

CSTE-hosted VBD Webinar: Emerging Tickborne Diseases

May 3, 2017

3:00-4:00 pm Eastern Standard Time



Council of State and Territorial Epidemiologists

Webinar Housekeeping

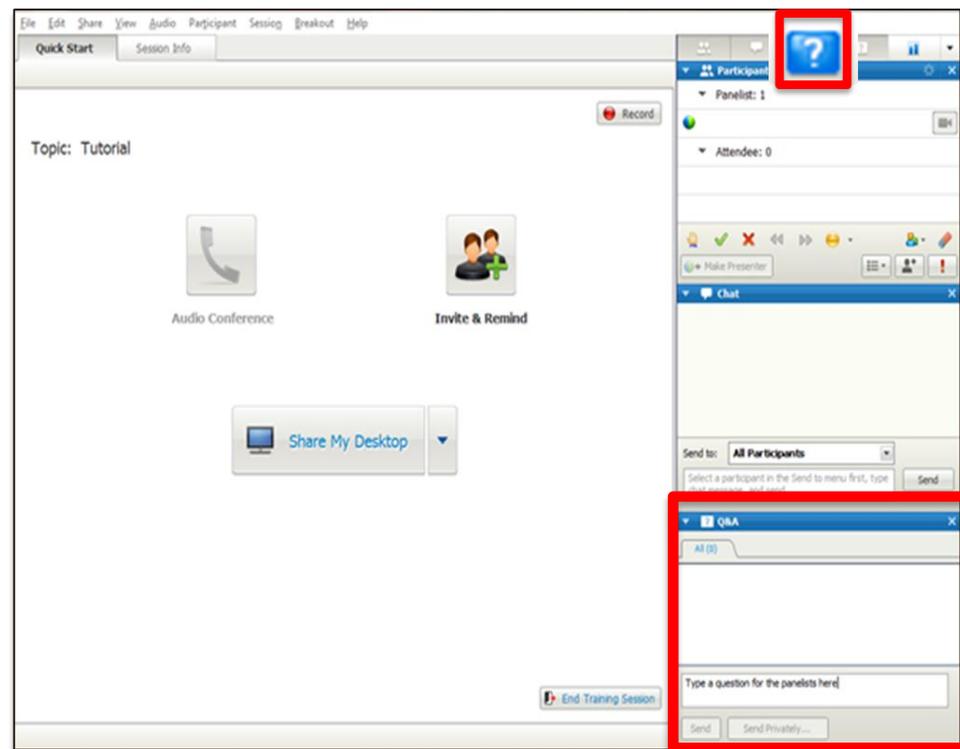


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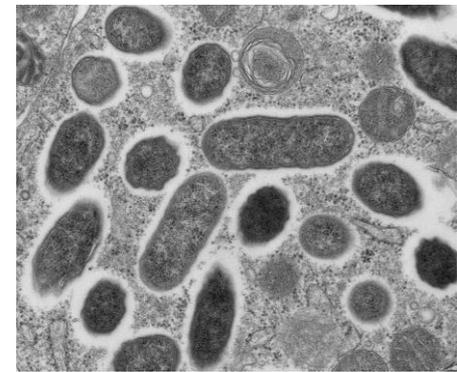
To Ask a Question



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- This will open the Q&A box on the bottom right panel on your screen
- Type a question
- Send questions to All Panelists
- Questions will be answered during the Q&A period



Expanding Recognition of *Rickettsia parkeri* Rickettsiosis in the United States



Christopher D. Paddock, MD

Medical Officer, Rickettsial Zoonoses Branch

Division of Vector-Borne Diseases

National Center for Emerging and Zoonotic Infectious Diseases

Ticks and *Rickettsia* in the United States, 1900-2004

- For more than 100 years after its discovery, Rocky Mountain spotted fever was considered the only tick-borne rickettsiosis of humans in the United States
- *Rickettsia rickettsii*, transmitted by *Dermacentor* spp. and *Rhipicephalus sanguineus* ticks



A Pathogen Emerges from the Past

1939

OBSERVATIONS ON AN INFECTIOUS AGENT FROM *AMBLIOMMA MACULATUM*¹

By **R. R. PARKER**, Director, Rocky Mountain Laboratory, **GLEN M. KOHLS**, Assistant Entomologist, United States Public Health Service, **GEORGE W. COX**, Executive Officer, Texas State Department of Public Health, and **GORDON E. DAVIS**, Bacteriologist, United States Public Health Service



Amblyomma maculatum,
the Gulf Coast tick

2004

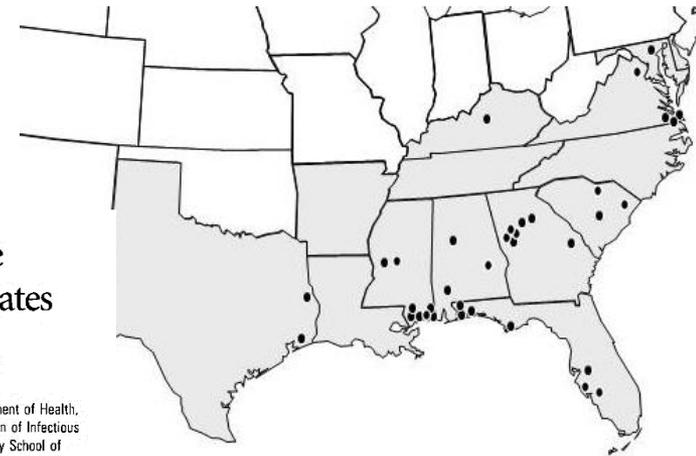
Rickettsia parkeri: A Newly Recognized Cause of Spotted Fever Rickettsiosis in the United States

Christopher D. Paddock,¹ John W. Sumner,¹ James A. Comer,¹ Sherif R. Zaki,¹ Cynthia S. Goldsmith,¹ Jerome Goddard,² Susan L. F. McLellan,³ Cynthia L. Tammimga,⁴ and Christopher A. Ohl^{1,5}

¹Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; ²Mississippi Department of Health, Jackson, Mississippi; ³Infectious Diseases Section, Tulane University Health Sciences Center, New Orleans, Louisiana; ⁴Division of Infectious Diseases, Portsmouth Naval Medical Center, Portsmouth, Virginia; and ⁵Section on Infectious Diseases, Wake Forest University School of Medicine, Winston-Salem, North Carolina

(See the editorial commentary by Raoult on pages 812–3)

2014



Rashes of Rocky Mountain Spotted Fever (RMSF) versus *Rickettsia parkeri* Rickettsiosis



RMSF



R. parkeri
rickettsiosis



Rickettsia parkeri Rickettsiosis: Primary Diagnoses for the First 12 Patients

Patient	Initial diagnosis
1	RMSF
2	RMSF
3	RMSF
4	rickettsialpox
5	rickettsialpox
6	RMSF
7	rickettsialpox
8	RMSF
9	spider bite
10	<i>R. parkeri</i> rickettsiosis
11	RMSF
12	cellulitis

Eschars of *Rickettsia parkeri* Rickettsiosis



Paddock CD, Sumner JW, Comer JA, et al. *Clin Infect Dis*. 2004 Mar 15;38(6):805-11.
Cragun WC, Bartlett BL, Ellis MW, et al. *Arch Dermatol*. 2010 Jun;146(6):641-8.

A case of “RMSF” with an Eschar

- 55 y/o man is bitten by a tick on his leg while playing golf in South Carolina
- Develops low-grade fever, eschar, and a maculopapular rash
- Rapid improvement with doxycycline
- Antibody titers to *R. rickettsii* rise from <64 to 512



RMSF versus *Rickettsia parkeri* Rickettsiosis

Clinical Feature	RMSF (n = 398)	<i>R. parkeri</i> rickettsiosis (n = 21)
Fever	99%	100%
Headache	80%	86%
Any rash	92%	90%
Petechial rash	52%	14%
Pustular/vesicular rash	---	33%
Eschar	---	95%
Nausea/vomiting	66%	10%
Coma/seizure	27%	---
Death	8%	---

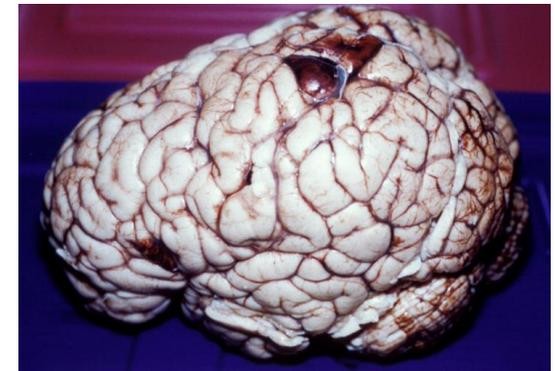
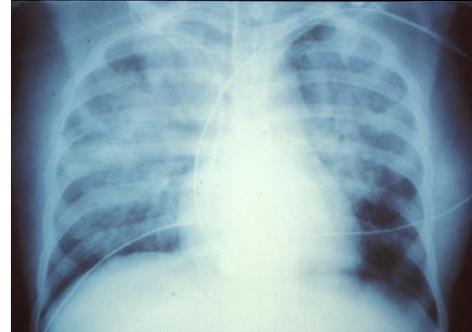
Paddock CD, Finley RW, Wright CS, et al. *Clin Infect Dis*. 2008 Nov 1;47(9):1188-96.

Cragun WC, Bartlett BL, Ellis MW, et al. *Arch Dermatol*. 2010 Jun;146(6):641-8.

Myers T, Lalani T, Dent M, et al. *Emerg Infect Dis*. 2013 May;19(5):778-80.

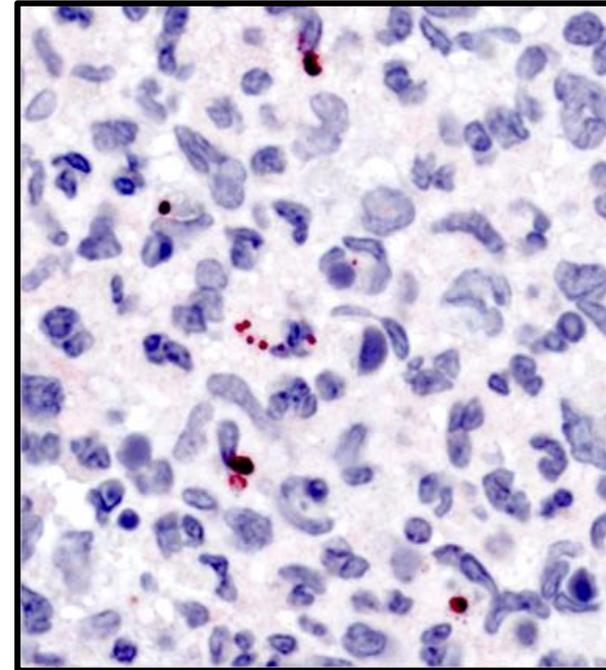
¹² Ekenna O, Paddock CD, Goddard J. *J Miss State Med Assoc*. 2014 Jul;55(7):216-9.

Severe or Life-threatening Complications of RMSF Not Identified with *R. parkeri* Rickettsiosis



Laboratory Diagnosis

- **Indirect immunofluorescence antibody (IFA) assay (serum)**
- **Immunohistochemical stain (rash or eschar biopsy specimen)**
- **DNA amplification by PCR assay (eschar biopsy or swab specimen)**
- **Isolation in cell culture (eschar biopsy specimen)**



IFA Titers of *Rickettsia parkeri*-infected Patients are Cross-reactive with *Rickettsia rickettsii*

	<i>Rickettsia parkeri</i>	<i>Rickettsia rickettsii</i>
Patient 1	512	1024
Patient 2	512	256
Patient 3	64	64
Patient 4	1024	1024
Patient 5	128	512
Patient 6	512	128

Eschar Swab Diagnosis of *Rickettsia parkeri* rickettsiosis

DISPATCHES

Detecting *Rickettsia parkeri* Infection from Eschar Swab Specimens

Todd Myers, Tahaniyat Lalani, Mike Dent,
Ju Jiang, Patrick L. Daly, Jason D. Maguire,
and Allen L. Richards

The typical clinical presentation of several spotted fever group *Rickettsia* infections includes eschars. Clinical diagnosis of the condition is usually made by analysis of blood samples. We describe a more sensitive, noninvasive means of obtaining a sample for diagnosis by using an eschar swab specimen from patients infected with *Rickettsia parkeri*.



Specimen Submission Guidelines Rickettsial Zoonoses Branch

Reference Diagnostic Laboratory Collection and Submission of Eschar Swab Specimens

Many rickettsial diseases, such as African tick bite fever and *Rickettsia parkeri* rickettsiosis, are characterized by a necrotic area at the site of an infected tick bite, known as an eschar. Sampling the eschar provides an important method for the detection of spotted fever group rickettsial DNA using polymerase chain reaction (PCR) assays. This procedure is less invasive than skin biopsies; however, it doesn't allow for IHC or cell culture evaluation.

The sample should be obtained before or within 24 hours of initiation of appropriate antibiotic therapy (i.e., doxycycline). **Antibiotic treatment should never be delayed to obtain a biopsy specimen.**

Collection of Eschar Swab

1. Disinfect the area of the eschar and remove disinfectant with sterile gauze soaked in sterile saline.
2. Use sterile tweezers to lift the scab partially or completely. If scab is removed completely, place it in a sterile container and submit with the swab.
3. Sample ulcerated area with a dry sterile cotton swab and collect the contents while rotating the swab and applying steady, gentle pressure.
4. Place swab in a sterile container.
5. Ship specimen(s) to CDC on cold packs by overnight delivery, or freeze at -70°C and ship on dry ice at your convenience.

We recommend the collection of an acute-phase serum at the time of swab collection, and a convalescent-phase serum sample 2-6 weeks later.

See the RZB Specimen Submission Guidelines for details on shipping requirements.

For questions, please call the Rickettsial Zoonoses Branch at (404) 639-1075 or email rzbepldiag@cdc.gov.

National Center for Emerging and Zoonotic Infectious Diseases
Division of Vector-Borne Diseases

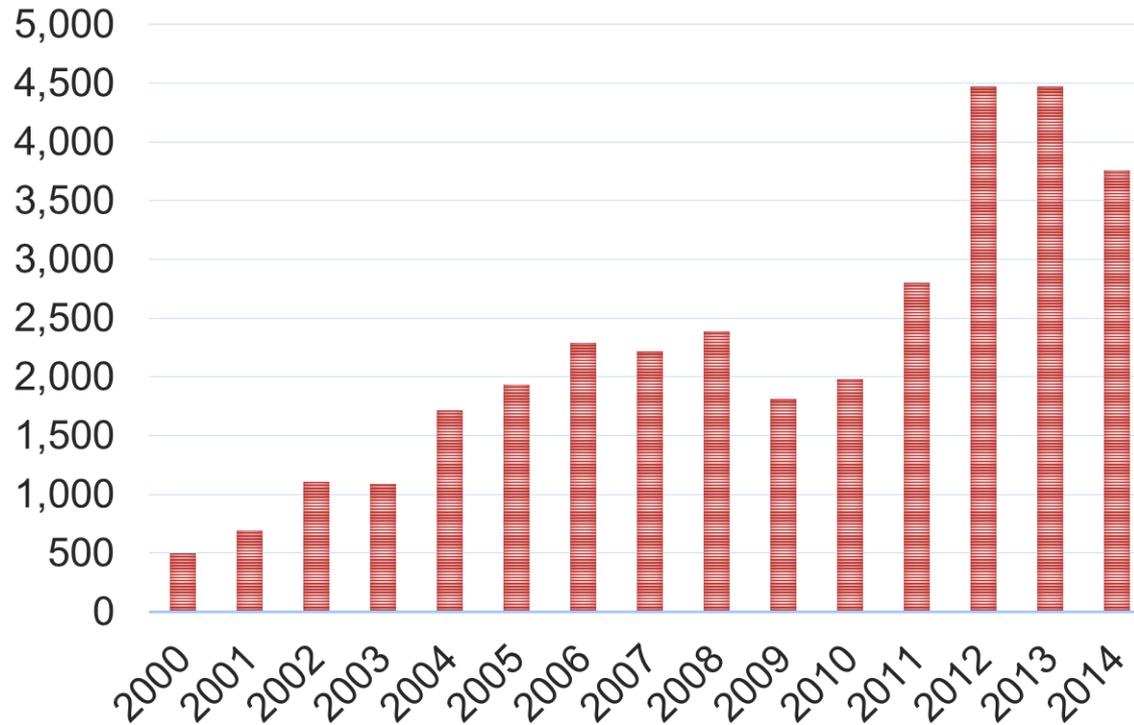


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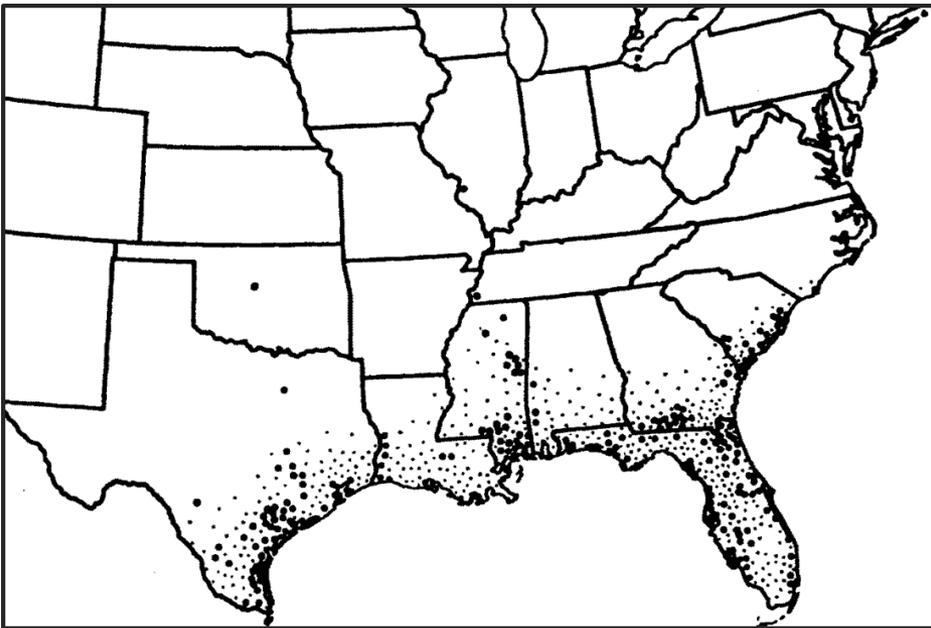
Doxycycline: Recommended Therapy for All Tickborne Rickettsioses

- **Adults and children of *all* ages**
- **100 mg orally twice per day to continue for at least 3 days after fever subsides (minimum treatment course is typically 5-7 days)**
- **Single short course in young children does not stain enamel**

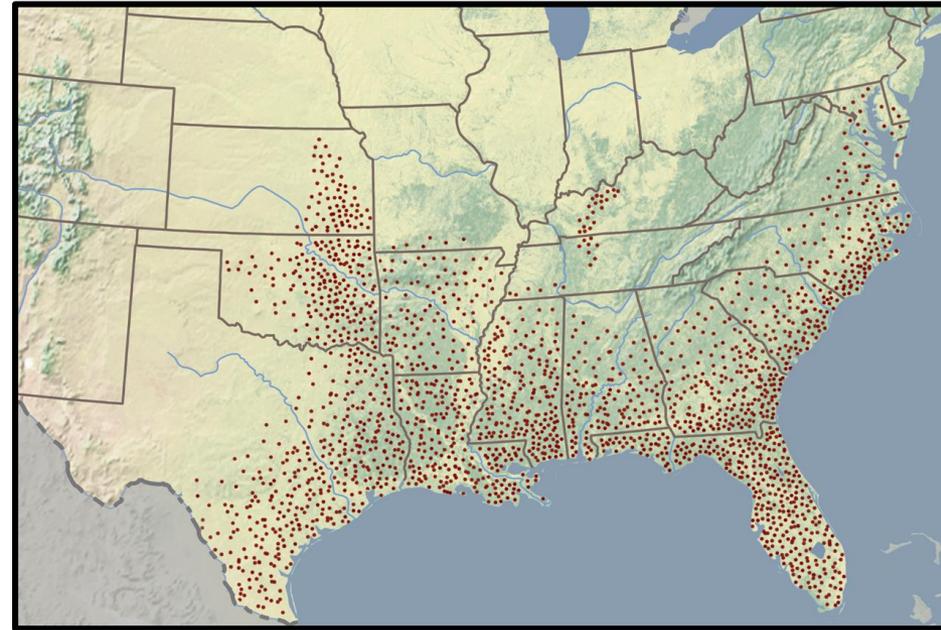
Reported Cases of Spotted Fever Group Rickettsiosis, 2000-2014



Recognized distribution of *Amblyomma maculatum* in the United States, 1944-2015



1944



2015

Cooley RA, Kohls GM. *J Parasitol* 1944;30:77-111.

Paddock CD, Goddard J. *J Med Entomol* 2015;52:230-52

Percentage of Ticks Infected with *R. parkeri* Greater than Percentage of Ticks Infected with *R. rickettsii*

Frequency of *R. rickettsii* in *D. variabilis* vs. *R. parkeri* in *A. maculatum*

	Pathogen	Location, years	No. (% infected)
<i>Dermacentor variabilis</i> 	<i>R. rickettsii</i>	North Carolina, 1982	2,123 (0.05)
		Ohio, 1984–1989	12,631 (0.06)
		Maryland, 2002	392 (0)
		Tennessee, 2007–2008	555 (0)
<i>Amblyomma maculatum</i> 	<i>R. parkeri</i>	Florida, 2005–2007	128 (22)
		Mississippi, 2008–2012	698 (15)
		North Carolina, 2009–2010	101 (31)
		Virginia, 2010–2011	293 (53)

Paddock CD, Fournier PE, Sumner JW, et al. *Appl Environ Microbiol*. 2010 May;76(9):2689-96.

Pagac BB, Miller MK, Mazzei MC, et al. *Emerg Infect Dis*. 2014 Oct;20(10):1750-2.

Ferrari FA, Goddard J, Paddock CD, et al. *Emerg Infect Dis*. 2012 Oct;18(10):1705-7.

Varela-Stokes AS, Paddock CD, Engber B, et al. *Emerg Infect Dis*. 2011 Dec;17(12):2350-3.

Nadolny RM, Wright CL, Sonenshine DE, et al. *Ticks Tick Borne Dis*. 2014 Feb;5(1):53-7.

Rickettsia parkeri rickettsiosis: How Much is Out There?

- **5 cases identified by one clinician in Mississippi during 2007–2012**
- **5 cases identified at one urgent care practice in Georgia during 2012–2014**

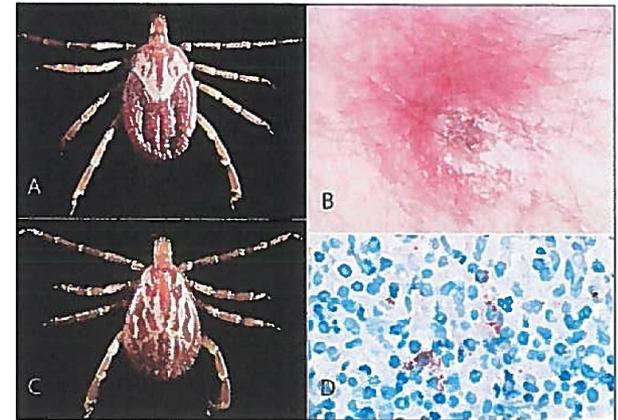
Notes from the Field

Rickettsia parkeri Rickettsiosis — Georgia, 2012–2014

Anne Straily, DVM^{1,2}; Amanda Feldpausch, MPH³; Carl Ulbrich, DO¹; Kiersten Schell⁴; Shannon Casillas, MPH³; Sherif R. Zaki, MD, PhD⁵; Amy M. Denison, PhD⁵; Marah Condit, MS²; Julie Gabel, DVM³; Christopher D. Paddock, MD²

During 2012–2014, five cases of *Rickettsia parkeri* rickettsiosis were identified by a single urgent care practice in Georgia, located approximately 40 miles southwest of Atlanta. Symptom onset occurred during June–October, and all patients had a known tick bite. Patients ranged in age from 27 to 72 years (median = 53 years), and all were male. The most commonly reported initial signs were erythema (n = 3) and swelling (n = 2) at the site of the bite. Two patients reported fever and a third patient reported a rash and lymphadenopathy without fever. Other symptoms included myalgia (n = 3), chills (n = 3), fatigue (n = 2), arthralgia (n = 2), and headache (n = 2). Eschar biopsy specimens were collected from each patient using a 4-mm or 5-mm punch and placed in 10% neutral buffered formalin or

FIGURE. Female (A) and male (C) Gulf Coast ticks (*Amblyomma maculatum*); (B) necrotic, ulcerated or scabbed lesion at the tick bite site, known as an inoculation eschar; and (D) immunohistochemical stain indicating the presence of a spotted fever group *Rickettsia* species in the tissue



Why is *Rickettsia parkeri* relevant?

1000 cases of
suspected RMSF with
10 deaths

**RMSF case fatality
rate = 1%**

vs.

100 *confirmed* cases of RMSF
with 10 deaths

+

900 cases of milder rickettsioses
caused by *Rickettsia parkeri* or
Rickettsia philipii with no deaths

RMSF case fatality rate = 10%

Conclusions

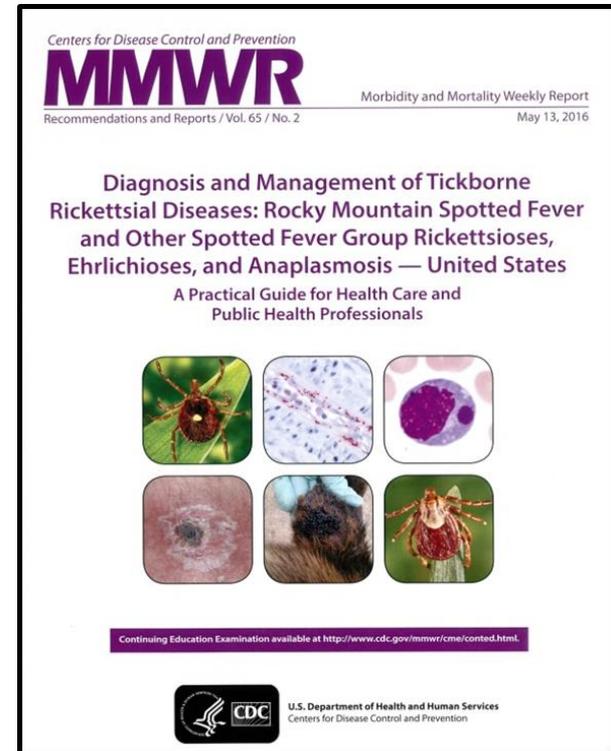
- **Etiologic spectrum of tickborne rickettsioses in the U.S. has expanded during the past 15 years**
- **Rocky Mountain spotted fever and *R. parkeri* rickettsiosis share many clinical features but differ considerably in severity**
- **Doxycycline is the drug of choice for all tickborne rickettsioses and in patients of all ages**
- **Correct diagnosis is crucial for epidemiological accuracy**

Contact Information and Recommended Reading

rzbepidiag@cdc.gov

cdp9@cdc.gov

404-639-1309



An Emerging Tick-borne Rickettsiosis in California: *Pacific Coast Tick Fever*



Kerry A. Padgett, Ph.D.

Supervising Public Health Biologist

California Department of Public Health

Tick-borne Spotted Fever Group *Rickettsia* in California

- ***Rickettsia rickettsii***

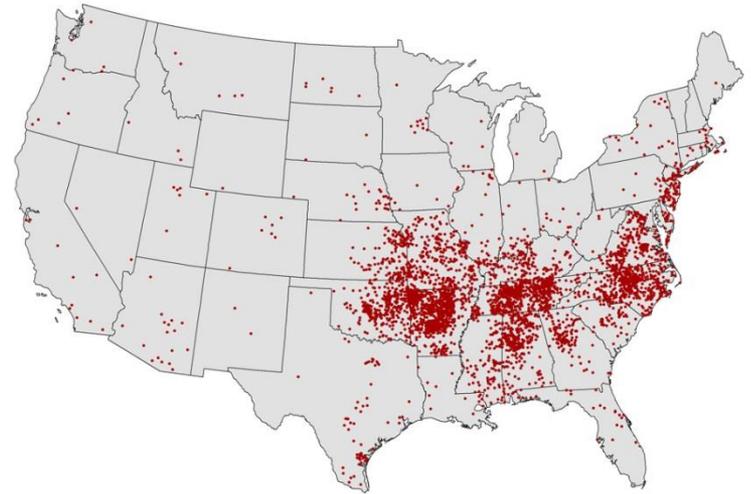
- Rocky Mountain Spotted Fever



- Fever, headache, petichial rash, confusion, and myalgia
- >20% case fatality rate if untreated

- **Rare**

- (<1 case per year in CA)



Common Human-Biting Ticks: California

Ixodes pacificus

(western blacklegged tick)



Dermacentor occidentalis

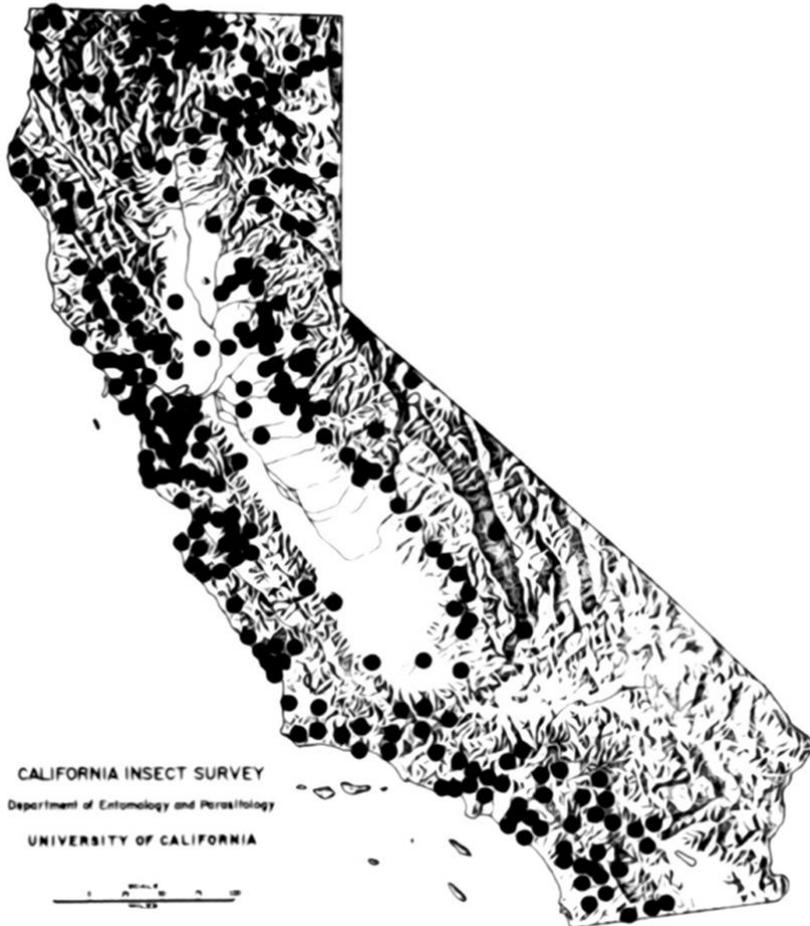
(Pacific Coast Tick)



There are 47 species of ticks in California - Only 8 species bite humans

Historical Background

Rickettsia 364D was first described from a Pacific Coast Tick collected from Ventura County, 1966



Pacific Coast Tick
(*Dermacentor occidentalis*)

Rickettsia* 364D = *Rickettsia philipii

- Robert Philip distinguished *Rickettsia philipii* from its nearest relative of *R. rickettsii*
- For over 30 years, *R. philipii* was suspected to cause human infection



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SEROLOGIC TYPING OF RICKETTSIAE OF THE SPOTTED FEVER GROUP BY MICROIMMUNOFLUORESCENCE

**ROBERT N. PHILIP, ELIZABETH A. CASPER, WILLY BURGDORFER, ROBERT K. GERLOFF,
LYNDAHL E. HUGHES, AND E. JOHN BELL**

From the U. S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Rocky Mountain Laboratory, Hamilton, Montana 59840

Pacific Coast Tick Fever



- Index case: 80 yr Male from Lake County, July 2008
- Local cutaneous **ESCHAR** (dark crusted ulcer); Suspected cutaneous anthrax
- Eschar biopsy sent to CDC; Molecular match to *R. philipii*!

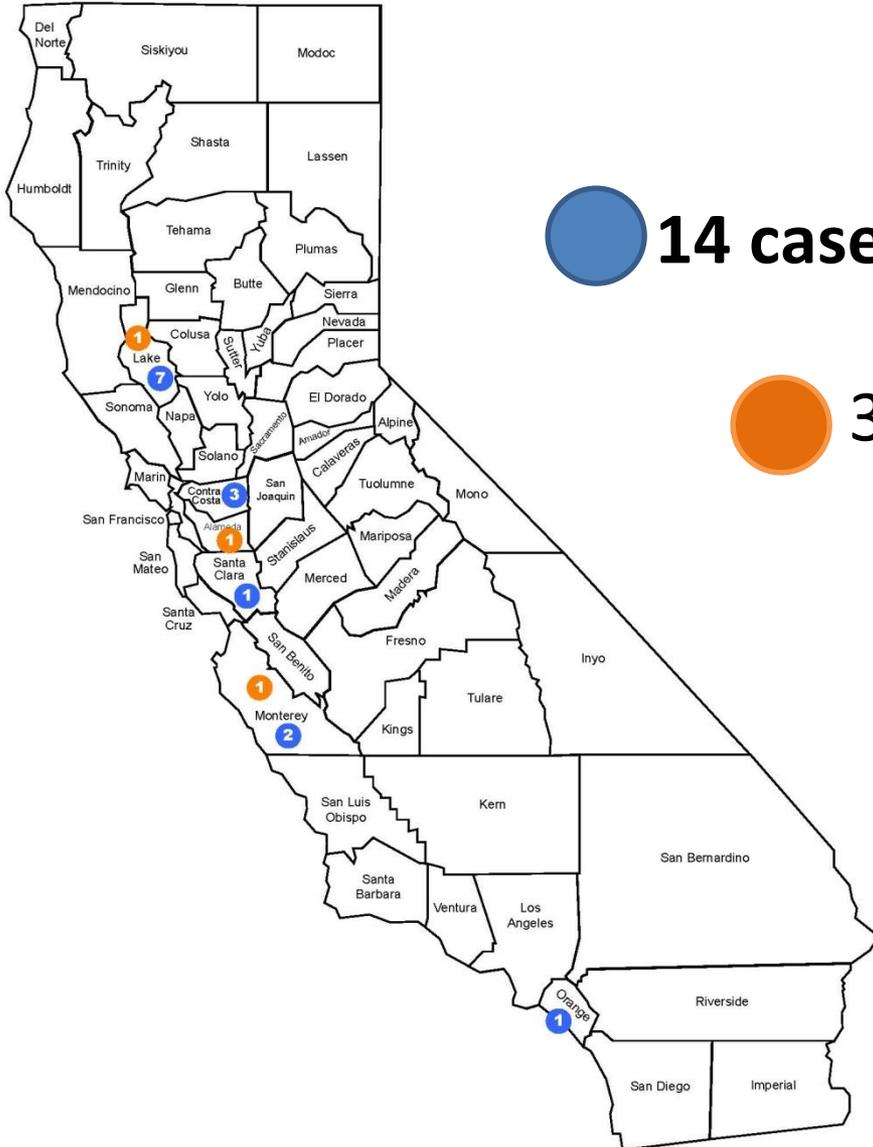
MAJOR ARTICLE

Rickettsia 364D: A Newly Recognized Cause of Eschar-Associated Illness in California

Marc R. Shapiro,¹ Curtis L. Fritz,² Karen Tait,³ Christopher D. Paddock,⁵ William L. Nicholson,⁵ Kyle F. Abramowicz,⁵ Sandor E. Karpathy,⁵ Gregory A. Dasch,⁵ John W. Sumner,⁵ Patricia V. Adem,⁵ Jamesina J. Scott,⁴ Kerry A. Padgett,² Sherif R. Zaki,⁵ and Marina E. Ereemeva⁵

¹St Helena Hospital Clearlake, Clearlake, ²Division of Communicable Disease Control, California Department of Public Health, Sacramento, and ³Lake County Health Services Department and ⁴Lake County Vector Control District, Lakeport, California; and ⁵Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

Pacific Coast Tick Fever



 **14 cases from 5 counties, 2008-2014**

 **3 probable cases from 3 counties**

PCTF-Clinical Signs



Onset of symptoms within one week after tick bite

- Common symptoms: ESCHAR, fever, headache, and lymphadenopathy
 - Multiple eschars in 4 cases
- Variable severity
 - 4 cases required hospitalization
 - 1/14 recovered with no antibiotic treatment

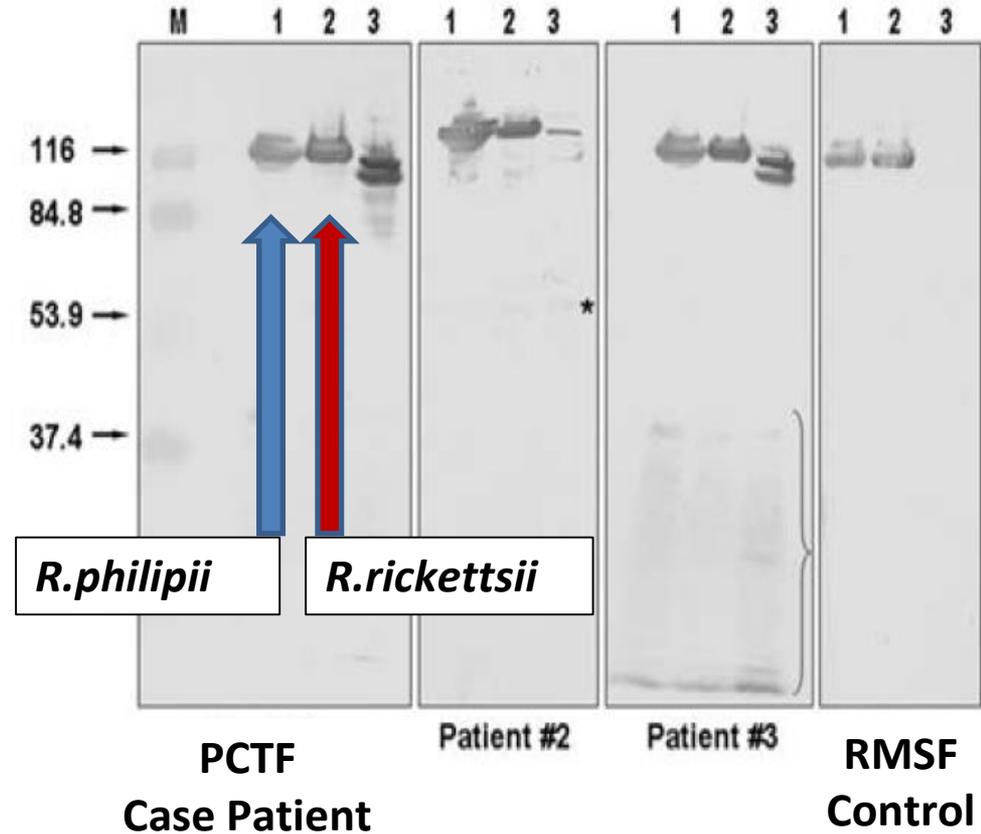


Symptom	<i>Pacific Coast Tick Fever</i> (% of current cases)	RMSF* (n=208)
Eschar	100%	Not documented
Fever	85%	100%
Headache	79%	72%
Lymphadenopathy	64%	20%
Rash	Uncommon (2/14)	92%

* Summary from Paddock et al., CID, 2008

Serological Diagnostics

- Serological tests (IFA and WB) are cross-reactive for SFG *Rickettsia*
 - Confirmatory tests **CANNOT** differentiate between *R. rickettsii* and other SFG *Rickettsia*
- Nevertheless, confirmatory serology of acute and convalescent samples recommended



Molecular Diagnostics

- To differentiate *R. rickettsii* and *R. philipii*: a dry swab sample of tissue from under eschar (scab) or piece of scab using SYBR Green PCR and sequencing of OmpA gene
- All 14 cases were diagnosed on PCR of swab or scab



If You Identify A Suspect Tick-Bite Associated Eschar...

<http://www.cdph.ca.gov/programs/vrdl/Pages/WhatsNew.aspx>

Minimum specimen requirement:

Paired serum specimens. Sera (5-10 cc)

Acute serum should be taken in the 1st week of illness (or within ~7-10 days post onset)

Convalescent serum should be taken at least 3-4 weeks following the acute sample

Additional desired specimens, as available:

- **Eschar/Scab** (if present)
- **Swab(s)** of open lesions, pustules or vesicles
- **Ticks** associated with suspected cases may also be submitted for identification and PCR testing



California Department of Public Health – July 2012

Laboratory Testing for Spotted Fever Rickettsiosis

A newly described eschar-associated illness has been identified in California caused by Spotted Fever Group (SFG) *Rickettsia* 364D and transmitted with tick bite. The most prominent clinical feature of *Rickettsia* 364D infection is

Specimen collection:

Minimum specimen requirement: Paired serum specimens. Sera (5-10 cc) should be collected in a red top or tiger top tube.

IMPORTANT NOTE: Treatment decisions should be based on epidemiologic and clinical evidence and should never be delayed while awaiting confirmation by laboratory results.

Of 14 case-patients, 13 were treated successfully with **14-day course of doxycycline**

- 3 case-patients were initially treated unsuccessfully with Ciprofloxacin, Cephalexin, or Trimethoprim/sulfamethoxazole

One patient recovered with no treatment

Multiple Eschars

Case Patient #11 (8/8/13)



Shoulder



Right Leg

- Four patients had multiple eschars

Case Patient #12 (8/8/13)



Shoulder



Neck



Back

- 3 of 4 hospitalized cases had multiple eschars

Spotted Fever Group Rickettsiosis

Disease	Organism	Rash/ Eschar
Rocky Mountain spotted fever	<i>Rickettsia rickettsii</i>	Rash/ No Eschar
<i>Rickettsia parkeri</i> rickettsiosis	<i>R. parkeri</i>	Eschar (rarely multiple)
Mediterranean spotted fever	<i>R. conorii</i>	Eschar (rarely multiple)
Rickettsialpox	<i>R. akari</i>	Eschar (rarely multiple)
North Asian tickborne rickettsiosis	<i>R. sibirica</i>	Multiple eschars
African tick bite fever	<i>R. africae</i>	Multiple eschars
Pacific Coast tick fever	<i>R. philipii</i>	Multiple eschars

**What are the Entomological Risk
Factors for
Pacific Coast Tick Fever?**

Field Methods



- 6,123 ticks were tested from 37 of 58 California counties, 2009-2014
- Primarily adults with >800 larval and nymphal ticks
- CDPH historic field surveillance database queried for *D. occidentalis*



Molecular Methods

R. philipii ompA
TCCCGTAGGTCTAAATATTACTCAAATACCGTCGTTGGTTCGATTATAACGAAAGGTAA
|||||
TCCCGTAGGTCTAAATATTACTCAAATACCGTCGTTGGTTCGATTATAACGAAAGGTAA
R. rickettsii (Sheila Smith)

R. philipii ompA
CTTGTTCCTGTACTCTTATGCGCGCAAAGCTTAACTTTAAATGGTAATAATGCTGT
|||||
CTTGTTCCTGTACTCTTATGCGCGCAAAGCTTAACTTTAAATGGTAATAATGCTGT
R. rickettsii (Sheila Smith)

- Ticks were tested by RZB, CDC, and CDPH
- Ticks were tested individually
 - Screening with 547-701 OmpA SYBR-GREEN PCR
 - Confirmatory sequencing of 70-701 OmpA



**Where is *Rickettsia philipii* found
in California?**

Rickettsia rickettsii: California

Almost 10,000 ticks have been tested for SFG *Rickettsia* from California **ONLY THREE** have tested positive for *R. rickettsii*!



Pacific Coast Tick
(*Dermacentor occidentalis*)



Brown Dog Tick
(*Rhipicephalis sanguineus*)



Brown Dog Tick
(*Rhipicephalis sanguineus*)

**What tick stage vectors
R. philipii to people?**

Transovarial and Transtadial Transmission



Male

Female



Eggs

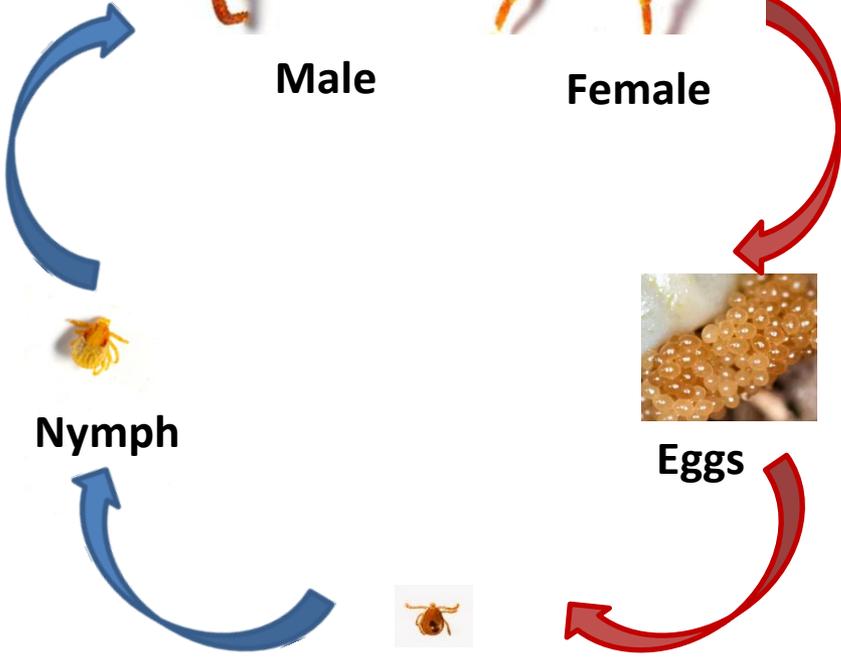


Larva

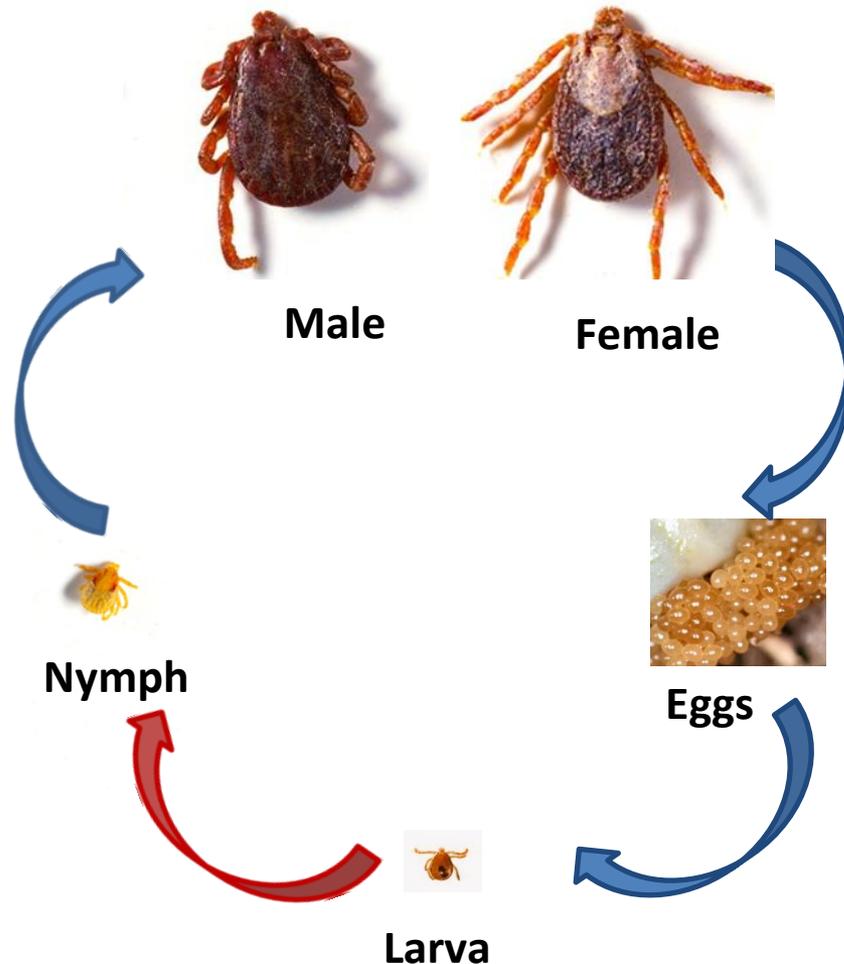


Nymph

- *Does R. philipii* transmit transovarially (from female to offspring)?
- *Are larvae infected?*

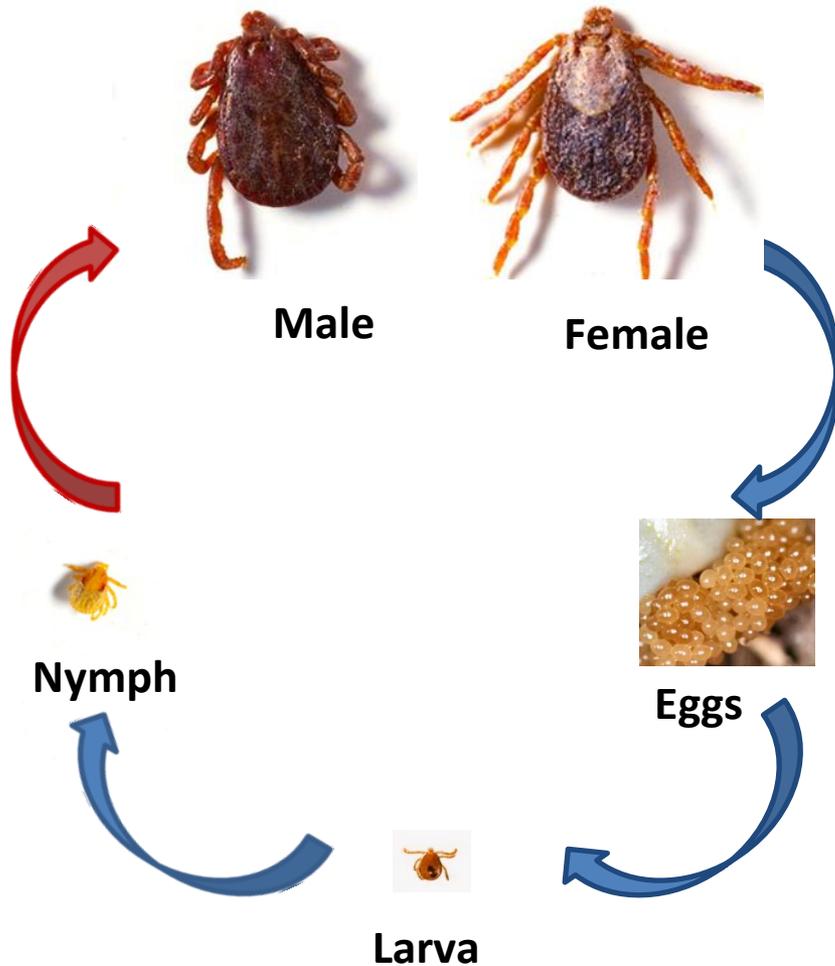


Transovarial and Transstadial Transmission



- *Is R. philipii effectively transmitted between life stages?*
 - *Transstadial transmission?*

Transovarial and Transstadial Transmission



- *Is R. philipii* effectively transmitted from life stages?
 - *Transstadial transmission?*

***Dermacentor occidentalis* tested for *Rickettsia*:
Lake, Sonoma, and Mendocino Counties
(2008-2014)**

<u>Stage</u>	<u>Number</u>
Larva	472
Nymph	398
Adult	1,586

***Dermacentor occidentalis* tested for *Rickettsia*: Lake, Sonoma, and Mendocino Counties (2008-2014)**

<u>Stage</u>	<u>Number</u>	<u><i>R. philipii</i> positive</u>
Larva	472	2 positive pools (0.4% MIP)
Nymph	398	
Adult	1,586	

MIP, minimum infection prevalence

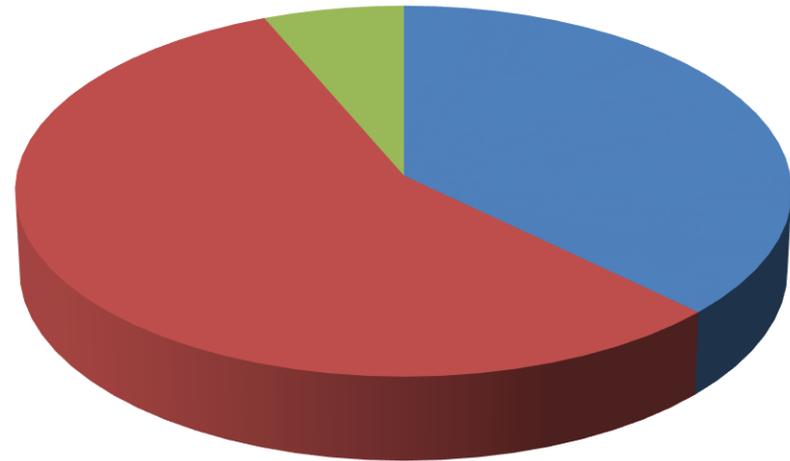
***Dermacentor occidentalis* tested for *Rickettsia*: Lake, Sonoma, and Mendocino Counties (2008-2014)**

<u>Stage</u>	<u>Number</u>	<u><i>R. philipii</i> positive</u>
Larva	472	2 positive pools (0.4% MIP)
Nymph	398	5 (1.3%)
Adult	1,586	16 (1.0%)

MIP, minimum infection prevalence

Pacific Coast Tick Human Biting Records

- 171 human bite records were recovered from CDPH surveillance database
- Nymphs most commonly bite people
- Larvae were found to bite people too!



■ Adult ■ Nymph ■ Larvae

Pacific Coast Tick

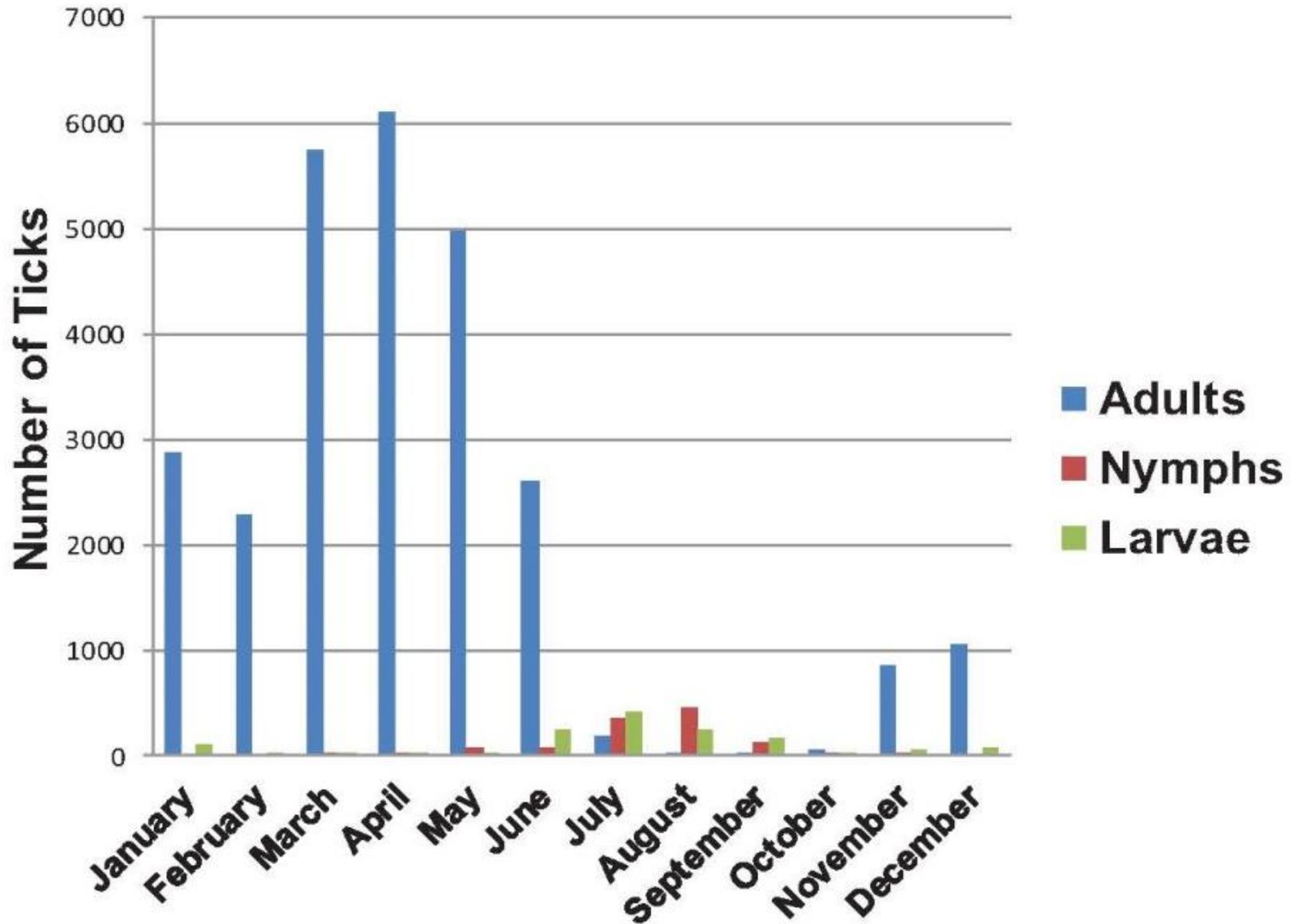
Dermacentor occidentalis

Despite being a common human biting tick...

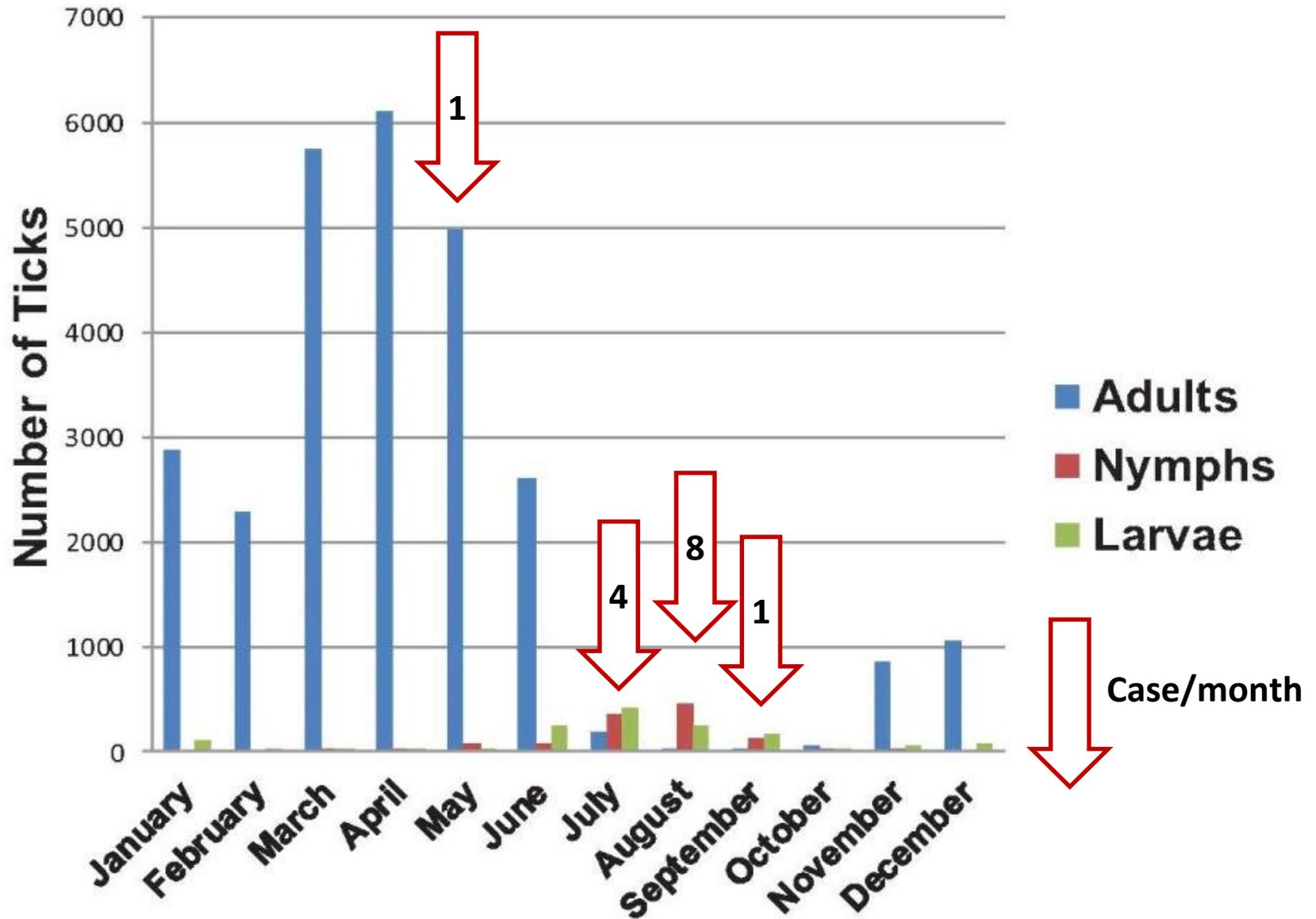
- When is each life stage active?
 - When are people at risk of tick bite?
 - When are people at risk of acquiring PCTF?
- What type of habitat is preferred by each life stage
 - Are there especially risky habitats for people?



Seasonality – *Dermacentor occidentalis*



Seasonality – *Dermacentor occidentalis*



Nymphs and Larvae: Vectors of PCTF



Supporting evidence:

- Both larvae and nymphs quest during summer
 - Coincident with PCTF cases!
- Tick bite records support role of nymphs in transmission
- Larvae/ multiple eschars?



Rickettsia philipii Reservoir Hosts?

- Unknown vertebrate host(s)...
- Common host species for *D. occidentalis* include **mammals** such as: Jackrabbits, Ground Squirrels, and Deer
- Due to transovarial transmission ticks likely reservoir host as well as vector



Rickettsia philipii



Dermacentor occidentalis (Pacific Coast Tick)

- Pacific Coast Tick Fever
- **Eschar**, fever, rash rare
- Multiple eschars
- US Range: California

Rickettsia parkeri



Amblyomma maculatum (Gulf Coast tick)

- *Rickettsia parkeri* rickettsiosis
- **Eschar**, fever, rash rare
- Multiple eschars (rare)
- US Range: Southeastern US

Collaborators – EcoEcology of *Rickettsia philipii*



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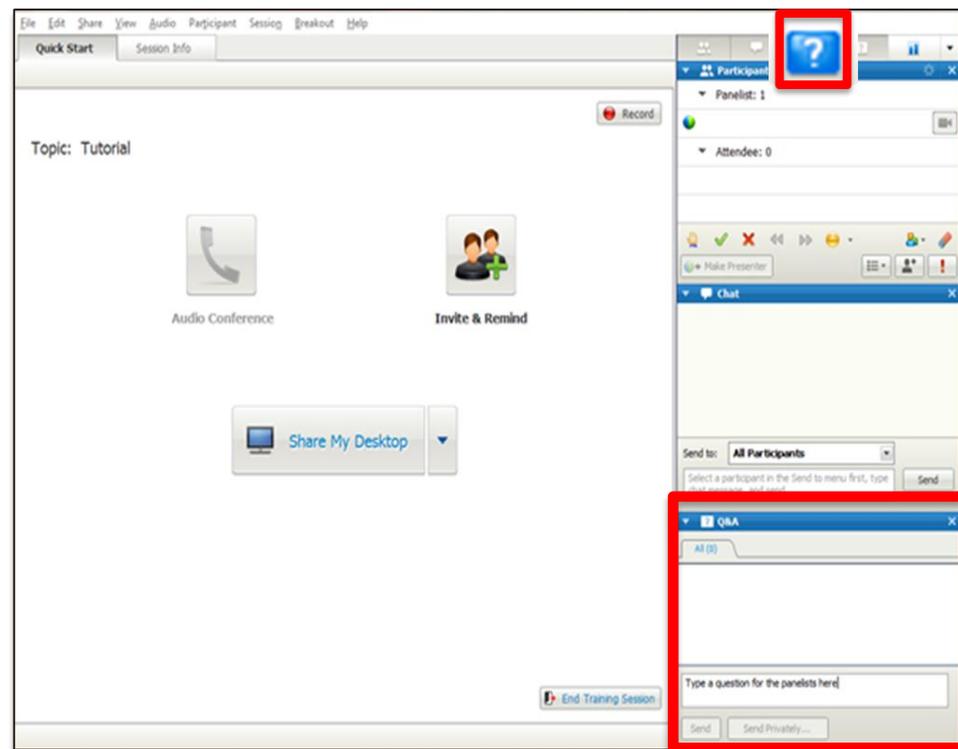
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- Send questions to All Panelists
- Questions will be answered during the Q&A period



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