Rocky Mountain Spotted Fever: Timely Recognition and Treatment

HS Clinical Rounds

May 10th, 2012

Host: Susan Karol, MD;
IHS Chief Medical Officer

Presenter: Marc Traeger, MD;
Whiteriver IHS Hospital

Objectives for Today's Rounds

- Understand the critical importance of timely recognition of Rocky Mountain Spotted Fever
- List the appropriate approach to diagnosis and treatment
- Identify key community-based prevention strategies

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- This activity is designated 1.0 contact hours for nurses.

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Topics for Future Rounds

June 7, 2012: *"Wound Care: A Multi-Disciplinary Approach"*
John J. Farris, MD; CMO, IHS Oklahoma Area

July 12, 2012: *"The Baby Friendly Hospital Initiative"*
Suzan Murphy RD MPH; Phoenix Indian Medical Center

August 9, 2012: *"An Update on the IHS Diabetes Standards of Care"*
Ann Bullock, MD; Cherokee Hospital

Sept 13, 2012: *"An Overview on Tele-Stroke Services"*
Dr. Bart Demaerschalk; Mayo Clinic

Meet the Presenter

Marc Traeger, MD is the preventive health officer and a staff physician at the Whiteriver IHS Hospital. Following a CDC epidemiology fellowship, in 2003 Dr. Traeger served as one of the primary investigators of an outbreak of Rocky Mountain Spotted Fever (RMSF) on the Ft. Apache Indian Reservation, Arizona. Since that time, he has been involved in the continuing investigation, surveillance, and intervention of RMSF on the Ft. Apache Indian Reservation, and has provided expertise to other Tribes identifying RMSF cases and outbreaks. Dr. Traeger has also contributed to a multi-agency workgroup to identify needs in tick-born illness at the CDC in 2009 and to a 2010 Institute of Medicine Report **Critical Needs and Gaps in Understanding Prevention, Amelioration, and Resolution of Lyme and Other Tick-Borne Diseases The Short-Term and Long-Term Outcomes - Workshop Report**. He works closely with the CDC, the AZ Department of Health Services, and other agencies and has co-authored 5 publications or reports on the topic of RMSF. Dr. Traeger completed his medical school training at the University of New Mexico School of Medicine and completed a Family Medicine residency program at the University of Arizona.

Rocky Mountain Spotted Fever (RMSF) Timely Recognition and Treatment

Marc Traeger, MD

Whiteriver Service Unit, IHS

With thanks to

Joanna Regan, MD, MPH, FAAP & Jennifer McQuiston DVM

Rickettsial Zoonoses Branch, CDC

Objectives

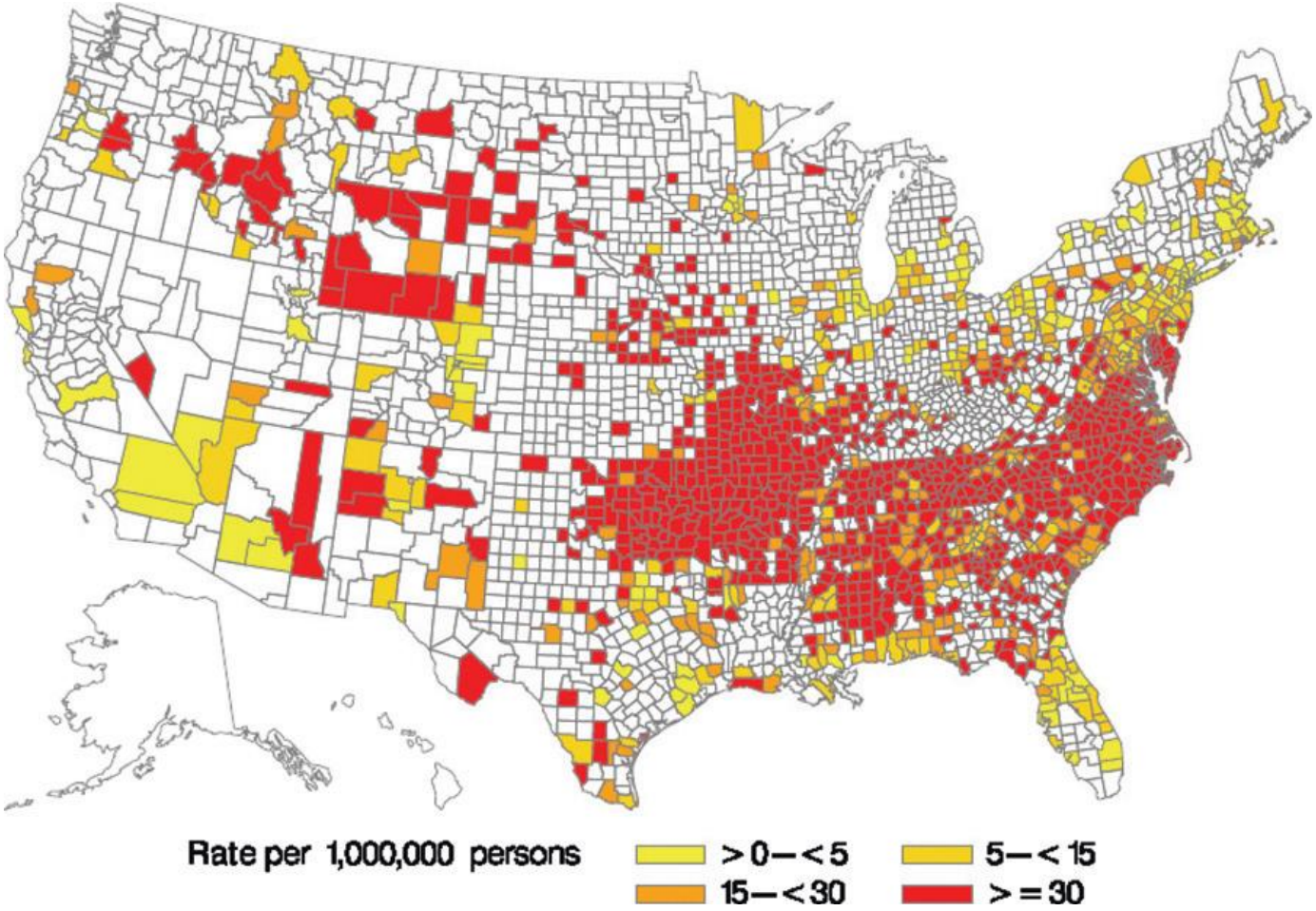
- Give background information about RMSF
- Contrast differences of RMSF in Arizona & other states
- Discuss diagnosis of RMSF
- Discuss treatment of RMSF
- Discuss bad outcomes & predictors
- Describe how to report cases

RMSF: Background

- Caused by *Rickettsia rickettsii*
  - Tickborne , no person-to-person transmission
  - Found in several species of ticks throughout North and South America
- Intracellular bacterial pathogen
- Infects endothelial cells, causes widespread vascular damage
- Effectively treated with doxycycline
  - Other antibiotics (even broad spectrum) ineffective

RMSF Incidence, U.S.

by county, 2000-2007

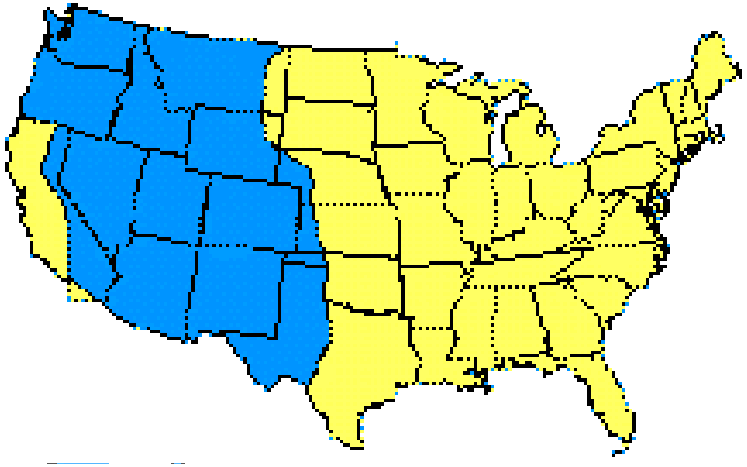


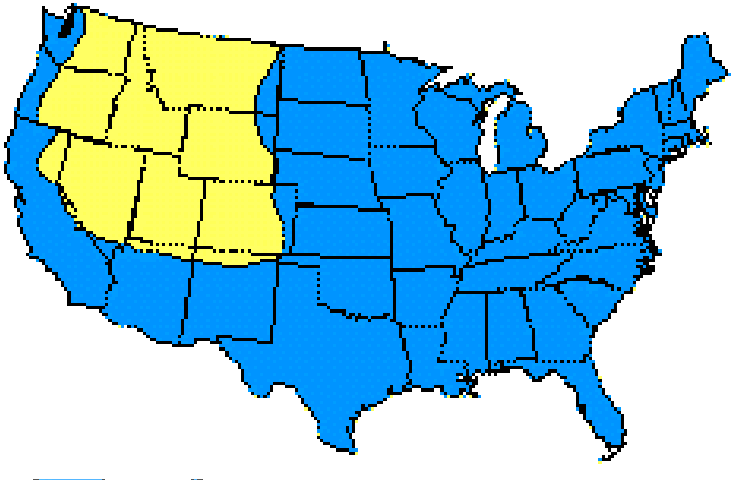
Openshaw, et. al. Am J Trop Med Hyg. 2010 July; 83(1): 174–182.

The Primary U.S. Tick Vectors of RMSF

Dermacentor variabilis
American dog tick

Dermacentor andersoni
Rocky Mountain wood tick

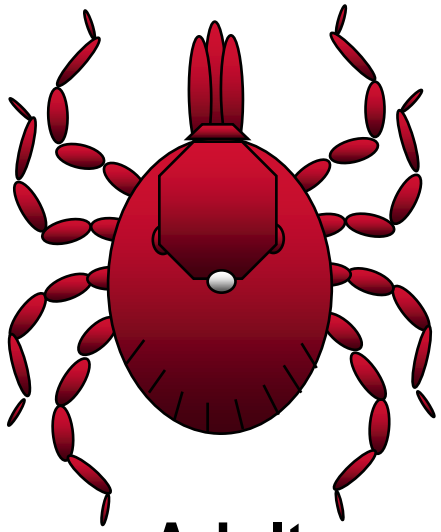




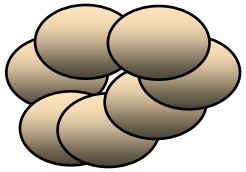
The Primary U.S. Tick Vectors of RMSF

Brown Dog Tick: Confirmed RMSF tick vector in Arizona

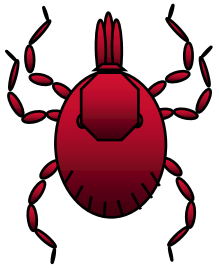
Generalized Tick Life Cycle



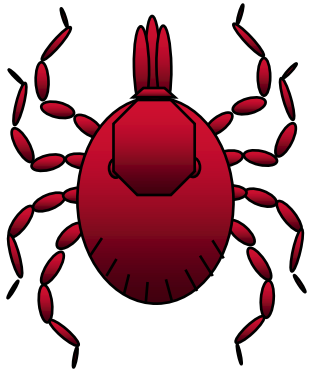
Adult



Eggs



Larva



Nymph

RMSF in Arizona

- **The Brown Dog Tick (*Rhipicephalus sanguineus)* was found to be the vector of RMSF in Arizona**

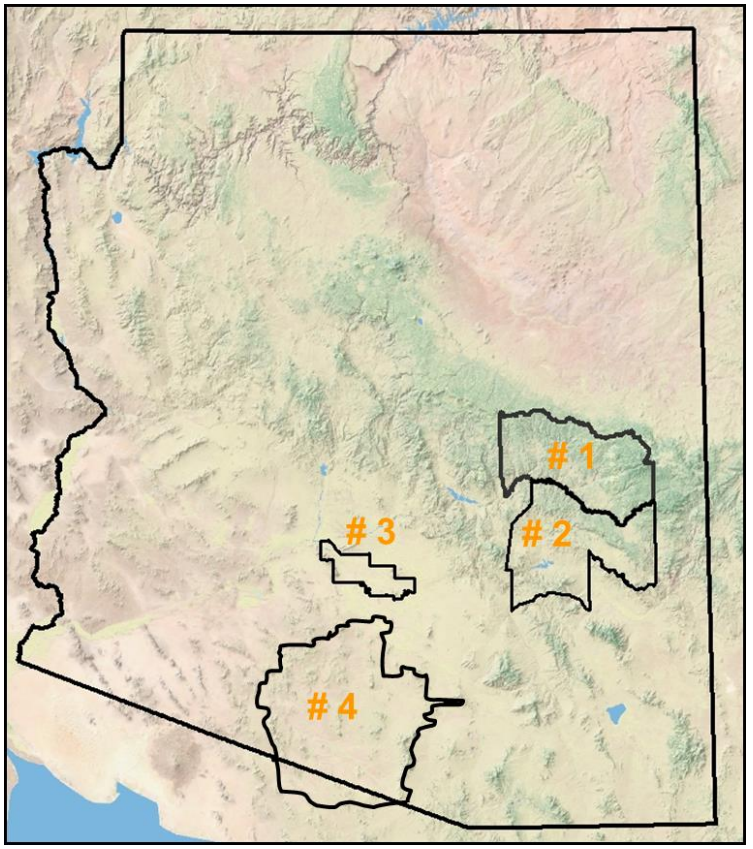
- **This tick is very common and can live in and around houses**

- **Feeds primarily on dogs during each of it's life stages**

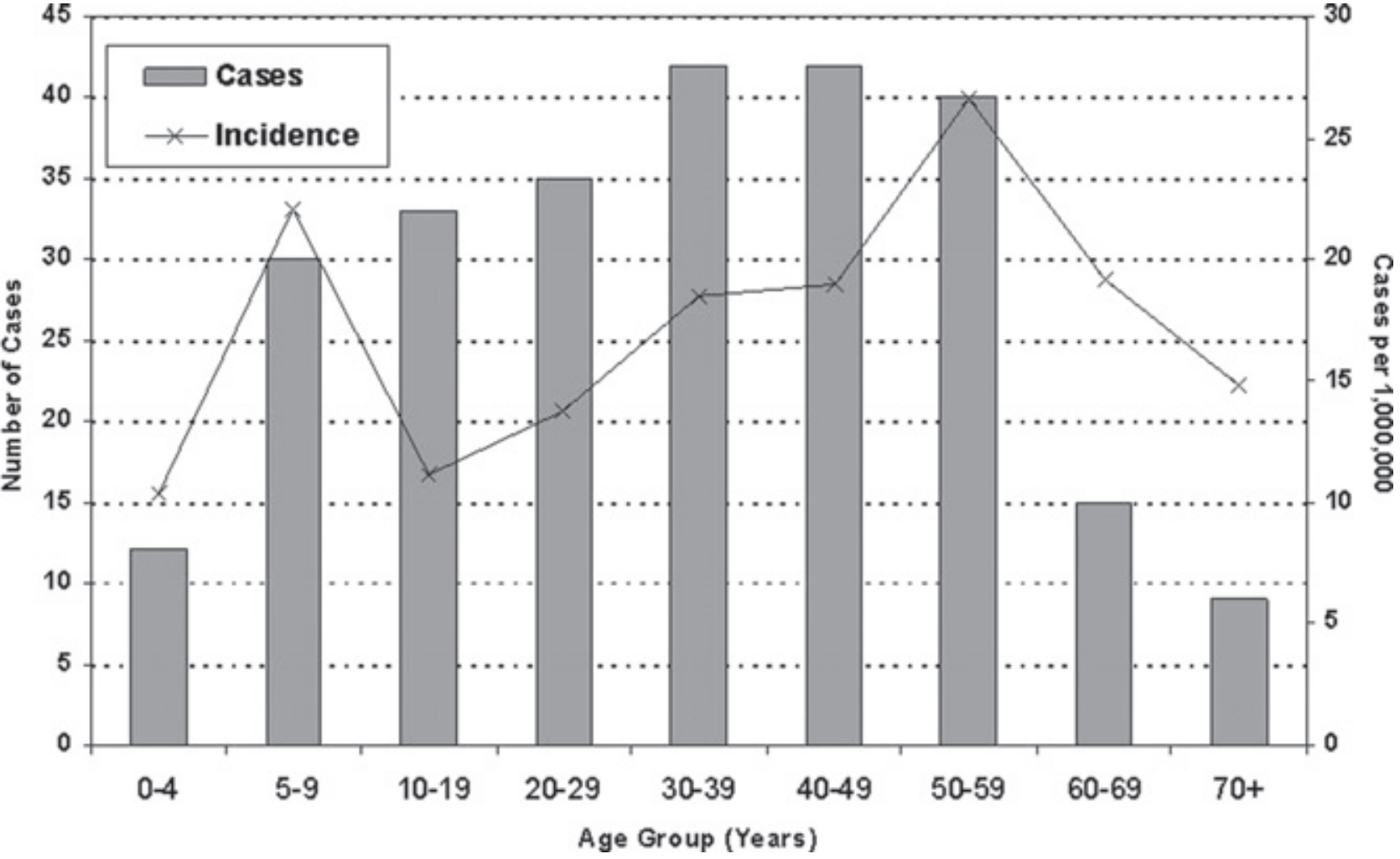
- **Can remain active year round**

RMSF in Arizona

- From 2002-present, over 250 cases of RMSF have been reported in Arizona
- Highest incidence in the U.S.
  - Incidence rate ~ 300 times higher than expected
- There have been 18 deaths
  - Case fatality 7%, ~ 15 X higher than the U.S. rate

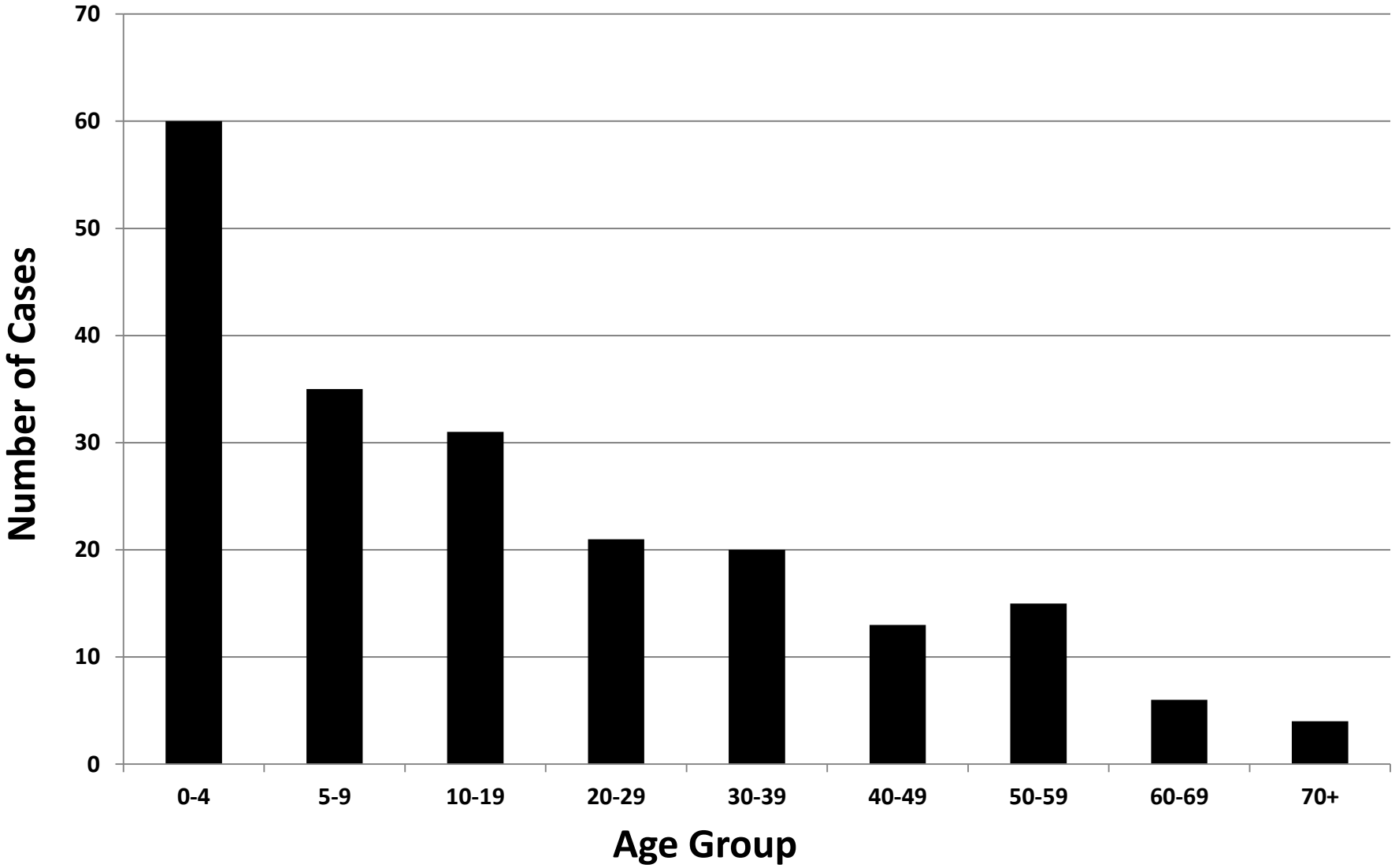


National AIAN Cases & Incidence by Age Group 2001-2005

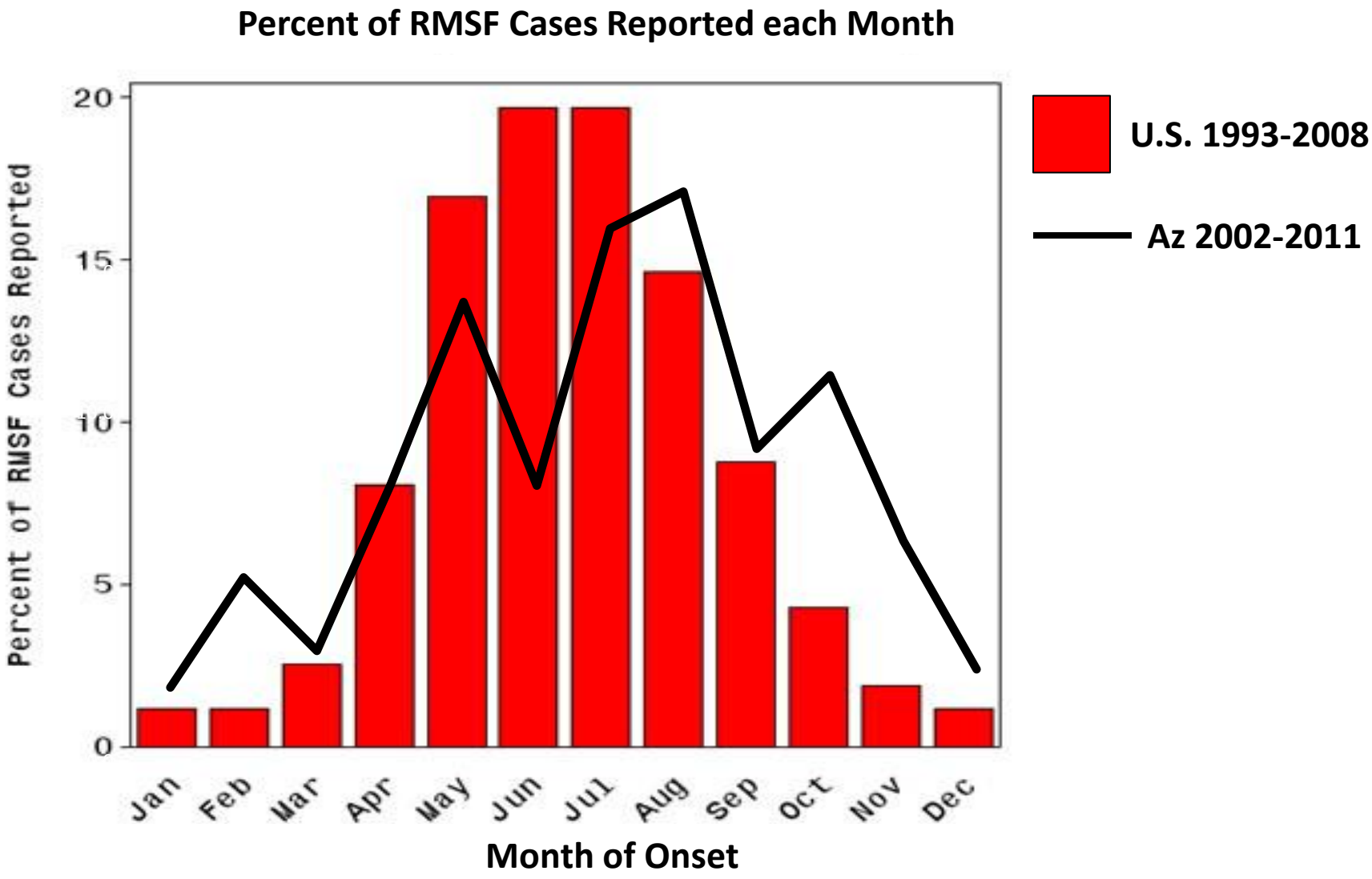


Holman et. al. Am. J. Trop. Med. Hyg., **80(4), 2009**

E. Arizona AIAN Cases by Age Group 2002-2011



Seasonality of RMSF in U.S. & Arizona



RMSF in Arizona

Several factors put American Indian tribes at risk

- large population of free roaming dogs
- lack of animal control
- lack of adequate waste disposal
- limited access to pest control

RMSF – Initial Presentation

- Most patients present for medical care within 2 days of onset of fever
  - Patients may return several times as the disease progresses (2.5 visits in AZ)
- Many patients, especially adults, don't have a rash at the time of initial presentation
- Not all patients recall a tick bite (30% report bite in AZ; 40-84% reported previously in other states)

RMSF: Clinical Manifestations

- Early (first 4 days): fever, headache, myalgia, and abdominal pain + N/V/D; light rash may be present
- Thrombocytopenia, hyponatremia, elevated liver enzymes (AST, ALT) may occur
- Late (day 5 or later): definitive petechial rash, altered mental status, seizures, cough, dyspnea, arrhythmias, hypotension, severe abdominal pain, multi-organ involvement

Symptoms - E. Arizona Cases

Symptom	Cases	%
Fever	164/202	81.2
Rash	130/192	67.7
Fever and Rash	108/190	56.8
Fever and Tick	58/131	44.3
Rash and Tick	48/128	37.5

More symptoms for Arizona RMSF

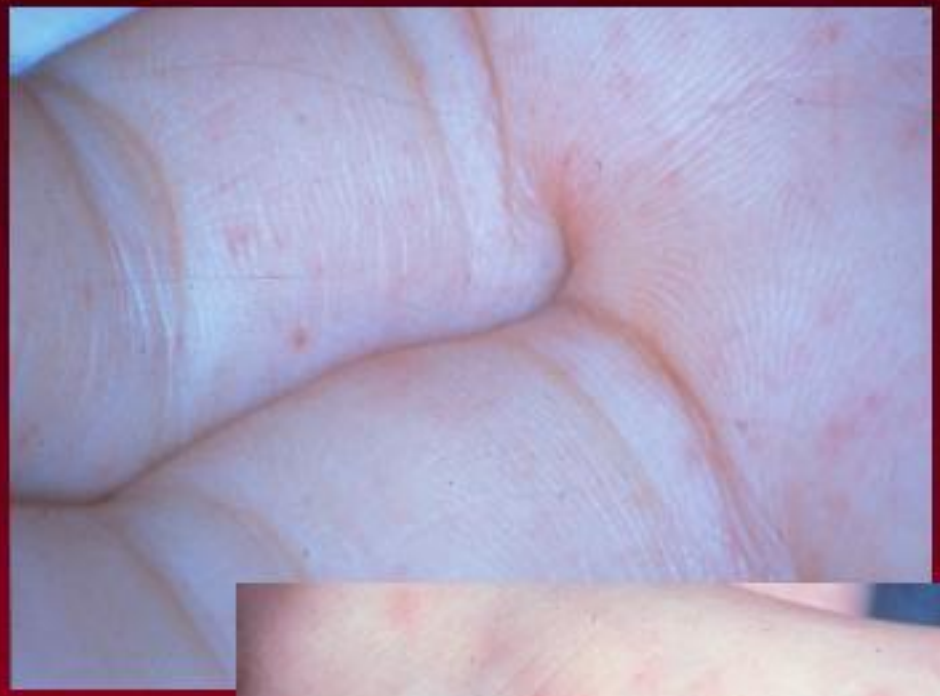
Symptom	Cases	%
Nausea*	74/156	47.4
Abdominal pain*	46/154	29.9
Anorexia*	48/125	38.4
Dizziness	21/110	19.1
Red, draining eyes	22/148	14.9
Neck pain	16/141	11.3
Mental status change	29/169	17.2
Peripheral edema	18/147	12.2
Cough	*68/169*	*40.2*
Nasal congestion	*43/155*	*27.7*
Ear pain	*13/126*	*10.3*
Irritability	*20/123*	*16.3*

*(Early symptoms associated with fatality

RMSF: The Rash

- Generally not apparent until day 2-5 of symptoms (only seen in 68% of AZ patients, 66-97% other U.S. reports)
- Appeared on average day 2.2 among cases; day 4-5 among fatalities
- Begins as 1 to 5 mm macules progressing to maculopapular
- May begin on ankles, wrists, and forearms, spreads to trunk
- Petechial rash is a late finding, occurs on or after day 6
- Rash may be asymmetric, localized, or absent

Rashes of RMSF

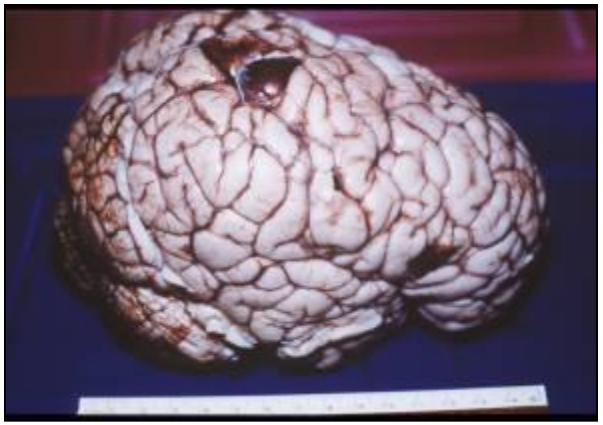


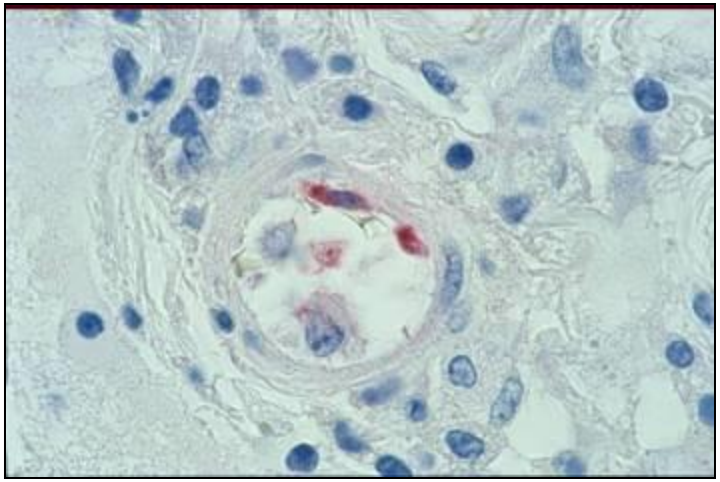
CDC
Centers for Disease Control and Prevention

Outcome by Day of Symptoms that Doxycycline was Started

Day of trxt (N)	# Outpatient (%)	# Hospitalized (%)	# ICU (%)	# fatal (%)
Day 1 (6)	5 (83%)	1 (17%)	0 (0%)	0 (0%)
Day 2 (11)	8 (73%)	3 (27%)	0 (0%)	0 (0%)
Day 3 (9)	4 (44%)	5 (56%)	1 (11%)	0 (0%)
Day 4 (7)	3 (43%)	4 (57%)	1 (14%)	0 (0%)
Day 5 (8)	2 (25%)	6 (75%)	4 (50%)	0 (0%)
Day 6 (9)	0 (0%)	9 (100%)	5 (55%)	3 (33%)
Day 7 (11)	0 (0%)	11 (100%)	4 (36%)	3 (27%)
Day 8 (5)	1 (20%)	4 (80%)	2 (40%)	2 (40%)
Day 9 (4)	0 (0%)	4 (100%)	4 (100%)	2 (50%)

Severe Sequelae





Deaths Attributable to RMSF

- Historic case-fatality rate 20%-80% in untreated patients
- ARDS, DIC and organ failure may begin around day 5 in severe cases
- Disease kills otherwise healthy adults and children
- Median time from symptom onset to death is 8 days
- Recall that patients seek medical care early.
- *Therefore, the cause of death is missed early diagnosis and delay in doxycycline treatment*

Risk Factors for Death

Lack of recognized tick bite

Late onset of rash

Symptoms consistent with more common diseases

Presentation outside of tick season (May-July)

Wrong antibiotic, especially in children

Early presentation to doctor

RMSF: Frequent Initial Diagnoses

1. Viral illness

2. Fever of undetermined etiology

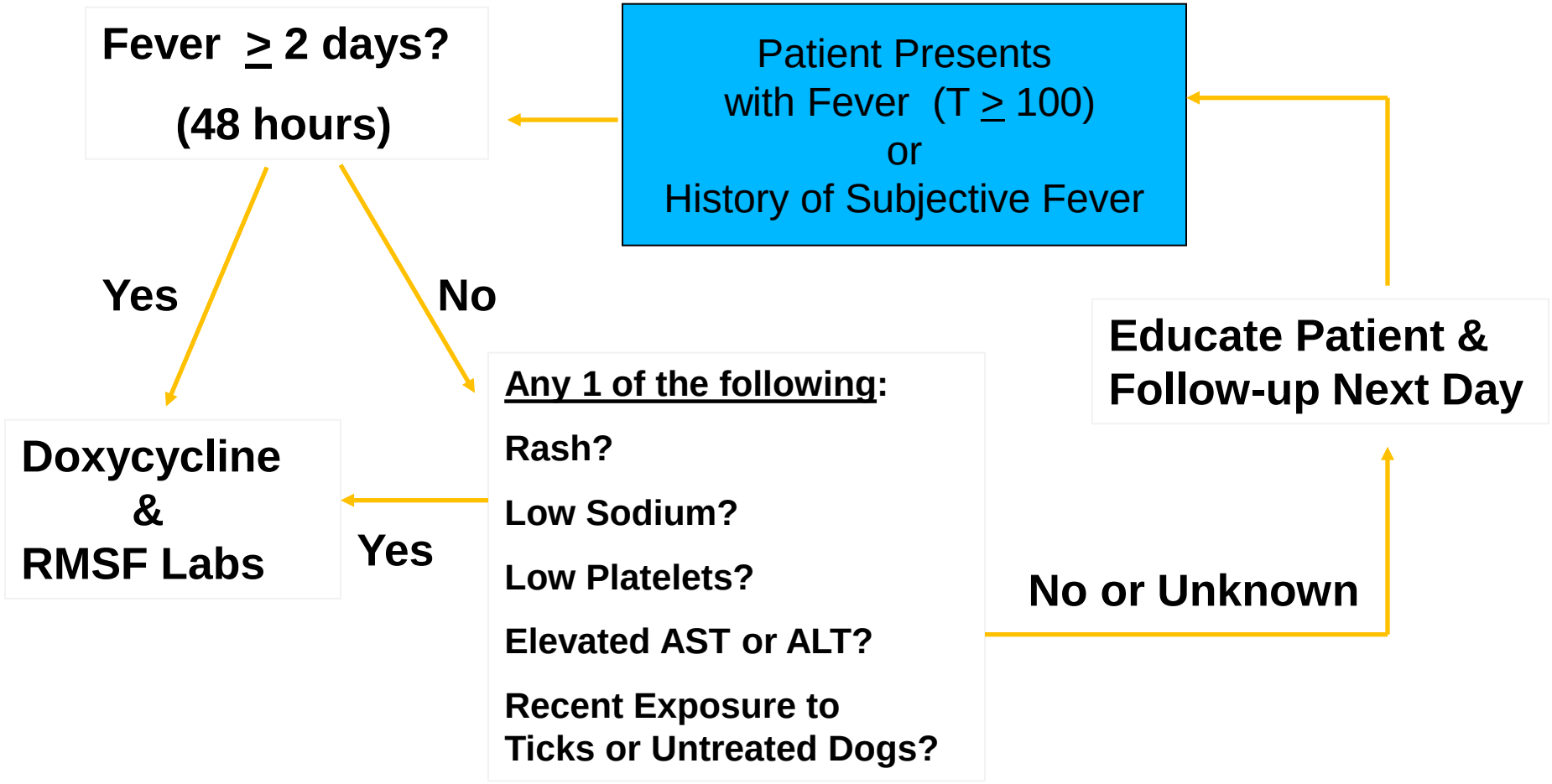
3. Bacterial sepsis (meningococcemia)

4. Upper or lower respiratory tract infections, acute appendicitis, cholecystitis, pyelonephritis

Diagnosis of RMSF

Clinical algorithm for treatment of RMSF in Arizona

The diagnosis and treatment algorithm for AZ



How do I treat RMSF?

RMSF Treatment

- Doxycycline is the drug of choice: clinical response within 24-72 h
  - *Chloramphenicol may be an alternative therapy for some patients with RMSF but less likely to prevent death*
- Other broad-spectrum antimicrobials are not effective, most fatal RMSF cases are on broad-spectrum antibiotics at the time of death

Antimicrobial Therapy of RMSF

Non-pregnant adult
or child ≥45 kg

Doxycycline
100 mg bid
p.o. or i.v.

Child <45 kg

Doxycycline
4.4 mg/kg/day
in 2 divided
doses p.o. or i.v.

Therapy should be continued at least 72 h after defervescence
AND until evidence of clinical improvement

Doxycycline and RMSF in Children

- Doxycycline is drug of choice to treat RMSF in children
- Therapeutic dose has not been shown to cause significant dental staining
- Recommended by AAP and CDC for suspected RMSF
- Withholding doxycycline may result in the death of the child

Antibiotics that fail to treat RMSF & have resulted in fatalities

Azithromycin

Ceftriaxone

Ceftazidime

Vancomycin

Ampicillin/Sulbactam

Clindamycin

Amoxicillin

Gentamicin

How do I confirm a case for reporting purposes?

Diagnostic tests are used for case reporting purposes and not clinical decision making. There is no RMSF test that can be used for clinical decision making.

Confirmation of *R. Rickettsii*

- Serology (RMSF titer)
  - Indirect immunofluorescence assay (IFA)
  - Requires paired sera (acute and convalescent)
  - Look for a rise (4-fold) in antibody titers for confirmed infections
  - Positive single titers or titers that do not rise are considered probable cases

- PCR (polymerase chain reaction)
  - Available at CDC. Can give a rapid result (48 hours)
  - Skin biopsy (2-4mm)
  - Whole blood of severely ill/fatal cases

More on Serology for RMSF

- Test for IgG instead of (or in addition to) IgM
  - IgM and IgG rise around the same time, and IgM can remain elevated for a long time
  - IgM tests for RMSF are prone to false positive results
- Test both samples (acute & convalescent) at the same lab, and ideally at the same time
- The acute serum is usually negative – do not stop treatment!
- Do not test or treat someone who has a tick bite and no symptoms. Most ticks do not carry *R. rickettsii.*
  - Watch them for symptoms
  - Tick bites indicate a public health concern and should be reported to the health department.

Surveillance and Reporting

- RMSF is a nationally reportable disease
- Cases should be reported to State Health Department
- Reports then submitted to CDC
- Reports help us know the level of activity and target prevention and control efforts
- Notify your health department immediately and they can investigate and treat the house

RMSF Prevention

- Disease awareness and recognition
- Treat dogs with collars year round
- Treat the yard and home
- Careful inspection and removal of ticks
- Where there is one case, there are likely to be others - Prevent clusters by alerting the health department and family

RMSF Prevention

- Wear light-colored clothing
- Perform tick checks on yourself and family members
- Tuck your pants legs into your socks
- Apply repellant (DEET) to discourage tick attachment

Electronic Health Record (EHR) patient education

- EHR contains RMSF patient education codes that should be entered when teaching patients about Rocky Mountain Spotted Fever

Summary

- RMSF can be rapidly fatal, even in previously healthy people
- Early disease difficult to diagnose even for experienced physicians
- Do not delay treatment pending lab confirmation
- Use the algorithm to diagnose and treat
- Use RMSF titers for surveillance purposes, not for treatment decisions

Summary Cont'd

- Doxycycline the drug of choice for all patients
  - Should be administered as soon as disease is suspected
  - Should be administered urgently in patients with signs of sepsis
- Prevent cases by educating patients about treating dogs and yards
- Prevent clusters by notifying families and alerting the health department immediately

Questions?

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Environmental Health: Kenny Hicks, IHS Phoenix Area, kenny.hicks@ihs.gov, 602-364-5078

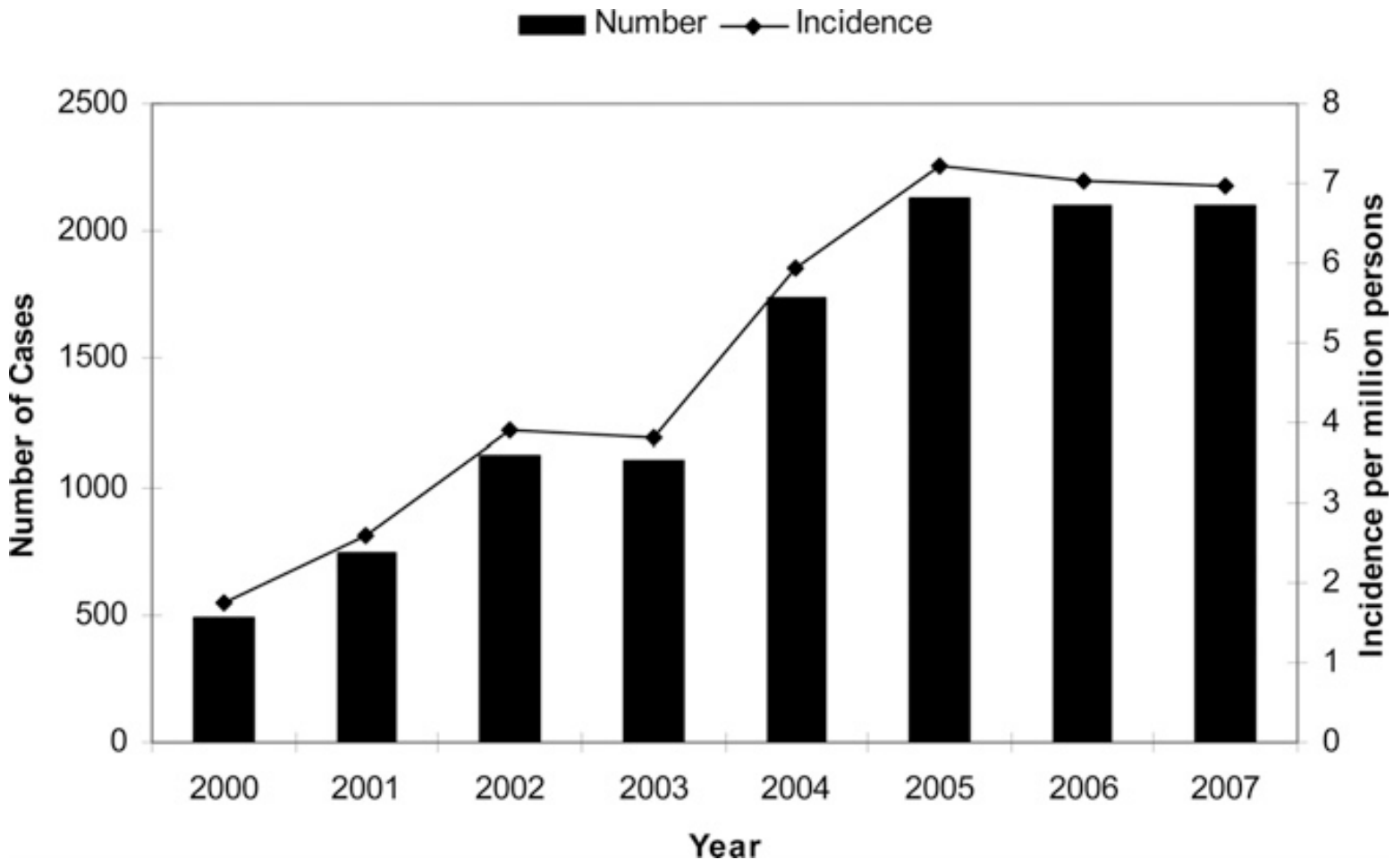
CDC RMSF Website: www.cdc.gov/rmsf

Jennifer McQuiston, CDC, jmcquiston@cdc.gov, 404-639-0041

Joanna Regan, CDC; jregan@cdc.gov, 404-639-4341

Thank you

RMSF Incidence, U.S.



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