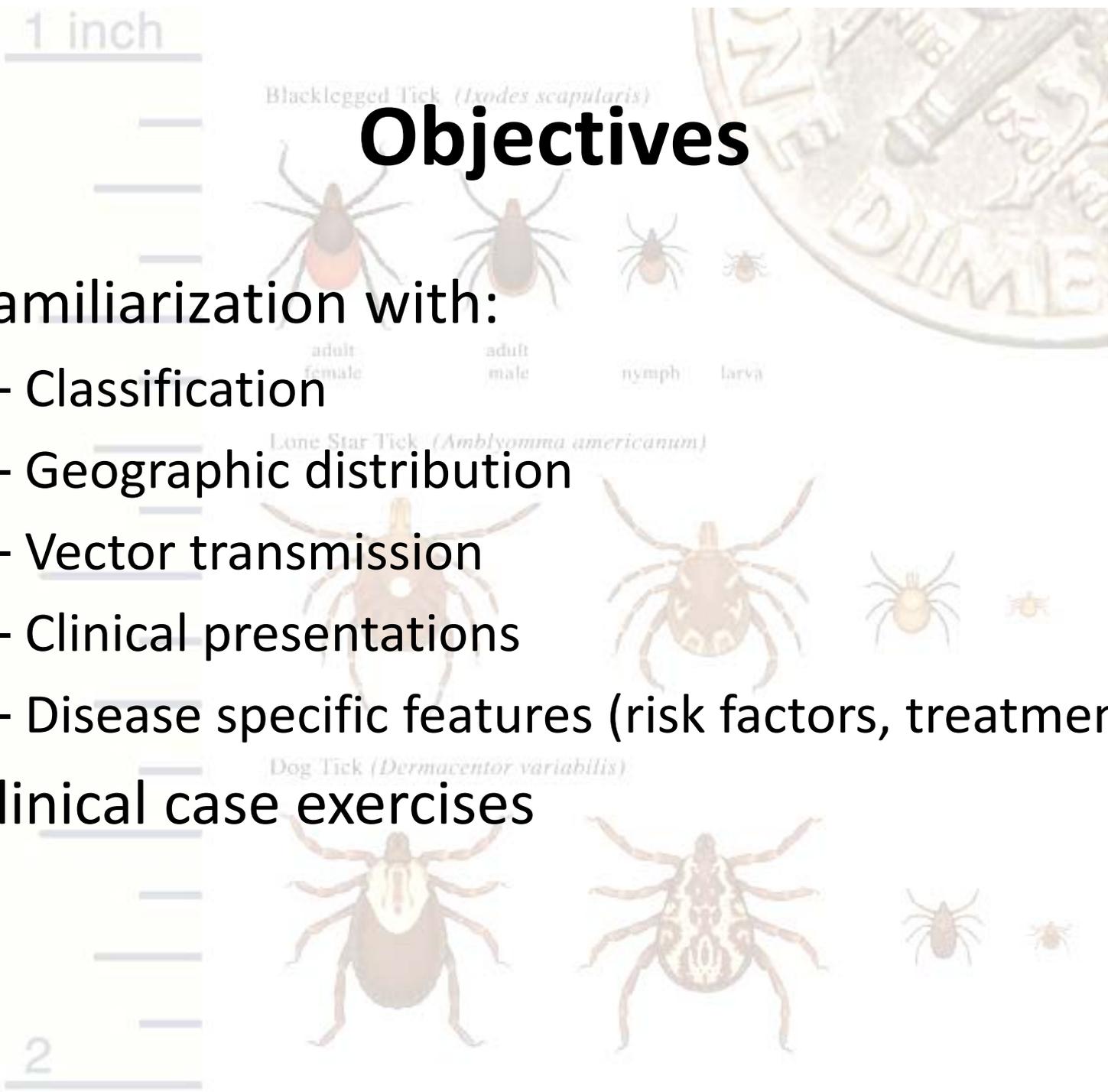
Dog Tick (*Dermacentor variabilis*)



***Acknowledgements: LTC Paige Waterman, MD,
MAJ Leyi Lin, MD**

Objectives

- Familiarization with:
 - Classification
 - Geographic distribution
 - Vector transmission
 - Clinical presentations
 - Disease specific features (risk factors, treatment)
- Clinical case exercises



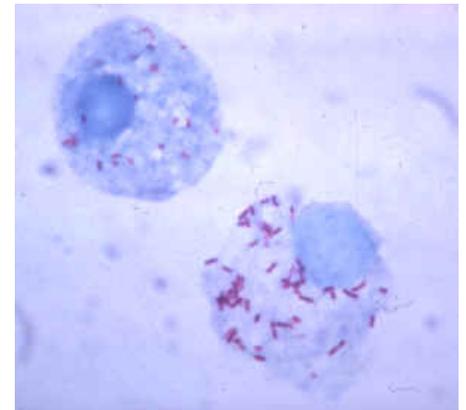
Common Rickettsial Infections

Rickettsiae

	Tick-Borne	Flea-Borne	Louse-Borne	Mite-Borne
Spotted Fever Group	<i>R. rickettsii</i>			
	<i>R. conorii</i>			
	<i>R. japonica</i>	<i>R. felis</i>		<i>R. akari</i>
	<i>R. africae</i>			
	<i>R. parkeri</i>			
Typhus Fever Group		<i>R. typhi</i>	<i>R. prowazekii</i>	
Scrub Typhus				<i>O. tsutsugamushi</i>
Anaplasma	<i>A. phagocytophilum</i>			
Ehrlichia	<i>E. chafeensis</i>			
	<i>E. ewingii</i>			
	<i>E. canis</i>			
Q Fever	<i>Coxiella burnetii</i>			
Lyme disease	<i>Borrellia burgdorferi</i>			

What's in Common?

- Obligate intracellular Gm-negative bacteria
- Transmitted by ectoparasites
 - Ticks, fleas, lice, mites (chiggers)
- Incubation: 1-2 weeks
- Some with bite eschar
- Rash not universal
- Non-specific symptoms
- Broad spectrum: mild flu-like to very ill
- ↓ platelets, ↓ WBCs, ↑ liver tests
- **Doxycycline is effective!**



Common things being common

Destination	No. travelers						
	SFG rickettsiosis	TG rickettsiosis	Indeterminate SFG/TG rickettsiosis	Scrub typhus	Anaplasmosis	Acute Q fever	Bartonellosis
Western Europe	7	1			1	2	1
Eastern Europe			1				
North Africa	3						
Sub-Saharan Africa	197	1				5	1
Middle East	1					2	1
Northeast Asia	2	1				1	
South central Asia	5	1	1	5			
Southeast Asia	3	6	2	9			1
Australia/New Zealand	1			1			
Oceania	1						
North America	1						
Central America	3						
Caribbean	1						3
South America							
Unknown	6			1		1	
Total	231	10	4	16	1	11	7

*SFG, spotted fever group; TG, typhus group.

Spotted fever group

Tick

Flea

Mite

R. rickettsii

R. conorii

R. japonica

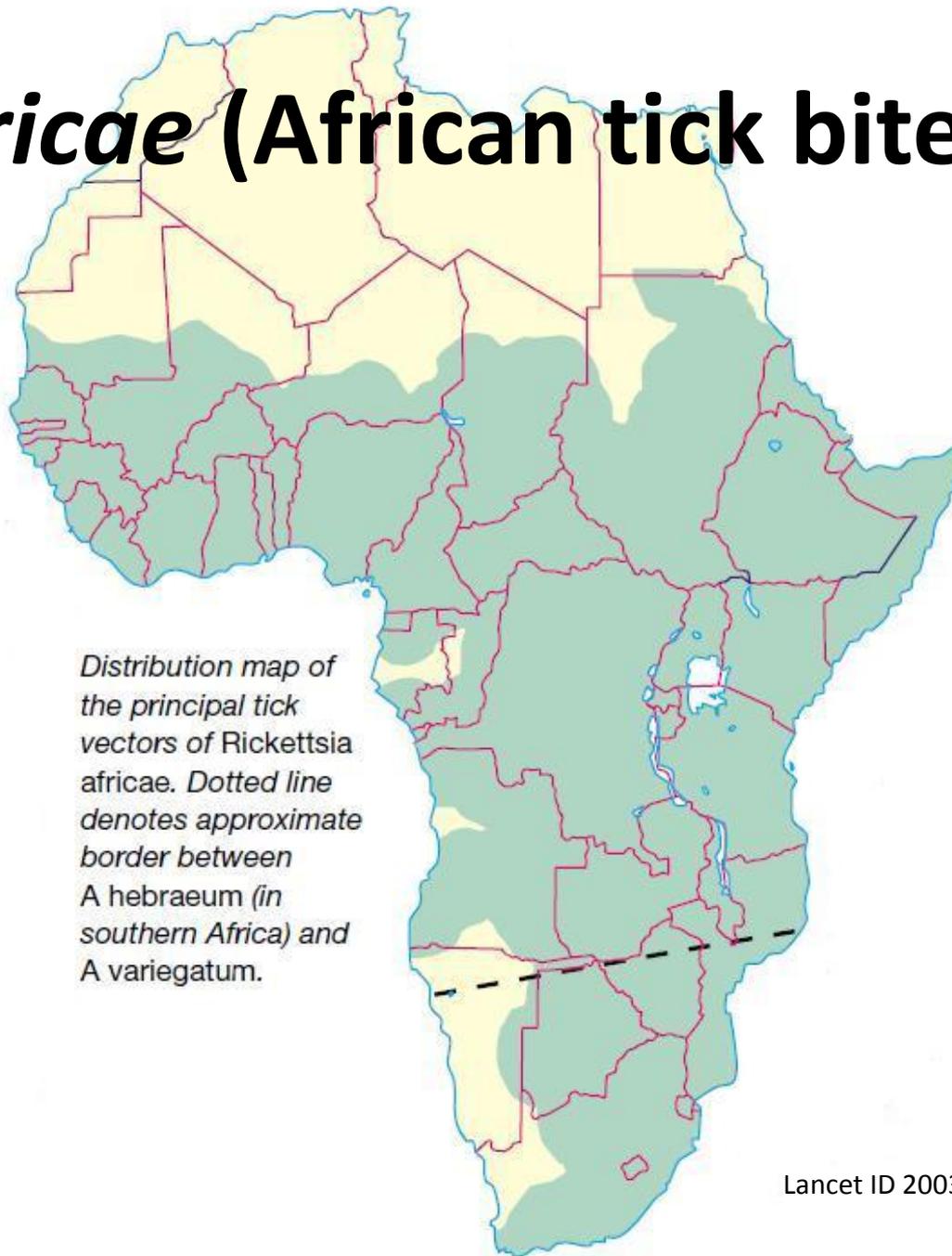
R. africae

R. parkeri

R. felis

R. akari

R. africae (African tick bite fever)



Distribution map of the principal tick vectors of Rickettsia africae. Dotted line denotes approximate border between A. hebraeum (in southern Africa) and A. variegatum.

R. africae (African tick bite fever)

- Incubation 5-7 days
- Acute, febrile, and influenza-like illness
 - severe headache, nausea, fatigue
 - Prominent myalgias (esp. neck)
- Inoculation eschar(s)
 - black crusts surrounded by a red halo
- +/- vesicular rash/apthous ulcers
- Regional lymphadenitis
- ~50% of patients have multiple eschars
- Rare complications; recovery is the rule



R. afr

(ever)



***R. africae* (African tick bite fever)**

- Habitat: tall grasses/bush; shade; rainy season
- Typical victims: soldiers, safaris, campers, cattle farmers
 - Aggressive: single host attacked by several ticks, multiple times
- Diagnosis: difficult (clinical)
- Treatment: Doxycycline 100mg BID 7d
 - or until 48hrs post defervescence
- Prevention: PPE; skin exam, careful tick removal

R. conorii (Mediterranean spotted fever AKA Boutonneuse fever)

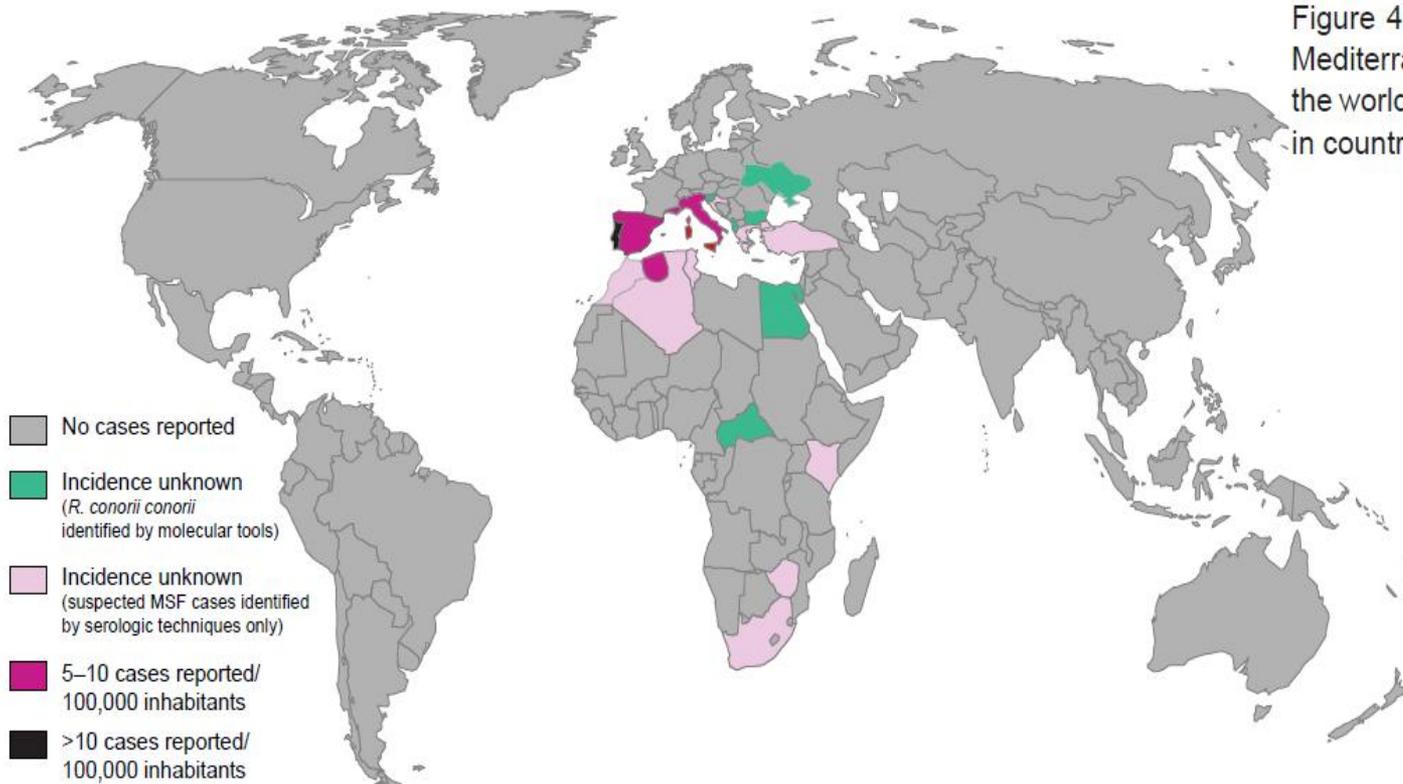


Figure 4. Distribution of the cases of Mediterranean spotted fever (MSF) in the world and incidence of the disease in countries where MSF is endemic.

R. conorii (Mediterranean spotted fever AKA Boutonneuse fever)

Rickettsia	Vector	Symptoms present, % patients			Fatal forms? (% patients)	Symptoms present, % patients		Fatal forms? (% patients)
		Fever	Inoculation eschar	Rash		Fever	Rash	
<i>R. conorii conorii</i> , isolates Malish, Moroccan Kenyan	<i>Rhipicephalus</i> sp <i>Haemaphysalis</i> leachi	91–100	20–87	93–100	Yes (0–18.1)	77	93–100	Yes (0–18.1)
<i>R. conorii israelensis</i>	<i>Rh. sanguineus</i>	100	0–46	98–100	Yes (0–3.5)	98–100	94	Yes (0–3.5)
<i>R. conorii caspia</i>	<i>Rh. sanguineus</i>	100	23	94	No	100 (frequently purpuric)		No
<i>R. conorii indica</i>	<i>Rh. sanguineus</i> <i>Boophilus microplus</i> <i>leachi</i>	100	Rare	100 (frequently purpuric)	No			

Unlike African tick bite fever, eschars RARELY multiple in MSF

***R. conorii* (Mediterranean spotted fever AKA Boutonneuse fever)**

- Incubation 5-7 days
- Fever, HA, maculopapular rash; tache noire
- Ecology of exposure: peridomestic; buildings where dogs kept
- Diagnosis tough (clinical) +/- biopsy (eschar); serology (IFA), PCR, culture
- Treatment: Doxy 100mg BID 5-10 days
- Prevention: PPE



Rocky Mountain Spotted Fever

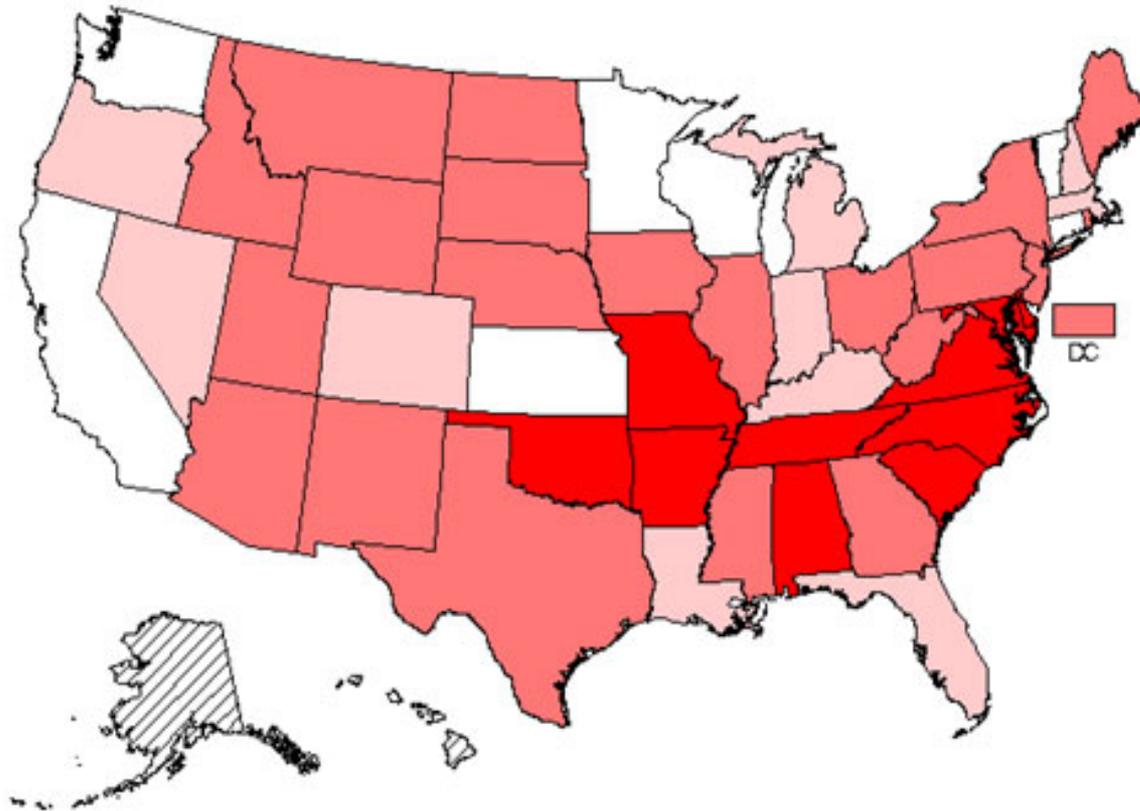
- RMSF, *R. rickettsii*
- USA, southern Canada, C/S Americas
- Vector: *Dermacentor variabilis* (American dog tick), *D. andersoni* (Rocky Mountain wood tick)
- Minimum attachment: 4-6hrs; Incubation: 2-14 days
- Fever, HA, nausea/vomiting
- abdominal pain, conjunctival injection
- Rash:
 - Occurs in 90%
 - Red to purple, spotted (petechial) rash in 35-60%
 - Usually not seen until after 6th day
- Can be fatal early if untreated (doxycycline)

RMSF Rash



RMSF

RMSF Incidence, 2008



Cases per million



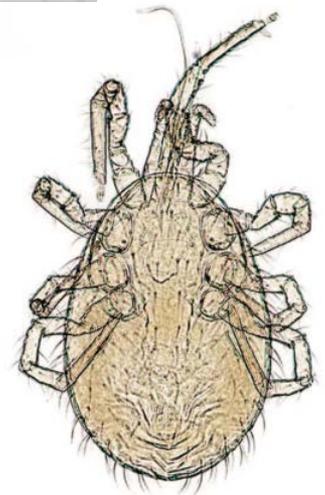
American dog tick



Rocky Mountain Wood tick

R. akari (Rickettsialpox)

- Morphologically identical to *R. rickettsii*
- Vector: house mouse mite
- Reservoir: common house mouse
- “urban zoonosis” since 1950s
 - NYC, Boston, West Hartford, Philadelphia, Pittsburgh, Cleveland
- Worldwide: Russia, Korea, South Africa



***R. akari* (Rickettsialpox)**

- Incubation 7-10 days
- Painless bite
- Papulovesicle -> eschar within 1-2 days
- Fever, malaise 1 week later
- Diffuse papulovesicular rash 2-3 days after fevers
 - Trunk, extremities, oral mucosa
- Generalized lymphadenopathy
- Self-limited (7-10 days after symptom onset)

Rickettsialpox



***R. akari* (Rickettsialpox)**

- Labs: mild leukopenia; thrombocytopenia, mild proteinuria
- Definitive Dx: rise in serum *R. akari* Ab during convalescence (CF, IFA)
 - Cross-reactive with RMSF Ab
- Treatment: Doxycycline 100mg BID until clinically improved for 48hrs (~ 5-7 days)
- Prevention: PPE

“Pox” DDX

Feature	Rickettsialpox	Chickenpox ²⁴	Smallpox (variola major) ²⁵
Eschar	Yes	No	No
Incubation period	9-14 days	14 days (range 10-23)	12 days (range 10-14)
Prodrome	Usually mild, may be severe. Fever, malaise, and headache.	Absent or mild and brief (less than one day)	Usually severe with high fever, headache, backache. Vomiting and severe abdominal pain may be present. Lasts 2 to 4 days.
Timing and evolution of lesions	Lesion develops at the site of the bite within 24 to 48 hrs and evolves into eschar. Rash begins 2 to 3 days after prodrome. Papules may eventuate in papulovesicles.	Lesions occur in “crops” over 2 to 4 days. Different stages characteristic: macules, papules, vesicles, pustules, crusts	Emerge over 1-2 days and then progress at same rate. The lesions progress over several days from macules (day 1), to papules (day 2), to vesicles (days 3-5), to pustules (days 7-14), to scabs (day 14-20).
Pruritus/pain	Exanthem usually asymptomatic: occasional pruritus.	Commonly pruritic	Pruritic during healing, otherwise may be painful.
Distribution	Anywhere. Palms, soles not usually involved.	Starts on trunk and face and spreads centrifugally. Palms, soles may be involved	Begins on the oral mucosa, face, and extremities and spreads centripetally. Palms, soles commonly involved.
Enanthem	Minority of cases.	Common, especially palate.	Starts in mouth
Scarring	Eschar leaves depressed scar, papulovesicles do not.	If bacterial superinfection occurs	Yes

Typhus group

Flea

Louse

Chigger mite

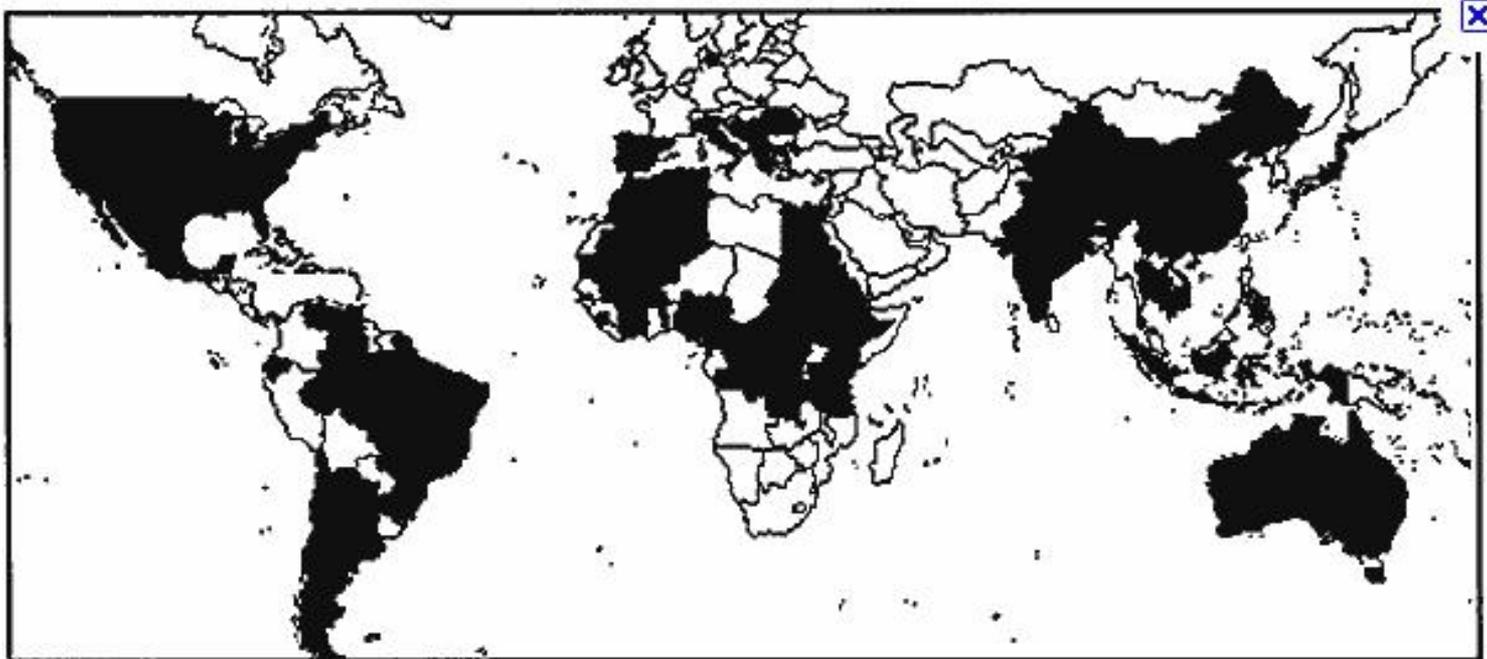
R. typhi

R. prowazekii

O. tsutsugamushi

R. typhi (murine/endemic typhus)

- Found sporadically worldwide
 - In US: Hawaii, California, Texas
- Hosts: Rats, cats, mice Vector: fleas



***R. typhi* (murine/endemic typhus)**

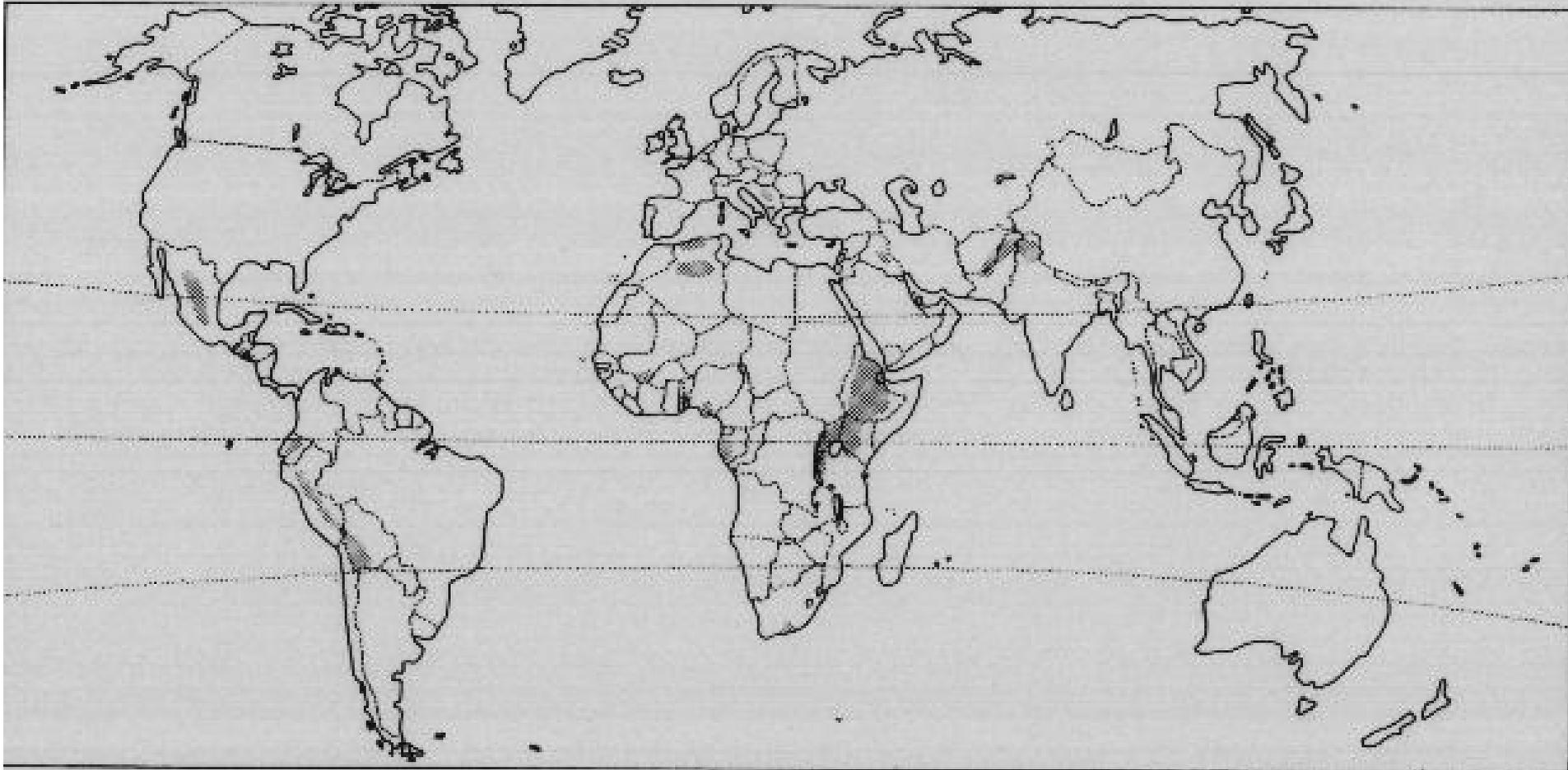
- Flea bites (infected feces contaminate skin) or aerosolization
- Incubation 6-14 days
- Fever, headache, rash (triad in 50%)
- Leukocytosis or mild leukopenia
- Anemia (severe with G6PD def)
- +/- ↓Na, hepatic/renal abnormalities

R. typhi (murine/endemic typhus)

- Ecology: Rat fleas; coastal areas
- Diagnosis (clinical): serology (IFA)
 - cross-reactive with *R. prowazekii* and RMSF Ab
- Spontaneous recovery in 2 weeks
- Treatment: Doxycycline 100mg BID for 48-72hrs after fever resolved
- Prevention: PPE



R. prowazekii (louse-borne/epidemic)



***R. prowazekii* (louse-borne/epidemic)**

- Incubation 6-14 days
- Fever, headache (abrupt), tachypnea, myalgias
- Rash (mac-pap/petechial) on days 4-7
 - spreads peripherally (unlike RMSF)
- CNS disease: confusion, drowsiness, coma
- Shock: multifocal/multi-organ vasculitis
 - Mortality 60% w/o abx; 4% w/ abx
- Recrudescence (Brill-Zinsser disease)
 - Mild illness, elderly, years after initial episode



Figure 4: (A) Skin rash and (B) toe gangrene in a patient outbreak, 1997



Figure 1: Scratching lesion on the upper arm of a homeless man



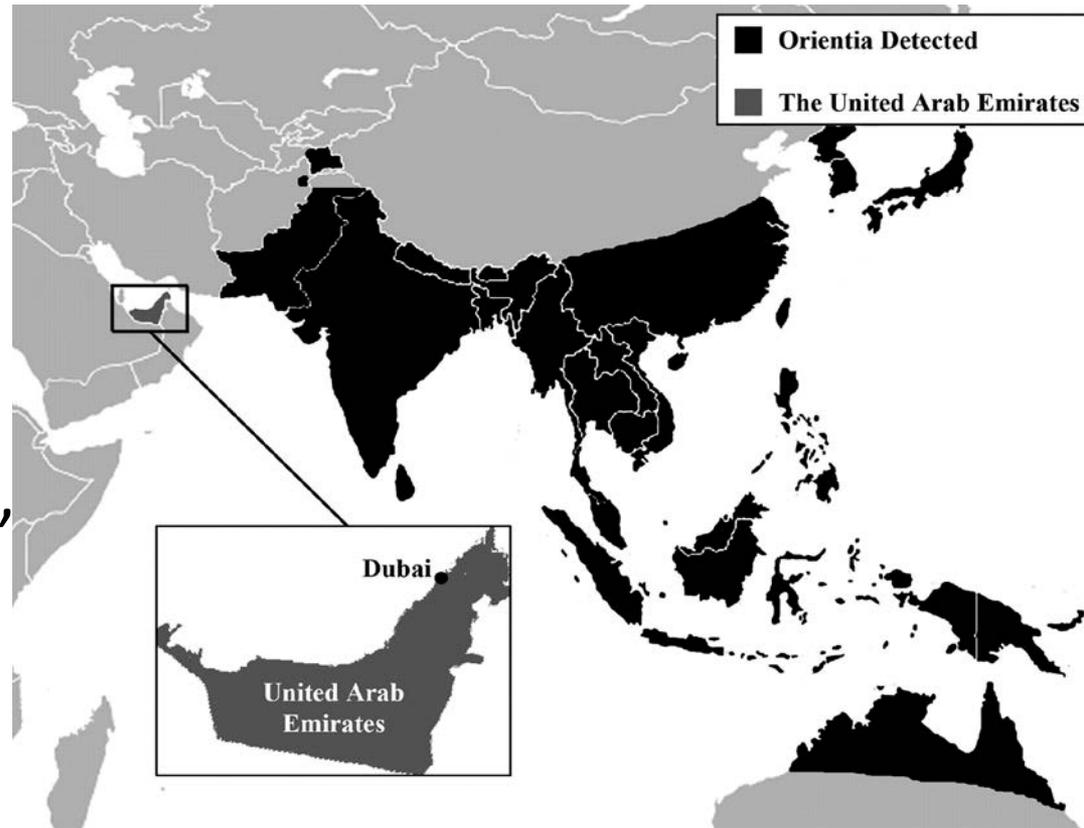
0-6 mm

***R. prowazekii* (louse-borne/epidemic)**

- Vector: body louse (*Pediculus humanus*)
- Reservoir: humans
 - flying squirrels
- Ecology: crowded, war/disasters, famine, poverty
- Diagnosis: serology (IFA), biopsy, PCR
- Treatment: Doxycycline (as endemic)
- Prevention: delousing (permethrin>lindane, malathion)
 - Boiling clothes, bedding
 - long-acting insecticides
 - prophylaxis (doxycycline)

O. tsutsugamushi (Scrub typhus)

- Chigger-borne zoonosis
- Vector: larval mites
 - “mite islands”
- “Tsutsugamushi Triangle”
 - Tropical Asia
 - west Pacific islands
 - UAE



O. tsutsugamushi (Scrub typhus)

- Painless bite
- Eschar - painless papule; central necrosis
- Fever, chills, HA, conjunctival suffusion
 - All prior to centrifugal rash
- Cough, tachypnea, pulmonary infiltrates
 - Most common
- Gastrointestinal symptoms
- Regional lymphadenopathy
- Acute hearing loss in 1/3 cases
- CFR 10% if untreated

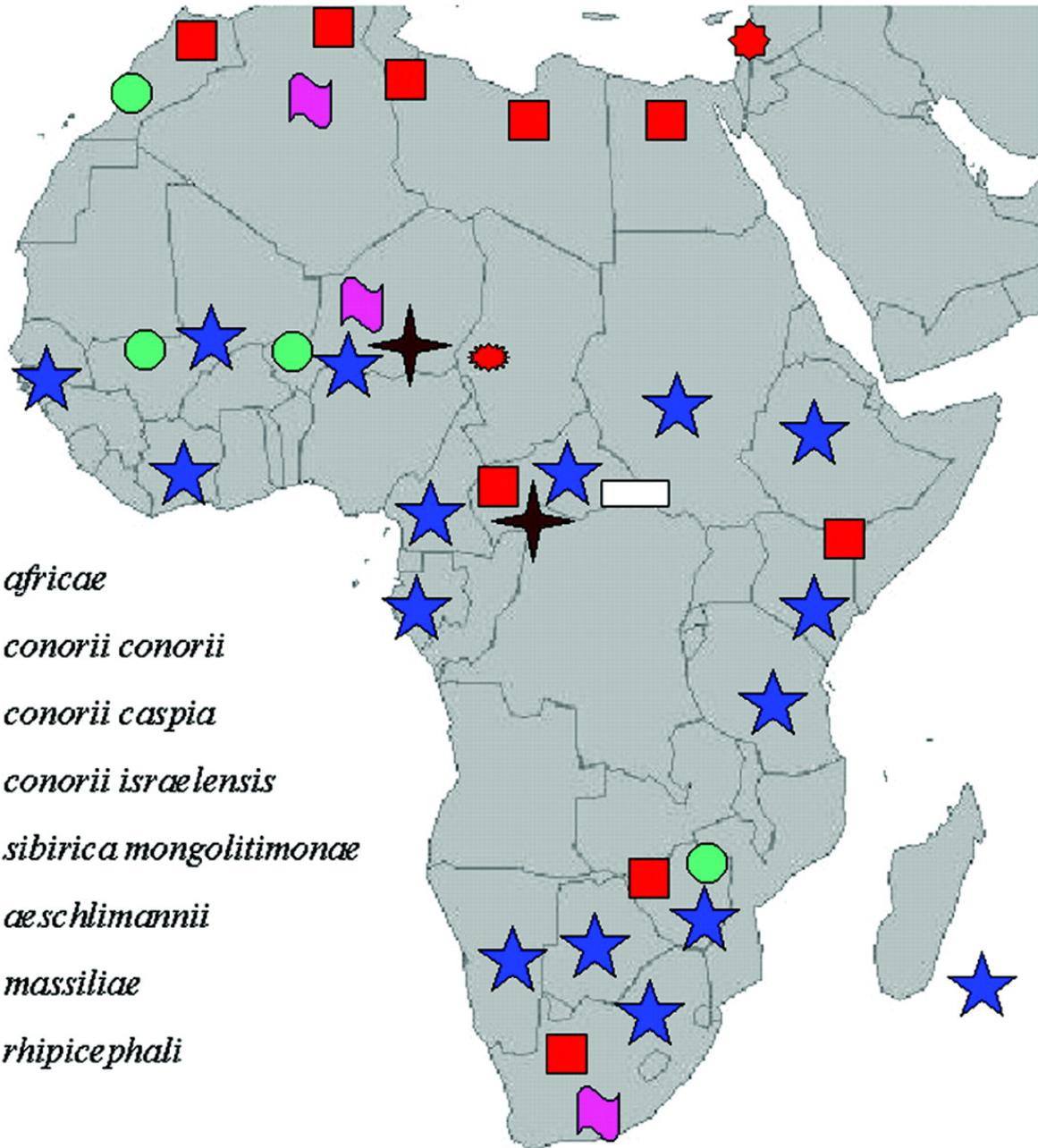


O. tsutsugamushi (Scrub typhus)

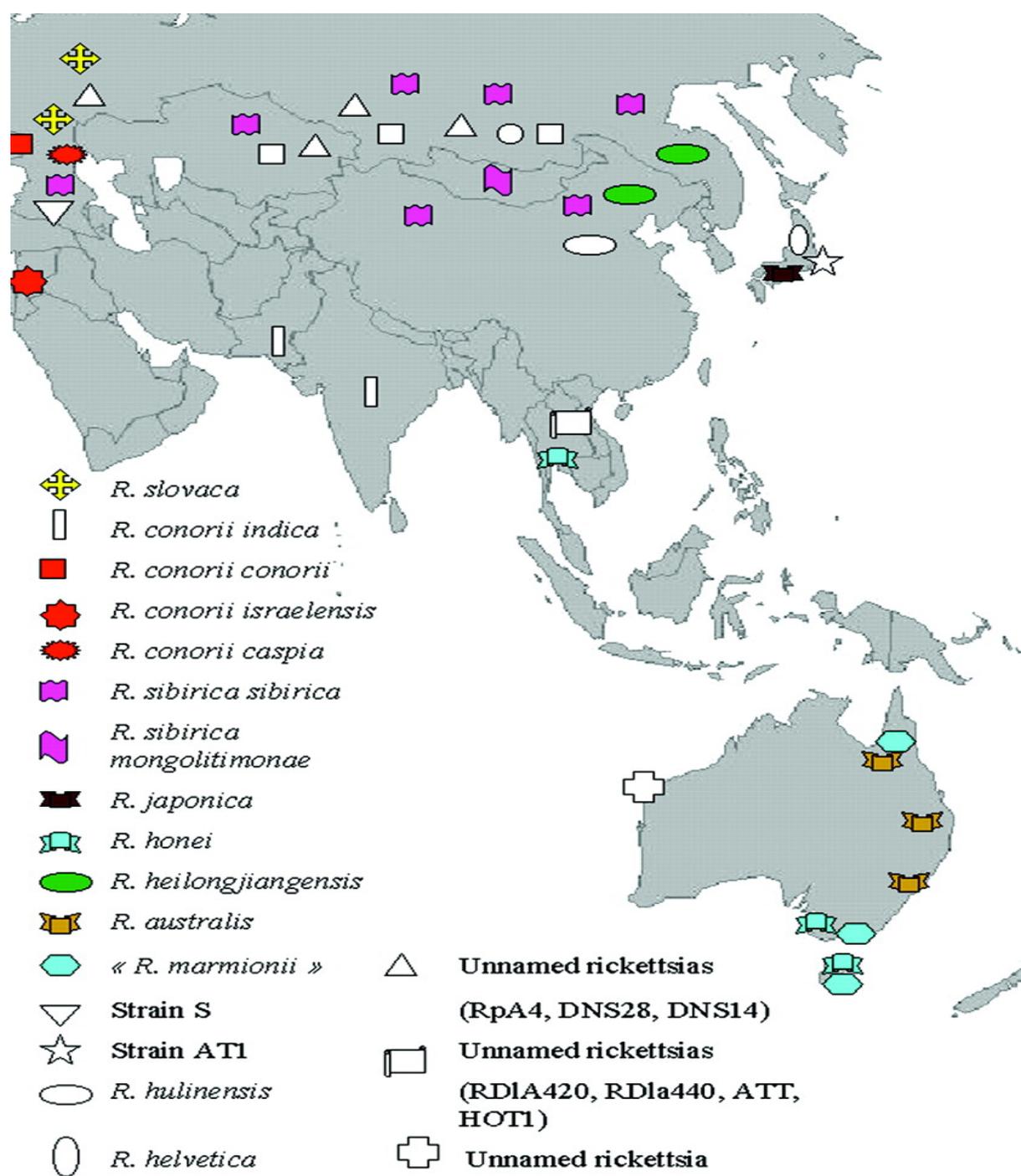
- Ecology: active rice fields, agricultural areas, warm humid tropics
- Rats key to population densities
- Diagnosis: clinical; IFA gold standard; PCR, isolation in blood
- Eschar in SE Asia pathognomonic
- Treatment: Doxycycline (resistance possible)
 - Azithromycin, rifampin
- Prevention: topical repellents to clothing, weekly doxycycline

Tick-Borne Rickettsiae in Africa

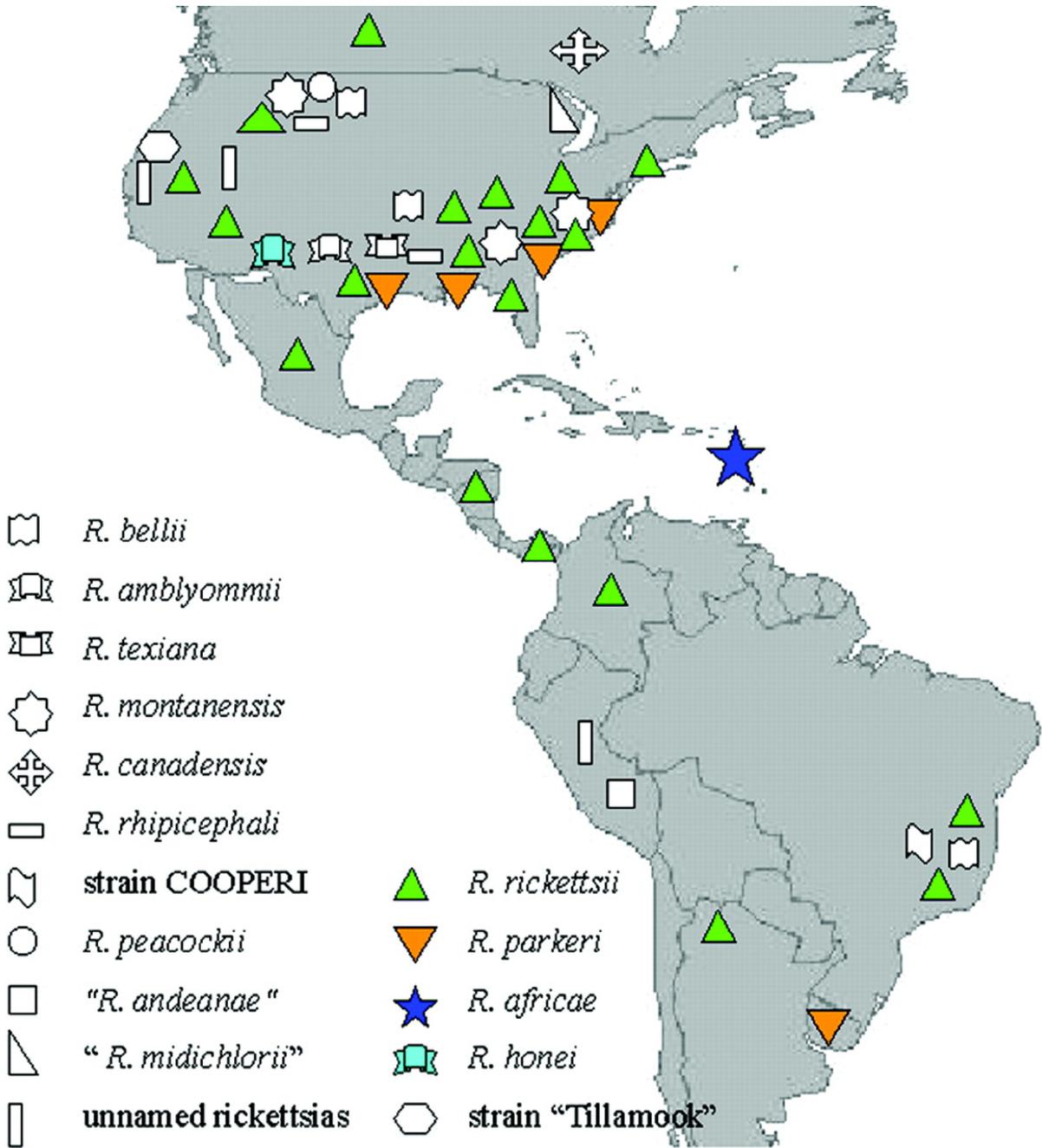
- ★ *R. africae*
- *R. conorii conorii*
- ⊛ *R. conorii caspia*
- ⊠ *R. conorii israelensis*
- ⊡ *R. sibirica mongolitimonae*
- *R. aeschlimannii*
- ✦ *R. massiliae*
- *R. rhipicephali*



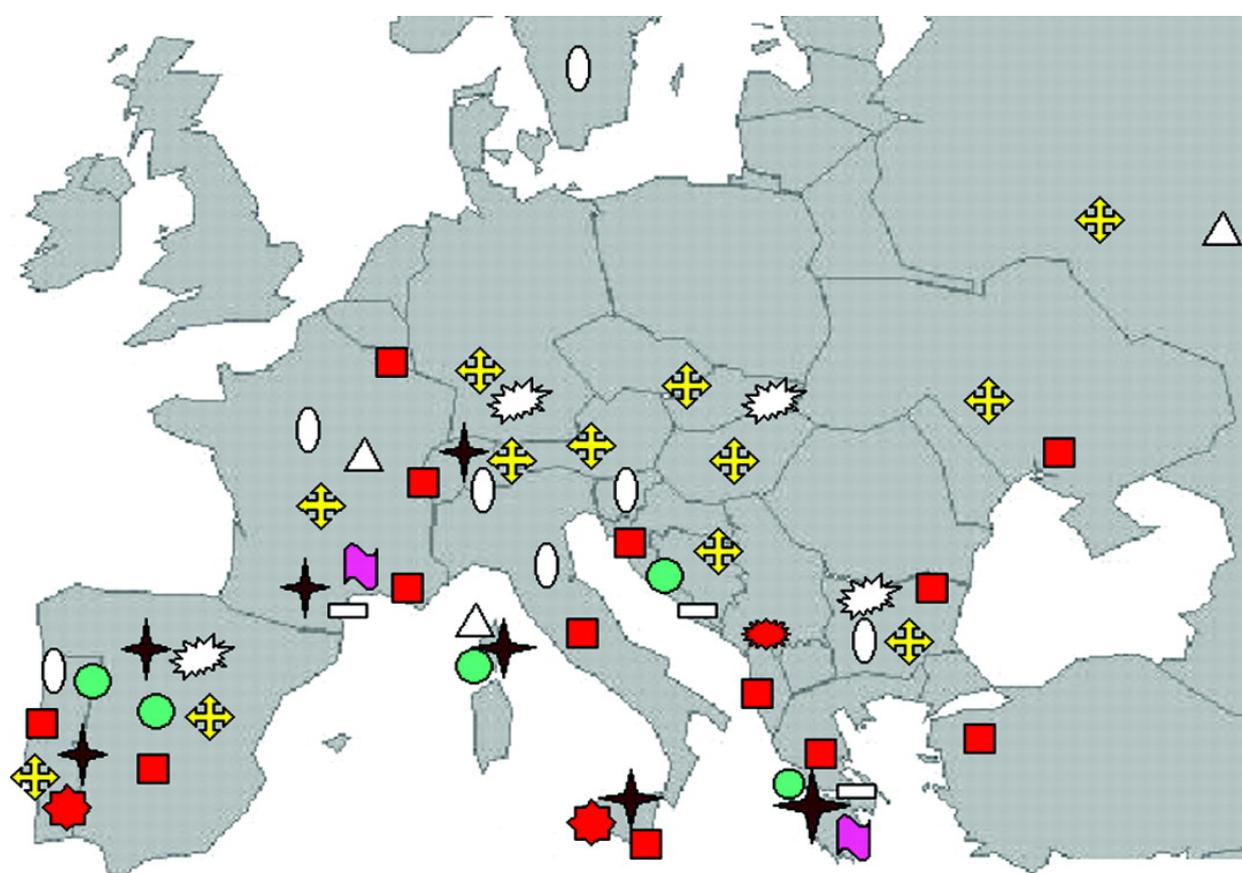
Tick-Borne Rickettsiae in Asia/Australia



Tick-Borne Rickettsiae in the Americas



Tick-Borne Rickettsiae in Europe



R. conorii conorii



R. conorii israelensis



R. conorii caspia



*R. sibirica
mongolitimonae*



R. aeschlimannii



R. slovaca



R. helvetica



R. massiliae



« *R. monacensis* »
and related rickettsias



R. rhipicephali



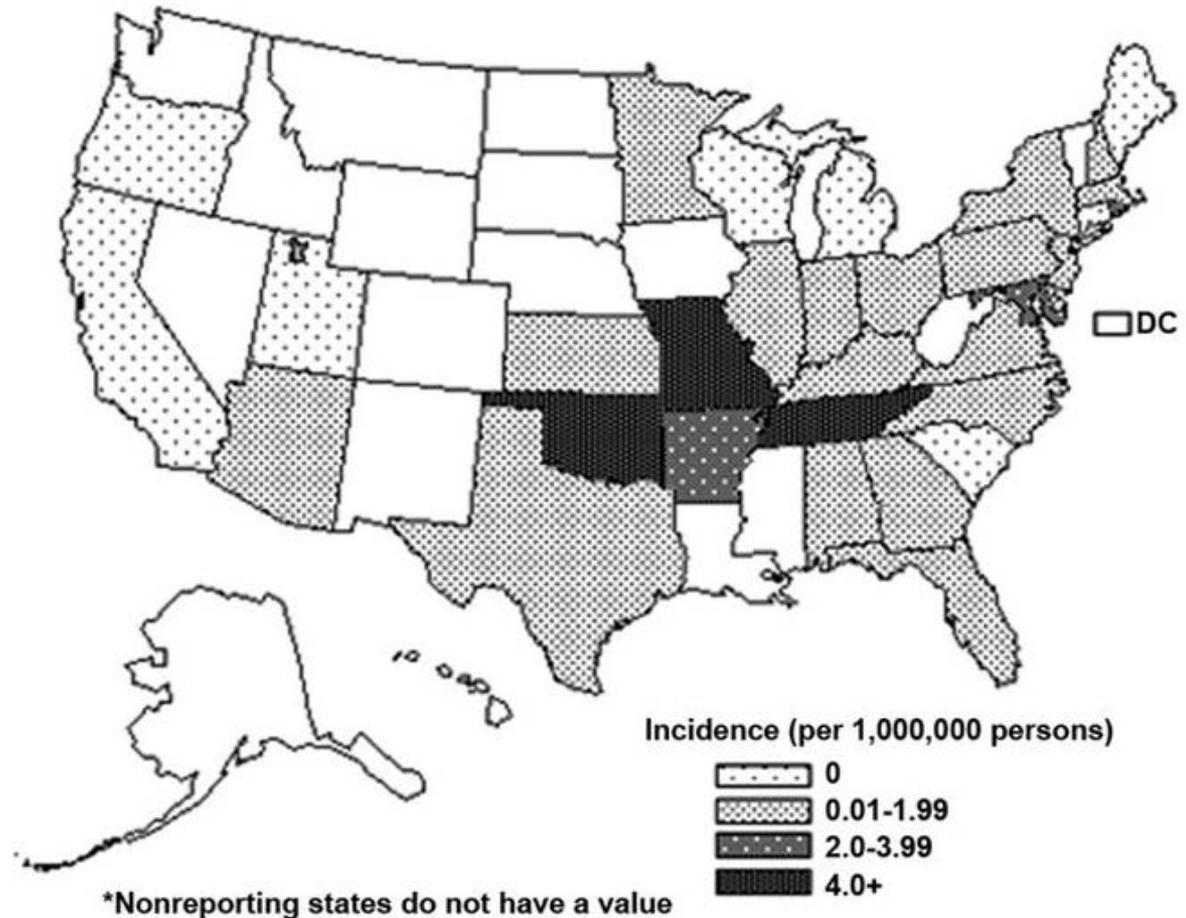
Rickettsia sp. RpA4

“Ehrlichiosis”

HME	HGA	<i>E. ewingii</i>
1987	1994	1999
<i>E. chaffeensis</i>	<i>A. phagocytophilum</i>	<i>E. ewingii</i>
Monocyte macrophage	Granulocyte	Granulocyte
>1600 cases/yr	>2100 cases/yr	~20 (immunocompromised)
SC, SE, mid-Atl	NE, MW, Pac coast	SC

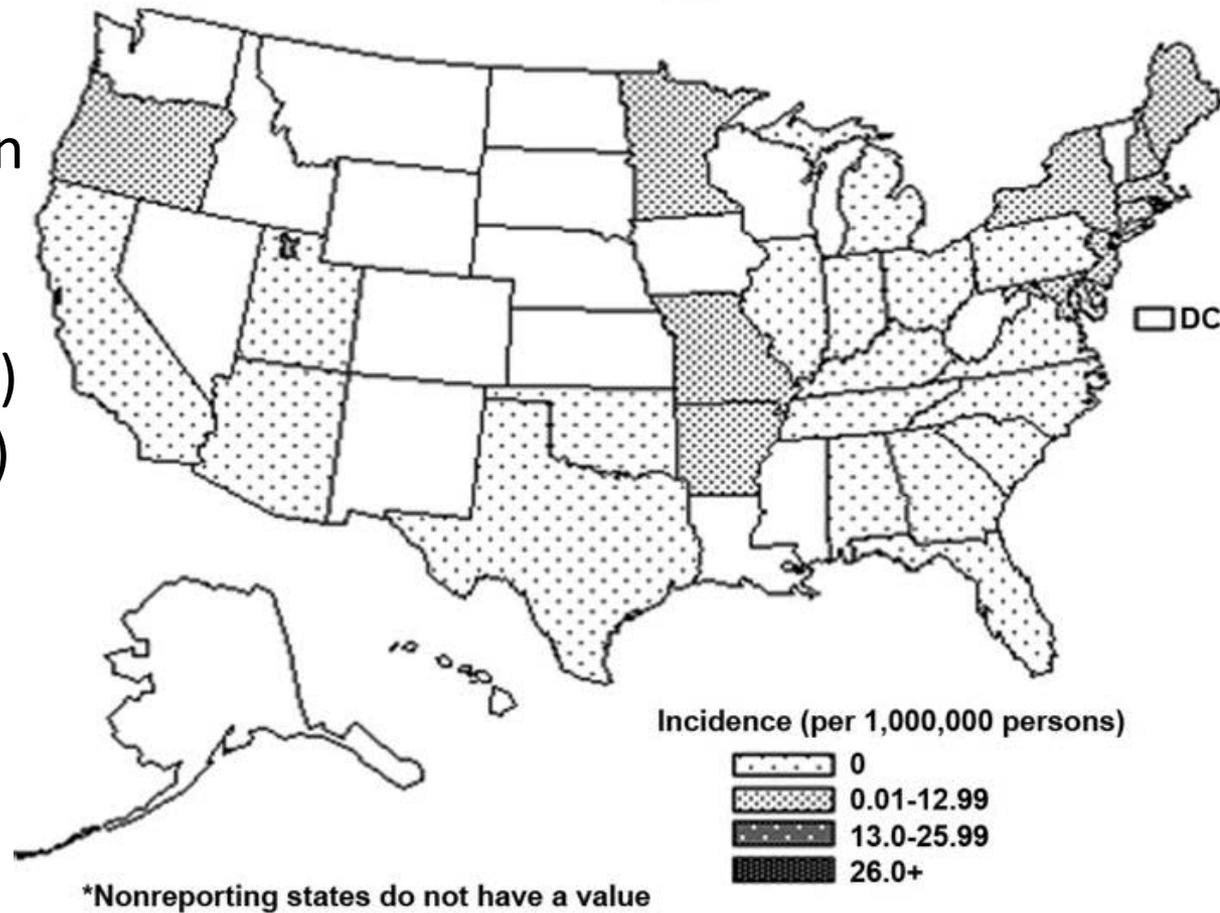
HME Distribution

- Vector: lone star tick
 - *Amblyomma americanum*
- Reservoir: White-tailed deer
- Only occurs in USA

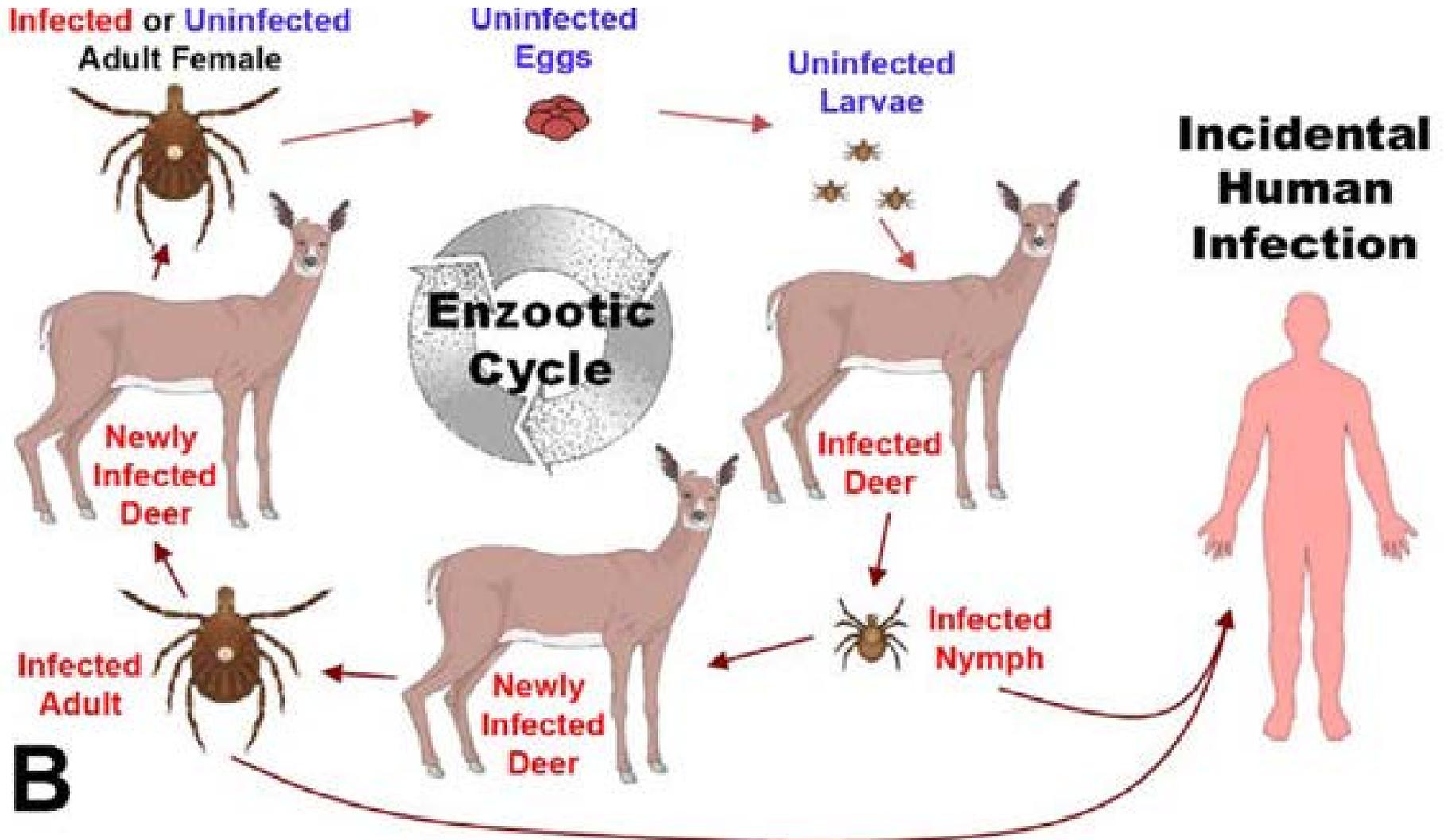


HGA Distribution

- International distribution
- Vector: *Ixodes* ticks
 - *I. scapularis* (East US)
 - *I. pacificus* (West US)
 - *I. ricinus* (Europe)
 - *I. persulcatus* (Asia)
- Reservoir: white-footed mouse



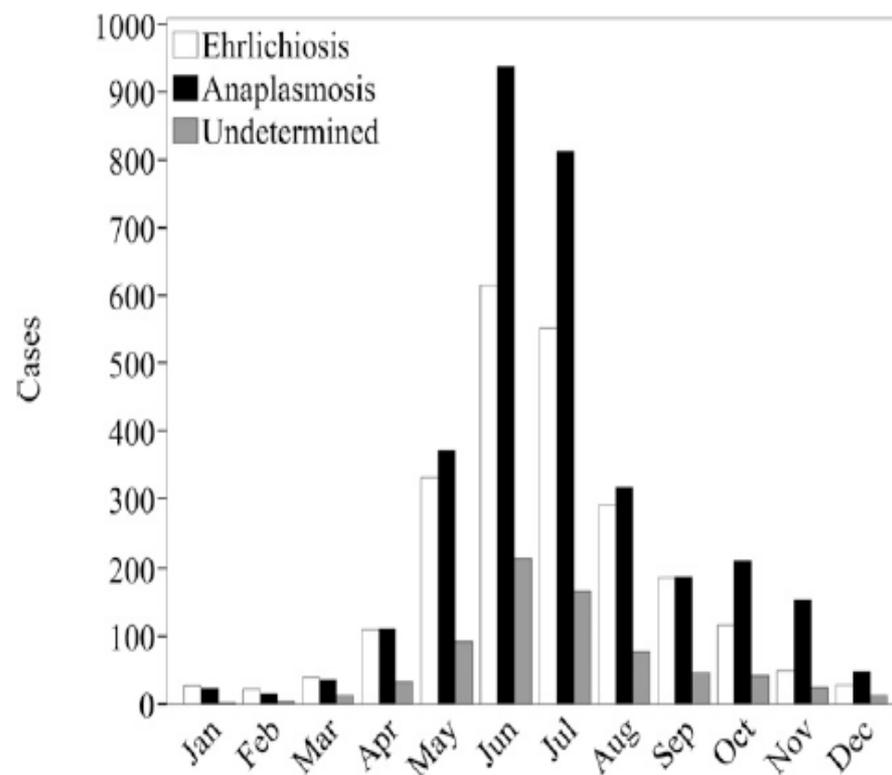
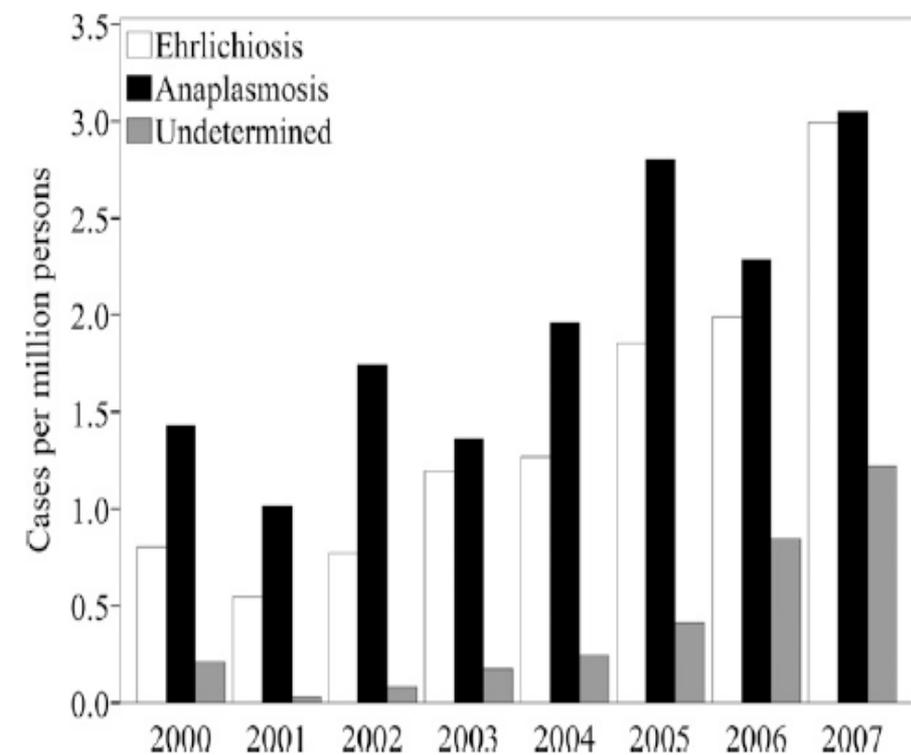
Anaplasma Life Cycle



Increasing Incidence of *Ehrlichia chaffeensis* and *Anaplasma phagocytophilum* in the United States, 2000–2007

F. Scott Dahlgren, Eric J. Mandel, John W. Krebs, Robert F. Massung, and Jennifer H. McQuiston*

Division of Vectorborne Infectious Diseases, National Center for Enteric, Zoonotic, and Infectious Disease, Centers for Disease Control and Prevention, Atlanta, Georgia



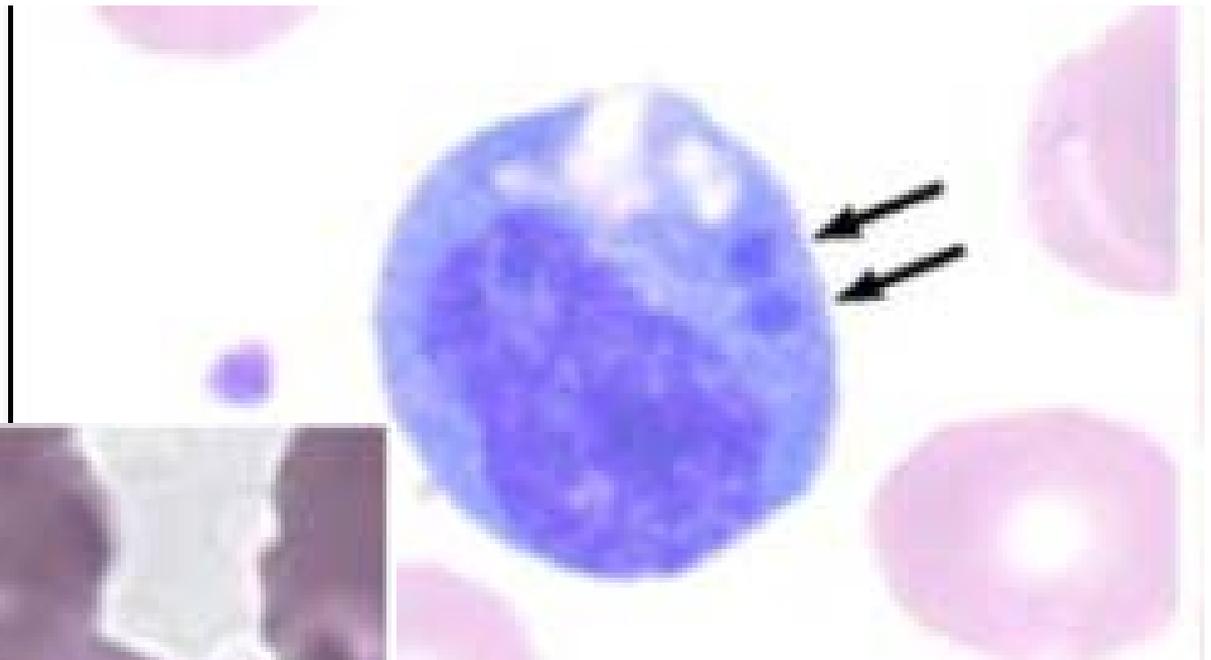
Ehrlichiosis

- Incubation 5-14 days
- Rash rare; NO vasculitis
- Ecology:
 - grassy areas, forest edge, un-mowed areas
 - May-Sept in USA
- Diagnosis: paired serology; peripheral blood smears (morulae=cytoplasmic inclusions); PCR
- Treatment: Doxycycline 100mg BID ~ 3d after afebrile (~5-7 days)
- Prevention: PPE

Ehrlichiosis and Anaplasmosis

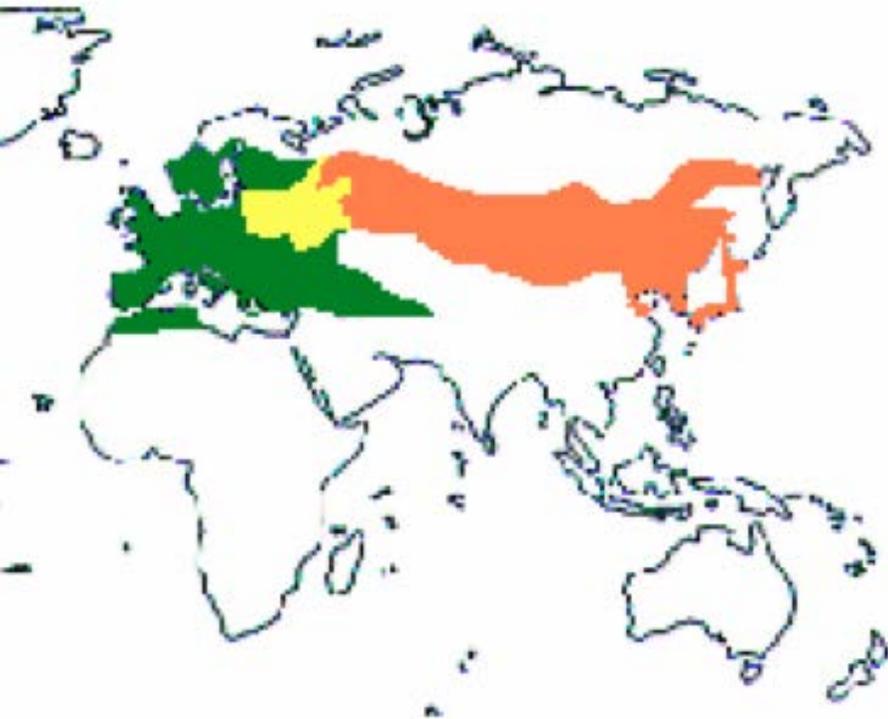
Symptom, sign, or finding	Patients, % (no. evaluated)	
	HME	HGA
Symptom or sign		
Fever	97 (633)	93 (521)
Myalgia	57 (250)	77 (516)
Headache	80 (240)	76 (385)
Malaise	82 (234)	94 (288)
Nausea	64 (143)	38 (258)
Vomiting	33 (192)	26 (90)
Diarrhea	23 (197)	16 (95)
Cough	26 (155)	19 (260)
Arthralgias	41 (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)

HME



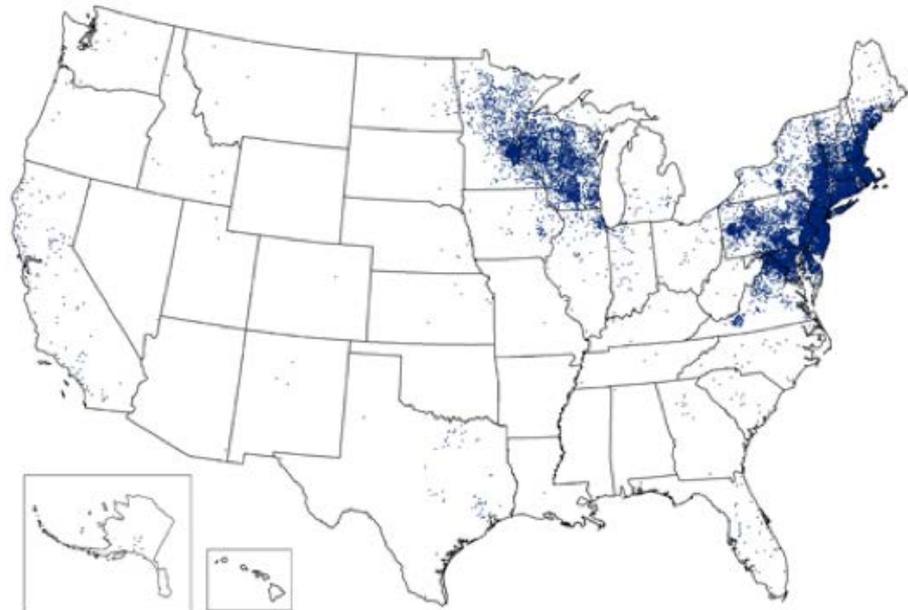
HGA

Lyme disease (*Borrelia* sp.)



Agent: *B. afzelii*, *B. garinii*
Vectors: *I. ricinus* – Europe
I. persulcatus – E. Europe, Russia

Reported Cases of Lyme Disease -- United States, 2010



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

Agent: *B. burgdorferi*
Vectors: *I. scapularis* – East
I. pacificus - West
Lancet 2003; CDC.gov

Common presenting symptoms

Early Infection

- Rash (erythema migrans) in ~ 70-80%
 - at site of tick bite after 3-30 days
 - Gradually expands over several days
 - Central clearing (Bull's-eye); warm but not painful
 - occasional additional EM lesions days later
- +/- fatigue, chills, fever, headache, swollen lymph nodes

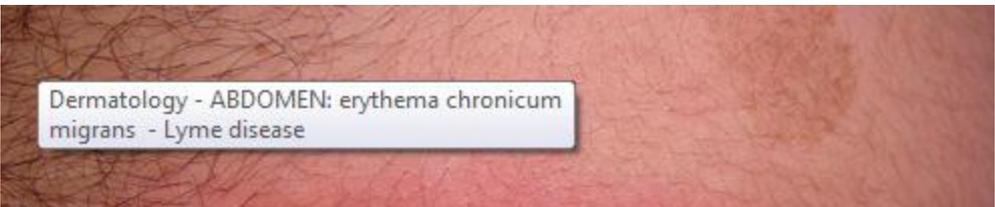
Late Infection

- Encephalomyelitis
- Carditis
- Arthritis in 60% untreated
 - Large and small joints, intermittent
 - Can develop chronic arthritis

Lyme disease (*B. burgdorferi*)



PHIL Image 9875



Dermatology - ABDOMEN: erythema chronicum migrans - Lyme disease



Table 3. Recommended therapy for patients with Lyme disease.

Indication	Treatment	Duration, days (range)
Tick bite in the United States	Doxycycline, 200 mg in a single dose ^{a,b} ; (4 mg/kg in children \geq 8 years of age) and/or observation	...
Erythema migrans	Oral regimen ^{c,d}	14 (14–21) ^e
Early neurologic disease		
Meningitis or radiculopathy	Parenteral regimen ^{c,f}	14 (10–28)
Cranial nerve palsy ^{a,g}	Oral regimen ^c	14 (14–21)
Cardiac disease	Oral regimen ^{a,c,h} or parenteral regimen ^{a,c,h}	14 (14–21)
Borrelial lymphocytoma	Oral regimen ^{c,d}	14 (14–21)
Late disease		
Arthritis without neurologic disease	Oral regimen ^c	28
Recurrent arthritis after oral regimen	Oral regimen ^{a,c} or parenteral regimen ^{a,c}	28 14 (14–28)
Antibiotic-refractory arthritis ⁱ	Symptomatic therapy ^j	...
Central or peripheral nervous system disease	Parenteral regimen ^c	14 (14–28)
Acrodermatitis chronica atrophicans	Oral regimen ^c	21 (14–28)
Post-Lyme disease syndrome	Consider and evaluate other potential causes of symptoms; if none is found, then administer symptomatic therapy ^a	...

Q fever (*Coxiella burnetii*)

- Worldwide distribution
 - ↓ USA, ↑ Netherlands, OIF
- Zoonosis: wildlife, ticks are main reservoir
- Transmitted from cattle, sheep, goats
 - Urine, feces, milk, birth products
 - Localizes to uterus/mammary glands
 - Via inhalation or ingestion
- Highly infectious
 - 1 organism can cause clinical infection



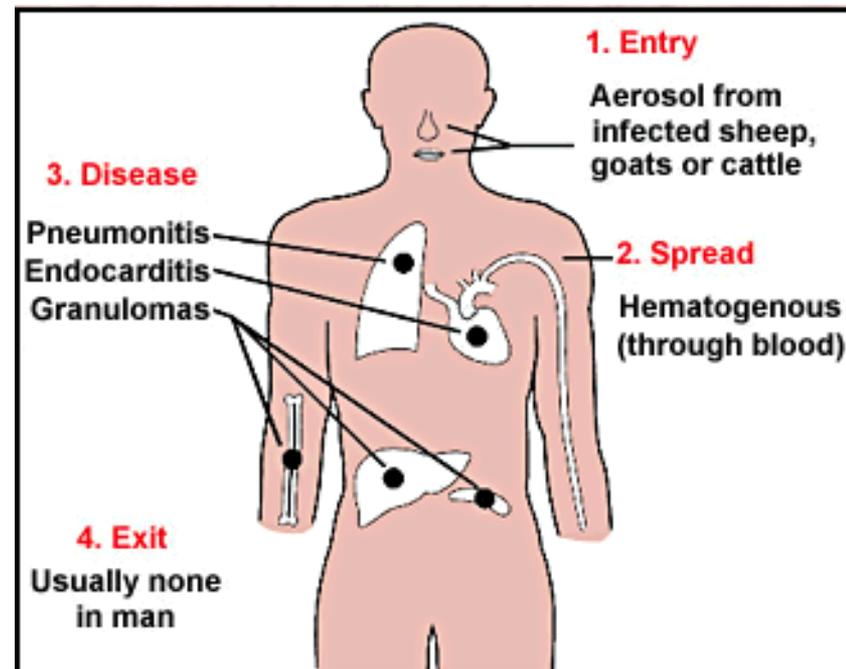
From Lancet 1984: 12 people were playing poker in the same room as a parturient cat. All 12 handled either the cat or litter and all 12 were diagnosed with acute Q fever (placentas carry 10^9 organisms).

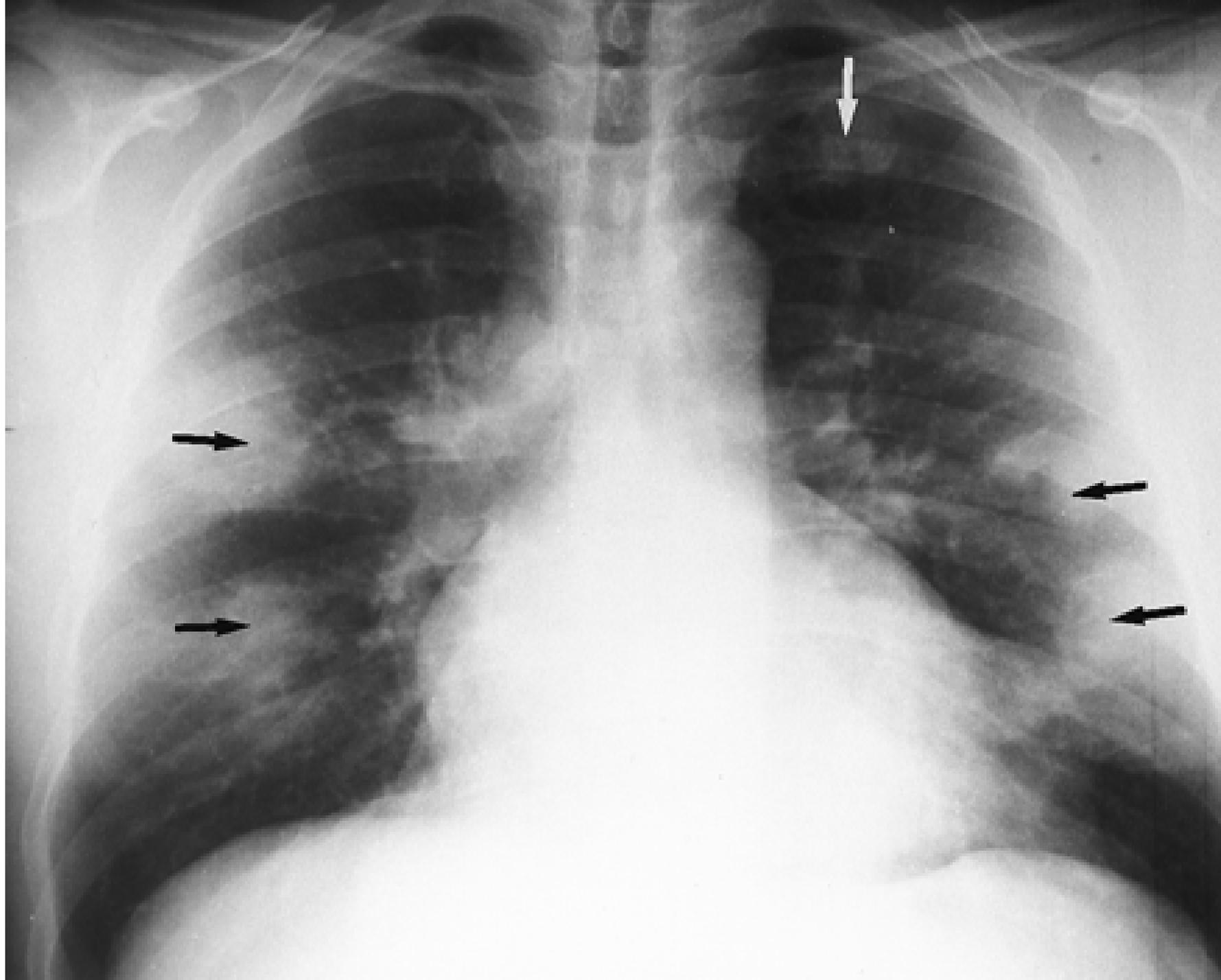
Q fever (*Coxiella burnetii*)

- 3 clinical presentations (major)
 - Febrile illness: self-limited; most common
 - Pneumonia (with fever): severe HA, retro-orbital pain
 - Hepatitis (with fever): “doughnut” granulomas”
 - * 60% asymptomatic

Complications:

- Endocarditis
 - culture negative; chronic
- Optic neuritis
- Encephalitis

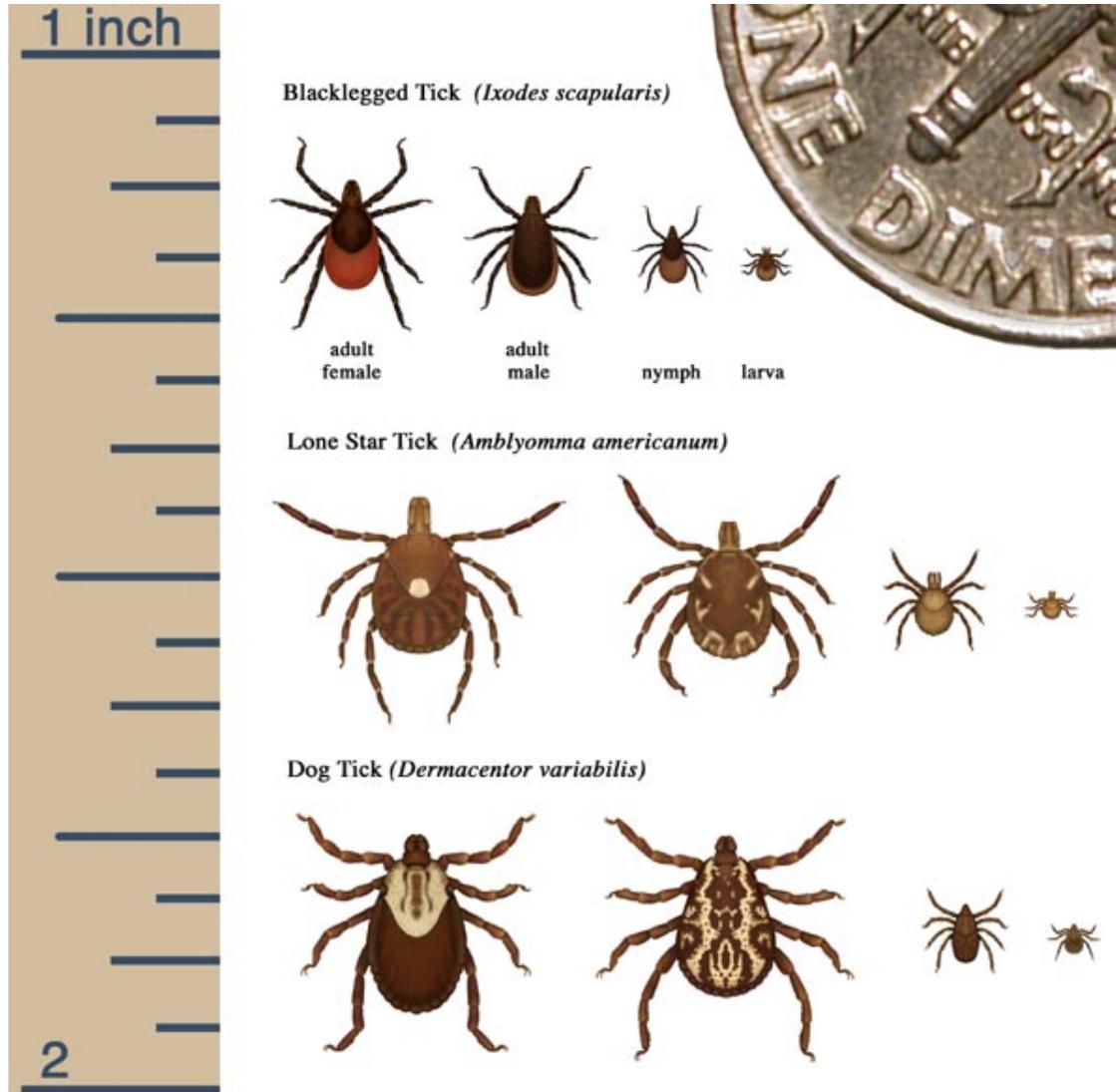




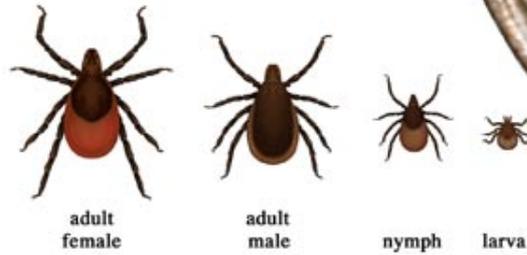
Q Fever (*Coxiella burnetii*)

- Ecology: farmers, vets, abattoir/lab workers
- Diagnosis: paired serology (Ph II, Ph I)
 - Culture (USAMRIID, CDC)
- Treatment:
 - Acute: fluoroquinolone or Doxy x 21 days
 - Chronic/endocarditis: FQ + rifampin or doxy + hydroxychloroquine x 18 mo.
- Prevention: educate (livestock, dairy)
 - disposal of birth products (animals)
 - quarantine/restriction of infected animals
 - caution high risk patients (valve disease)

Size comparison



Blacklegged Tick (*Ixodes scapularis*)



Lone Star Tick (*Amblyomma americanum*)



Dog Tick (*Dermacentor variabilis*)



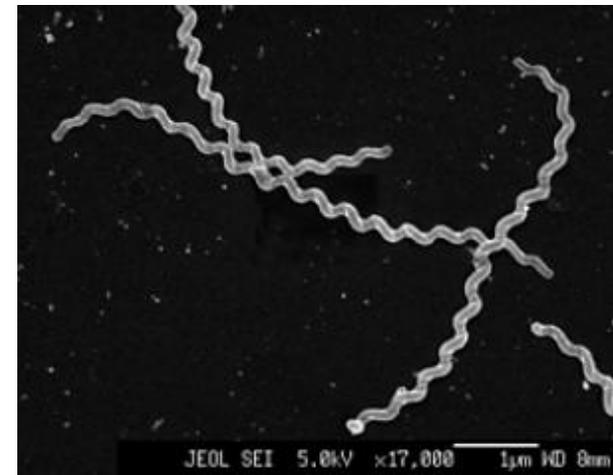
**Lyme
Anaplasma**

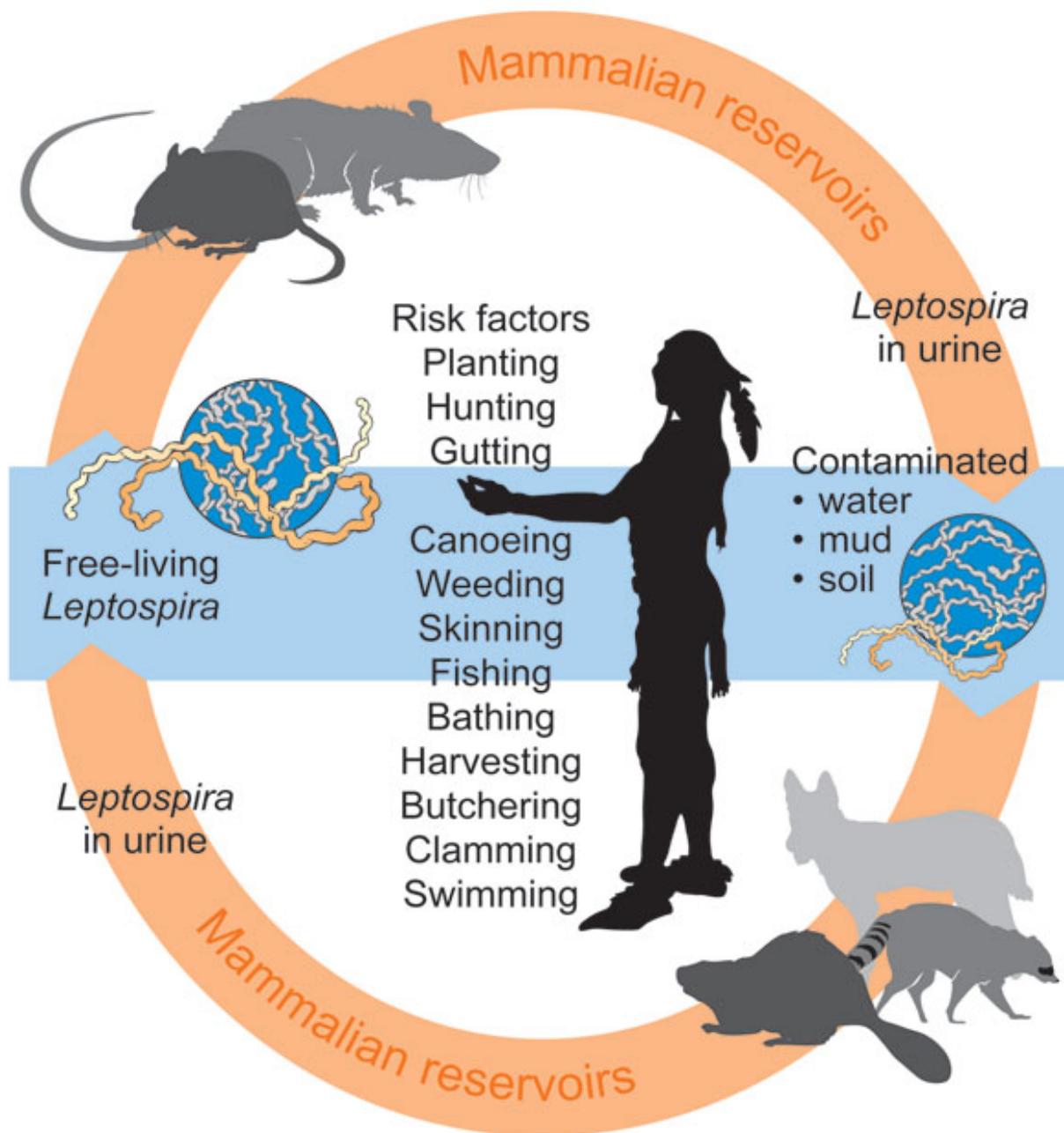
Ehrlichia

**Rocky
Mountain
Spotted
Fever**

Leptospirosis

- Obligate spirochete bacteria
- Wide array of animal reservoirs
 - Rodents, cattle, swine, dogs, sheep, goats, horses
- Infection via abrasions, conjunctiva, mucous membranes
- Exposure to: animal urine, contaminated water/soil, infected animal tissues (placenta, etc.)
 - Rarely ingestion, aerosolization
- US outbreaks: Hawaii, Puerto Rico
- Isolated cases worldwide

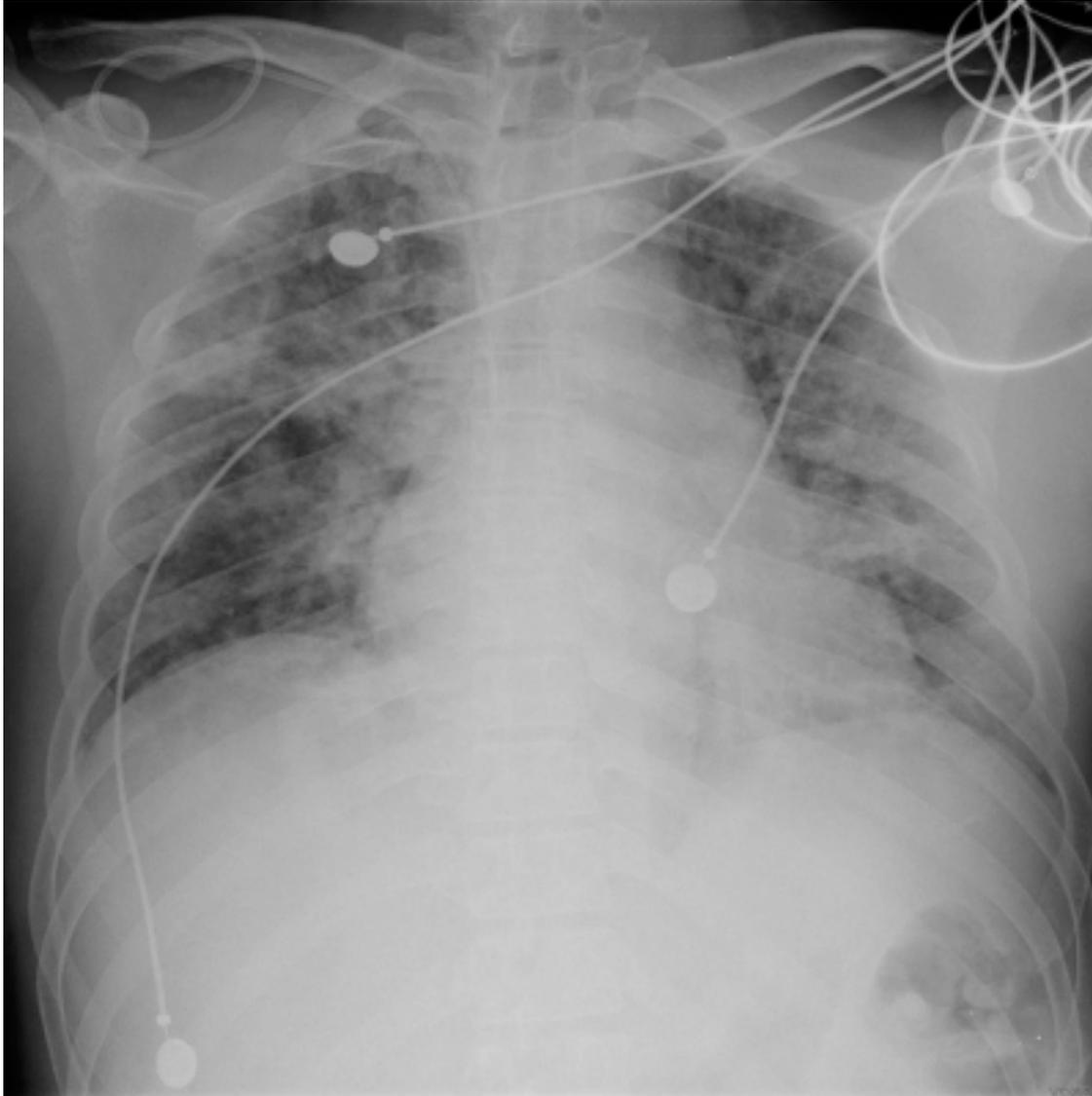




Leptospirosis: Clinical Presentation

- Incubation 2-26 days
- Broad spectrum of symptoms
 - Biphasic
 - Mild to life-threatening
 - Abrupt onset fever, rigors, myalgias, HA (75-100%)
- Weil's Disease (severe)
 - 5-10%
 - **Jaundice, renal failure**, hemorrhage, cardiac arrhythmias, pneumonitis, hemodynamic collapse.
 - 5-15% mortality

Leptospirosis



Diagnosis

- Clinical – always consider in the differential!
 - Fevers, myalgias, jaundice, HA
- Labs: ↓Plt, ↓Na, ↓K, sterile pyuria, AKI, mild ↑LFTs, ↑bilirubin, ↑CK
- Serology: microscopic agglutination test (MAT), ELISA
- Molecular tests: PCR
- Culture: blood, urine, CSF (takes weeks)

Treatment / Prophylaxis

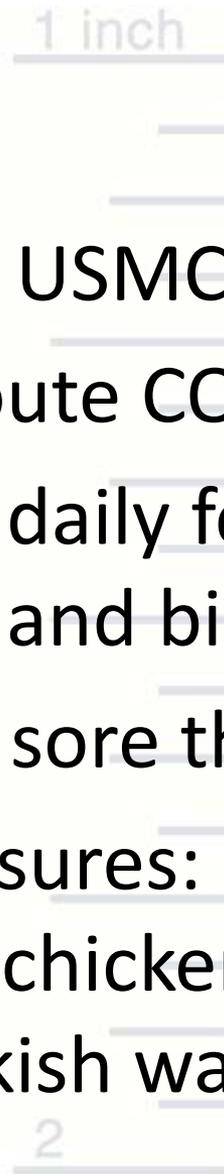
- Start early in severe disease
- IV Penicillin: DOC for severe disease
 - Jarish-Herxheimer reactions
 - Acute response to clearance of organism
 - fever, rigors, hypotension
- Doxycycline (oral) 100 mg twice daily x 7 days
 - Toxicity in children and pregnant women
- Alt: ceftriaxone, azithromycin
- Antibiotic prophylaxis
 - At risk individuals: 200 mg PO WEEKLY, start 2 days before entry

Matching

-
1. Rat-infested grain stores
2. Close living quarters, poverty
3. Sheep or cattle exposure
4. Transitional vegetation
5. Land navigation exercises
- A. Spotted fever (*R. rickettsii*)
- B. Q fever (*C. burnetii*)
- C. Scrub typhus (*O. tsutsugamushi*)
- D. Murine typhus (*R. typhi*)
- E. Louse-borne Typhus (*R. prowazekii*)

Case #1

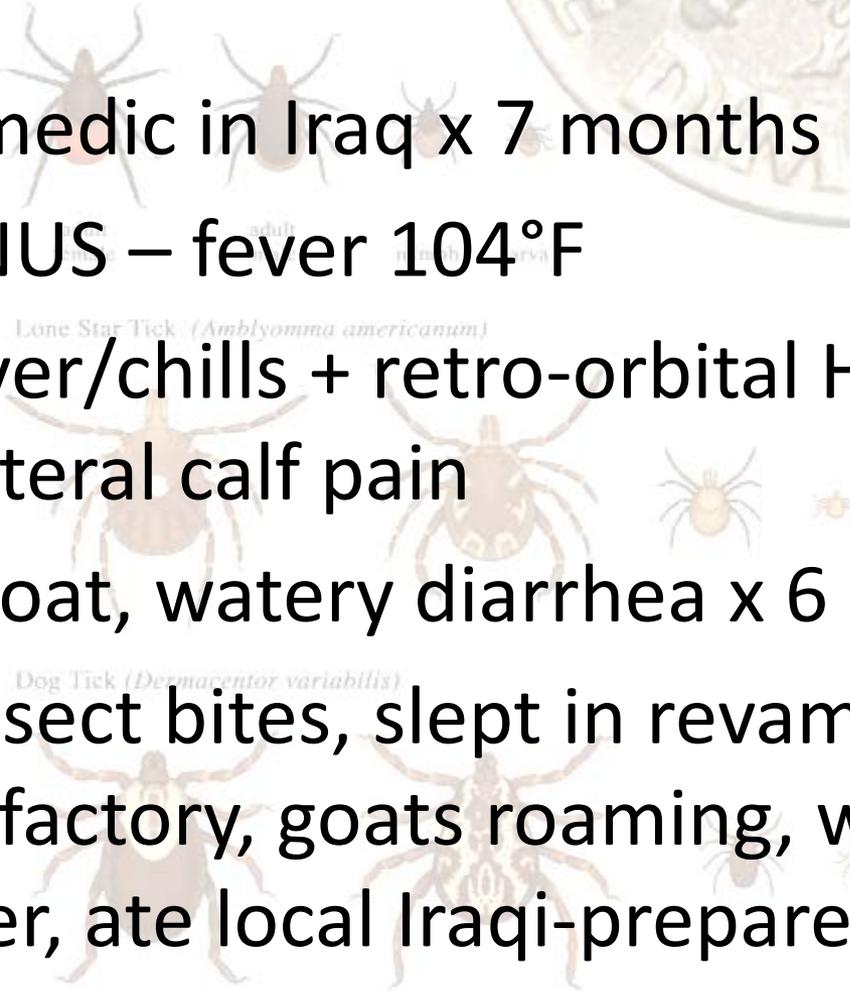
- 35yo USMC medic in Iraq x 7 months
- En route CONUS – fever 104°F
- Now daily fever/chills + retro-orbital HA, lower back and bilateral calf pain
- ROS: sore throat, watery diarrhea x 6 days
- Exposures: insect bites, slept in revamped Iraqi chicken factory, goats roaming, walked in brackish water, ate local Iraqi-prepared food



Blacklegged Tick (*Ixodes scapularis*)

Lone Star Tick (*Amblyomma americanum*)

Dog Tick (*Dermacentor variabilis*)



1 inch

Case #1



- PE:

- T-103°F, HR-90, BP-110/60, O₂ Sat-99% (RA)
- Unremarkable

- CXR, abdominal CT both normal

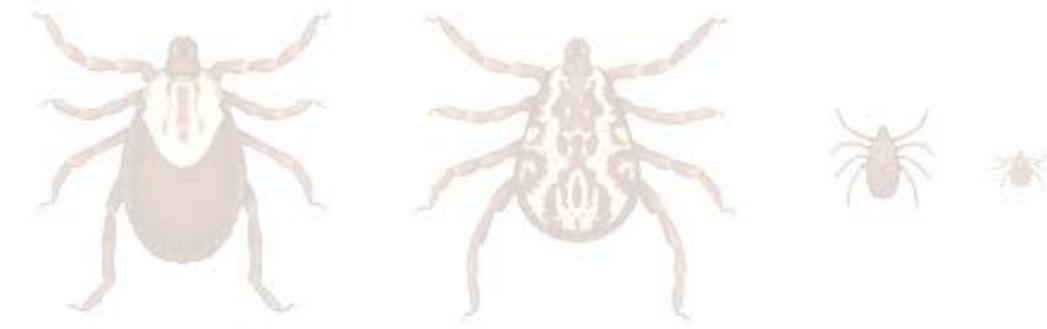


adult female
adult male
nymph
larva

Long Star Tick (*Amblyomma americanum*)



Dog Tick (*Dermacentor variabilis*)

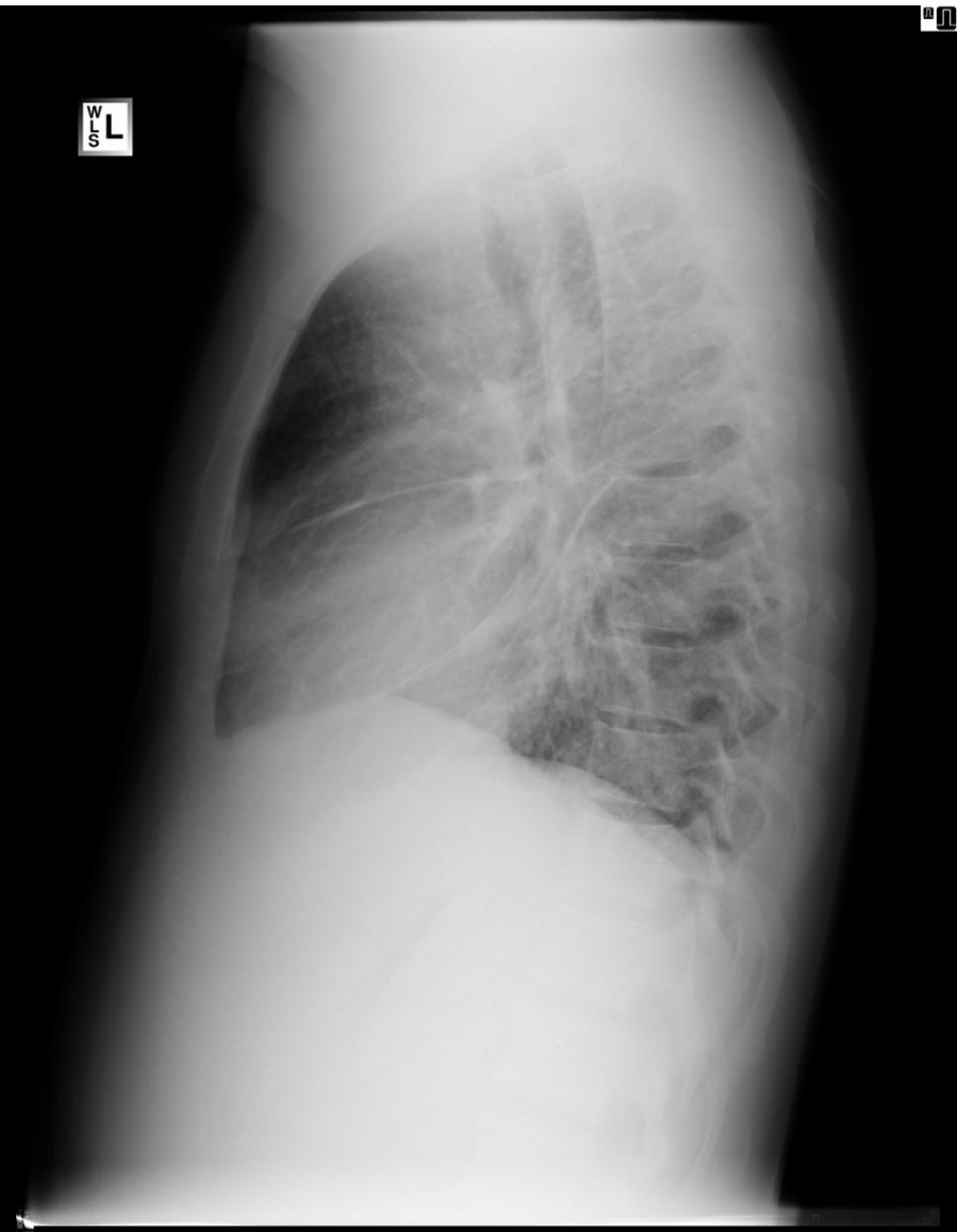
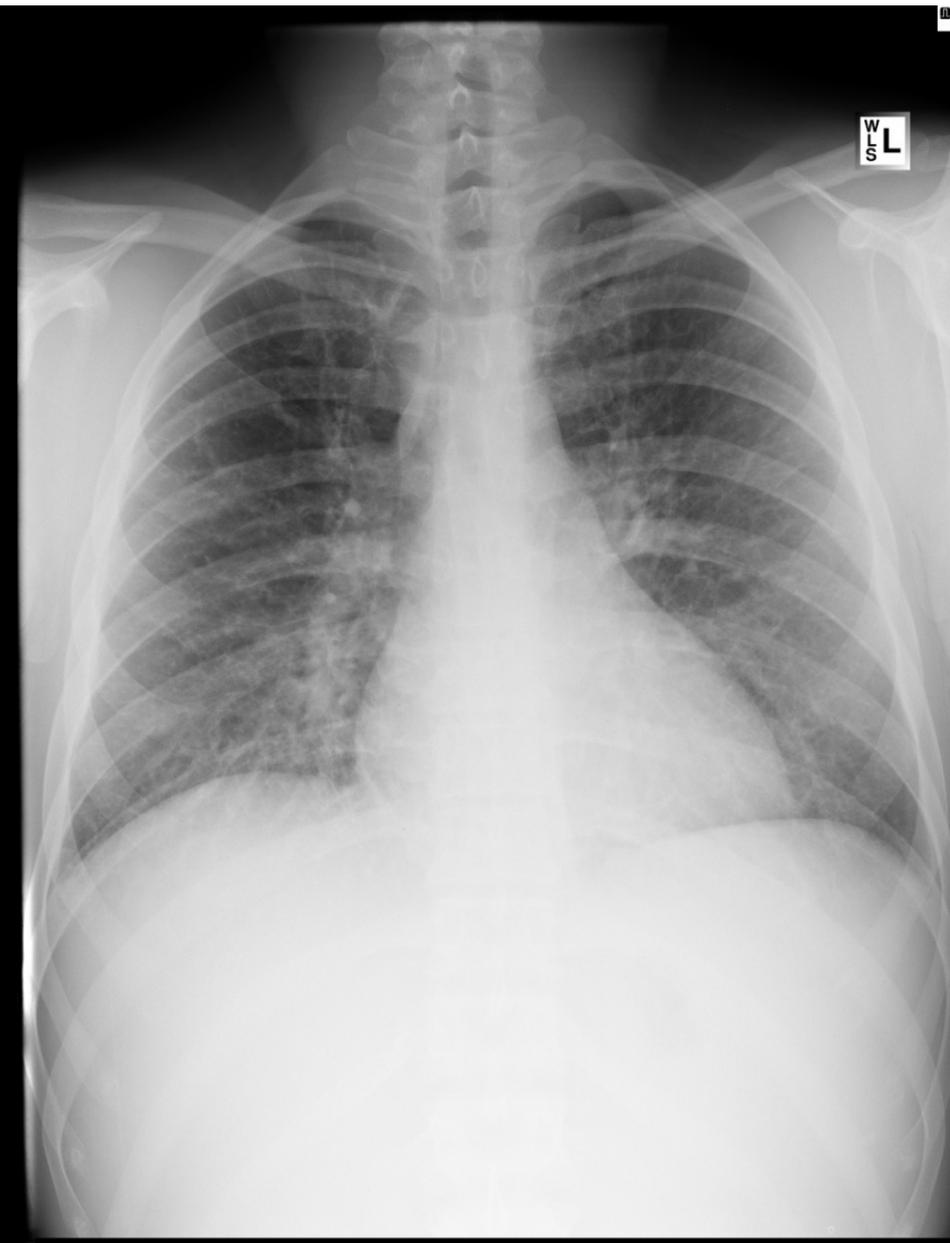


2

Case #1 part B

- 23yo USMC – becomes ill 3 days after #1
- Similar fever, chills, sore throat, diarrhea
- ROS: blisters on feet (waded through sewage); only ate MREs, did not sleep in chicken factory (500yds away)
- PE: T-106°F, HR-104, BP-120/70, O₂ Sat - 98%
 - Mild jaundice o/w normal

Case #1B



Lab data

Patient 1

- Na-130 (137-145)
- K-3.0 (3.6-5.0)
- Alkphos-310 (36-126)
- AST-125 (17-49)
- ALT-130 (7-56)
- Tbili 1.8 (0.2-1.3)
- WBC 4.5 (4.0-11.0) 74N/E2
- Plt-120 (150-450)

Patient 2

- Na-130
- K-2.9
- Alkphos-137
- AST-173
- ALT-131
- Tbili-2.8
- WBC-4.8
- Plt-45

1 inch

Blacklegged Tick (*Ixodes scapularis*)



adult female

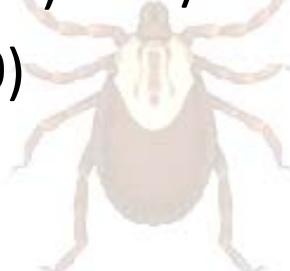


adult male

Lone Star Tick (*Amblyomma americanum*)



Dog Tick (*Dermacentor variabilis*)



2

1 inch

Blacklegged Tick (*Ixodes scapularis*)

Case #1

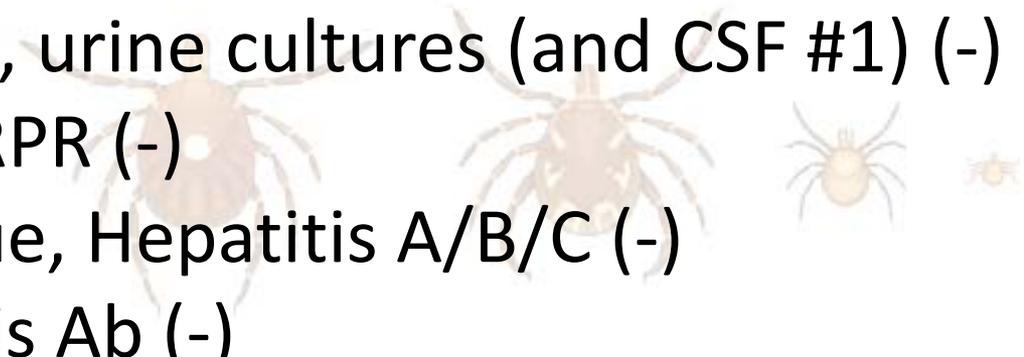


- Differential?



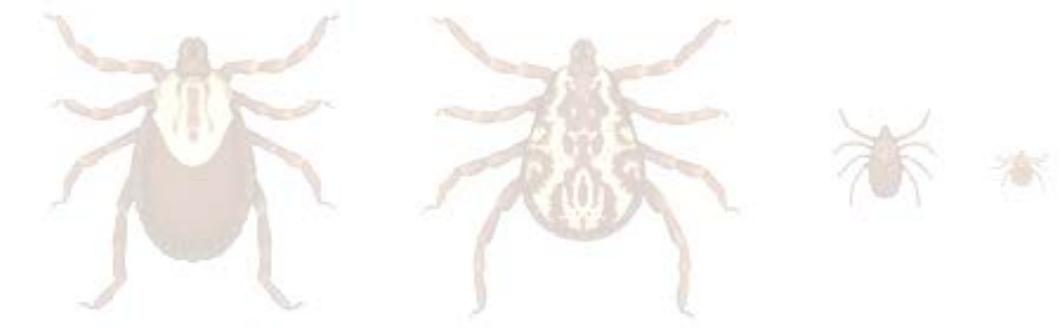
- Malaria smears (-)
- Blood, stool, urine cultures (and CSF #1) (-)
- Acute HIV, RPR (-)
- Viral, Dengue, Hepatitis A/B/C (-)
- Leptospirosis Ab (-)

American Star Tick (*Amblyomma americanum*)



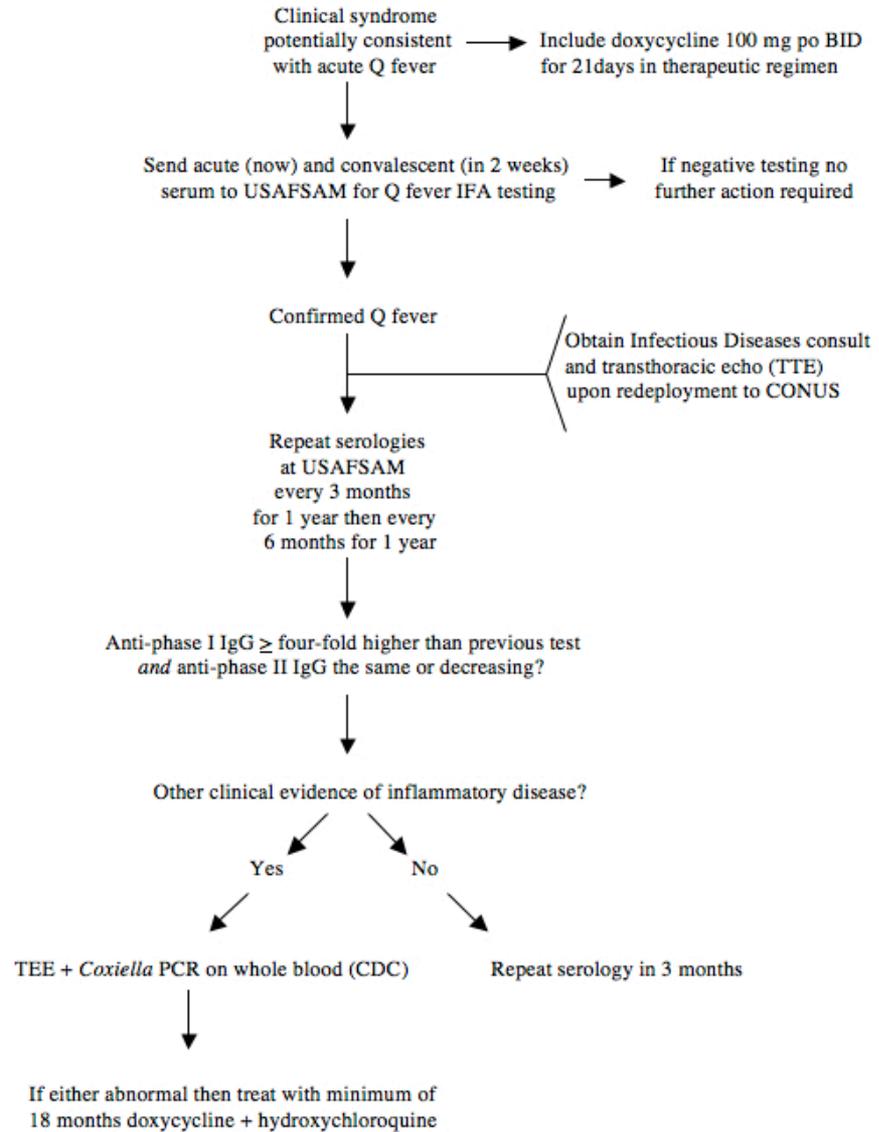
Dog Tick (*Dermacentor variabilis*)

- **Q fever**



2

Current Recommendations of the Tri-Service Infectious Diseases Q Fever Working Group



Fevers, sweats, weight loss, chest pain, elevated erythrocyte sedimentation rate, C reactive protein, liver-associated enzymes, white blood cell count, rheumatoid factor

1 inch

Blacklegged Tick (*Ixodes scapularis*)

Case #2

- 44yo Indian subsistence farmer with fever x 7 days
- Fever unremitting, initially abrupt onset
- Previously well
- One day severe frontal HA, N/V, photophobia, DOE and now tender swelling in left groin

Lone Star Tick (*Amblyomma americanum*)

Dog Tick (*Dermacentor variabilis*)

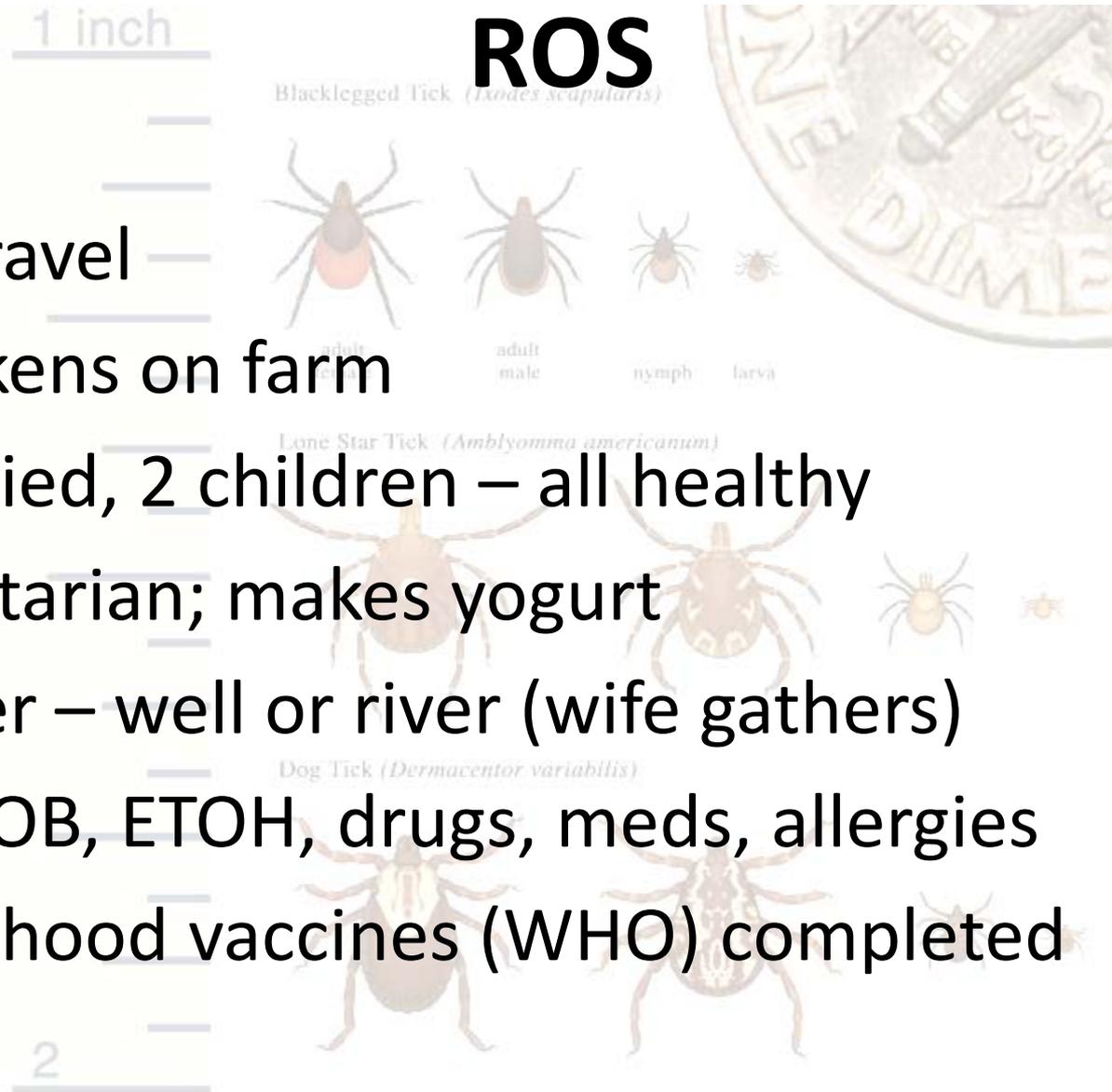
2

TAMIL NADU



ROS

- No travel
- Chickens on farm
- Married, 2 children – all healthy
- Vegetarian; makes yogurt
- Water – well or river (wife gathers)
- No TOB, ETOH, drugs, meds, allergies
- Childhood vaccines (WHO) completed



1 inch

Blacklegged Tick (*Ixodes scapularis*)



Courtesy: N. Aronson, MD

More clinical information

- Following incubation (6-21 d), sx appear
- After initial sx (F, HA, chills, fever, ↓ hearing, conjunctivitis/suffusion, LAD), ulcer seen then centrifugal rash within 1 wk
- 2nd wk (if untreated):
 - Splenomegaly
 - Pneumonia
 - Myocarditis
 - Delirium
 - Death
- Diagnosis?

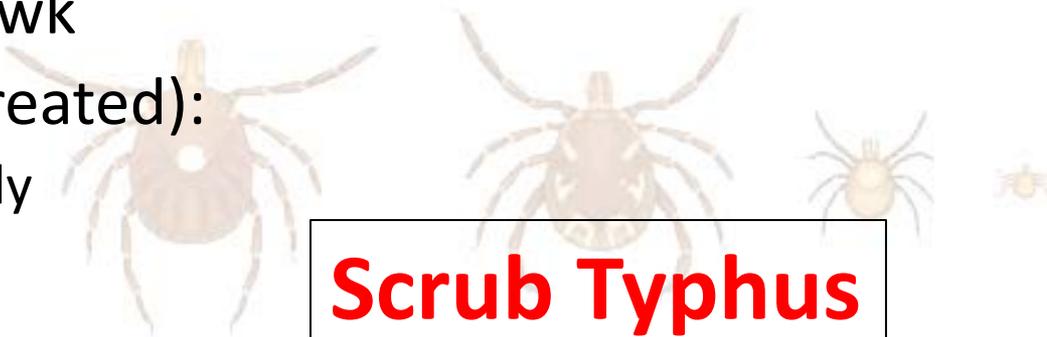
Scrub Typhus

1 inch

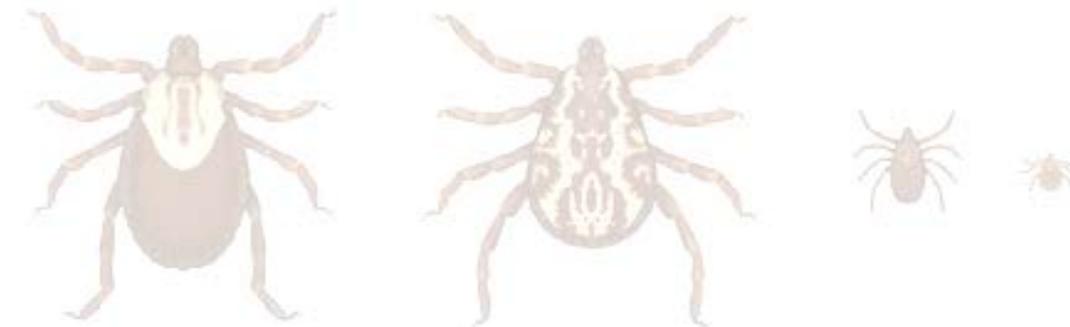
Blacklegged Tick (*Ixodes scapularis*)



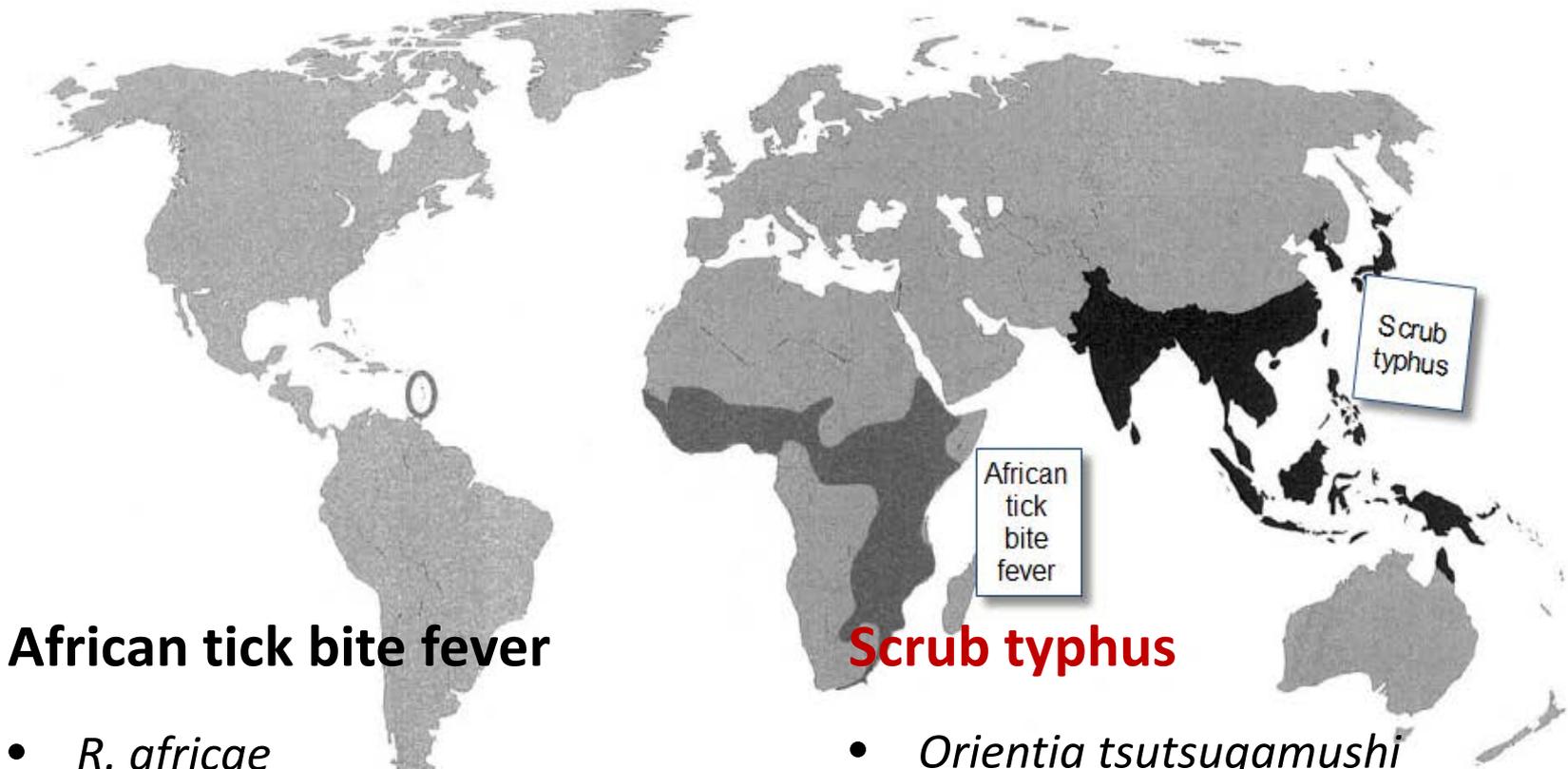
Lone Star Tick (*Amblyomma americanum*)



Dog Tick (*Dermacentor variabilis*)



2



African tick bite fever

- *R. africae*
- *Amblyomma* tick
- ↑ tourists (~5%)
- HA, myalgias, eschar/s
- Vesicular rash, mouth blisters 30%
- Reactive arthritis (5%)
- Self-limited

Scrub typhus

- *Orientia tsutsugamushi*
- Mites
- Loggers, rice farmers, military
- F, LAD (70%), eschar (50%)
- **PNA**, CNS, DIC, renal failure
- Indep. predictor mort: met. acidosis (↑ ast, wbc, ↓ plt)

1 inch

Blacklegged Tick (*Ixodes scapularis*)

Case #3

40yo male Thai subsistence farmer is brought to clinic with report of headache, chills, hearing loss, and cough. You note an eschar on his leg and elicit confusing responses to simple questions. What would be your drug of choice for treatment?

Lone Star Tick (*Amblyomma americanum*)

- A. Doxycycline
- B. Atovaquone
- C. Azithromycin
- D. Gentamicin

Dog Tick (*Dermacentor variabilis*)

2

1 inch

Blacklegged Tick (*Ixodes scapularis*)

40yo male Thai subsistence farmer is brought to clinic with report of headache, chills, hearing loss, and cough. You note an eschar on his leg and elicit confusing responses to simple questions. What would be your drug of choice for treatment?

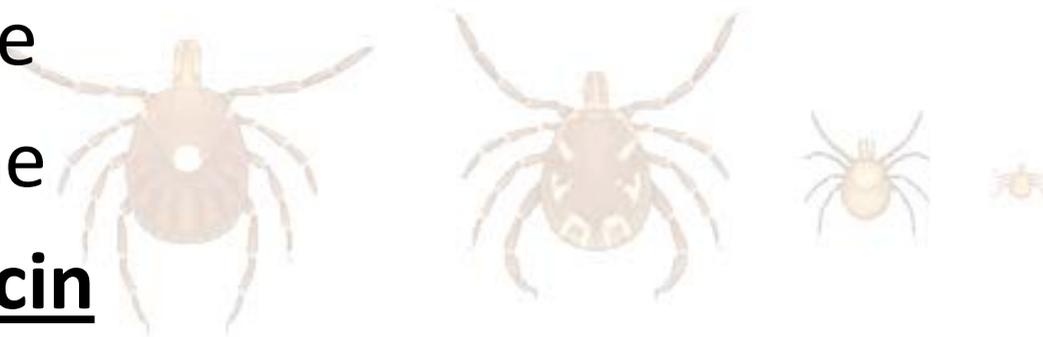
A. Doxycycline

B. Atovaquone

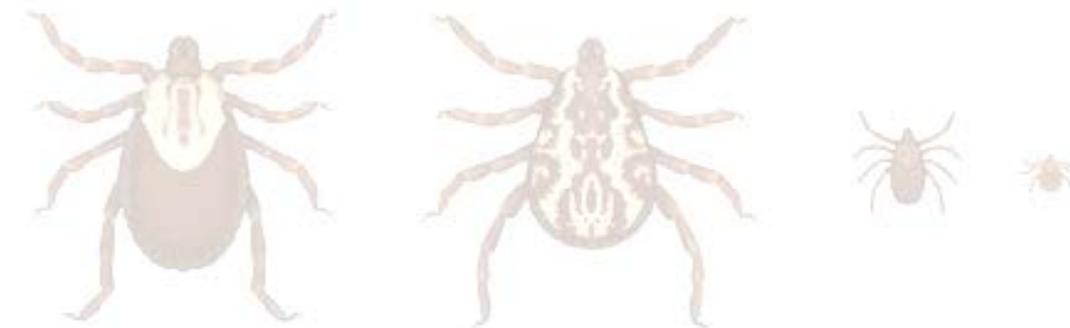
C. **Azithromycin**

D. Gentamicin

Lone Star Tick (*Amblyomma americanum*)



Dog Tick (*Dermacentor variabilis*)



2

Case #4

A 44-year-old male traveler returning from Tanzania presents 7 days after return with fever and respiratory symptoms. Among rickettsial diseases to be considered, which of the following is most likely to be the cause of his illness?

- A. Ehrlichiosis
- B. Spotted fever group rickettsiosis
- C. Bartonellosis
- D. Typhus group rickettsiosis

A 44-year-old male traveler returning from Tanzania presents 7 days after return with fever and respiratory symptoms. Among rickettsial diseases to be considered, which of the following is most likely to be the cause of his illness?

A. Ehrlichiosis

B. Spotted fever group rickettsiosis

C. Bartonellosis

D. Typhus group rickettsiosis

#5

Which of the following is the most commonly used treatment for rickettsial disease among returning international travelers?

- A. Tetracycline
- B. Minocycline
- C. Septra
- D. Doxycycline

Which of the following is the most commonly used treatment for rickettsial disease among returning international travelers?

A. Tetracycline

B. Minocycline

C. Septra

D. Doxycycline

#6

During war with many displaced people, which organism would you be most concerned about because of its high mortality rates, complications, and epidemic potential?

- A. *Orientia tsutsugamushi*
- B. *Rickettsia rickettsii*
- C. *Rickettsia prowazekii*
- D. *Rickettsia typhi*

#6

During war with many displaced people, which organism would you be most concerned about because of its high mortality rates, complications, and epidemic potential?

- A. *Orientia tsutsugamushi*
- B. *Rickettsia rickettsia*
- C. *Rickettsia prowazekii***
- D. *Rickettsia typhi*

Location, location, location...

<u>Rickettsial disease</u>	<u>Geographic locations where most prevalent</u>
RMSF	•Primarily in the continental United States and rarely elsewhere
Rickettsialpox	•Large cities in Russia, South Africa, and Korea
Boutonneuse fever	•Mediterranean countries, such as Spain, Italy, and Israel
Louse-borne typhus (Epidemic) Brill-Zinsser disease	•Europe, Asia and Africa •In the last 2 decades African countries, especially Ethiopia and Nigeria, have reported most cases
Murine	•Large cities around the world with high rate infestations
Tsutsugamushi disease	•Japan, Solomon Islands and Pakistan
Q fever	•Australia, Canada and other parts of the world where humans come into contact with infected animals

Transmission

<u>Disease</u>	<u>Causative rickettsia</u>	<u>Transmitting vector/carrier</u>
Rocky Mountain Spotted Fever (RMSF)	<i>R rickettsii</i>	Vector: wood tick, dog tick, and Lone Star tick Humans become incidental host after being bitten by infected adult tick
Rickettsialpox	<i>R akari</i>	Vector: house mouse is the natural host of the mouse mite transmitting rickettsialpox Distribution: Russia, South Africa, Korea
Boutonneuse fever	<i>R conorii</i>	Vector: various ticks including dog ticks
Louse-borne typhus	<i>R prowazekii</i>	Vector: Human lice
Brill-Zinsser disease	<i>R prowazekii</i>	Vector: lice Reactivation of the organism from a latent state up to decades after primary infection
Murine	<i>R typhi</i> and <i>R felis</i>	Transmitted between rats by a rat flea Humans accidentally infected by the faeces of infected fleas
Tsutsugamushi disease	<i>O tsutsugamushi</i>	Vector: larval trombiculid mites in soil and scrub
Q fever	<i>C burnetii</i>	Vector: Airborne droplets from infected cattle , sheep goats, rodents and cats Slaughterhouse and animal research workers at risk Ticks transmit disease to rodents and domestic animals but are seldom the cause of human infection Organism remains latent in infected host until stressor such as birth activates it. Then multiplies and contaminates animals' surrounding, persisting as potential source of infection for months

Summary

- Rickettsial diseases have nonspecific symptoms
- Thorough skin exam: look for eschars
- Rashes are not always present

NO ONE DIES WITHOUT DOXYCYCLINE ON BOARD!!

- Know what is endemic where you are
- Mortality is high for some conditions
- Treat with doxycycline when in doubt



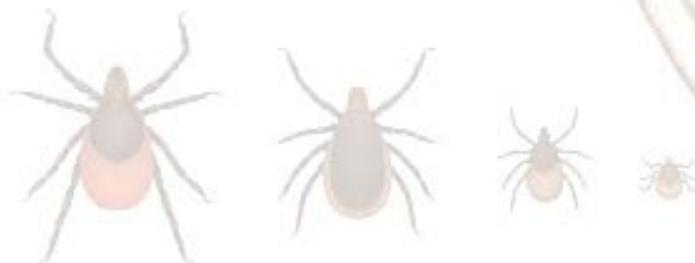
WRAIR

Walter Reed Army
Institute of Research

Soldier Health • World Health



Blacklegged Tick (*Ixodes scapularis*)



adult
female

adult
male

nymph

larva

Lone Star Tick (*Amblyomma americanum*)

QUESTIONS?



Dog Tick (*Dermacentor variabilis*)



2