



# Tick-borne Infections

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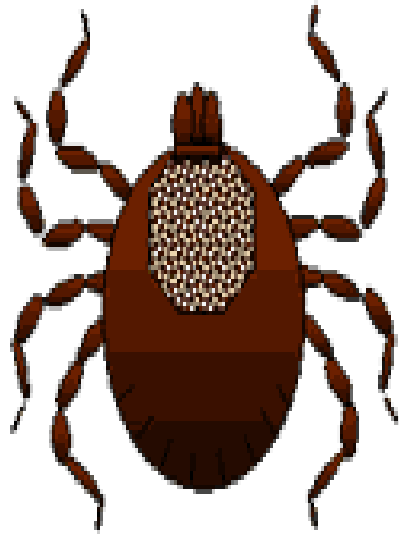
# Ticks in General

**Class: Arachnida**

□ **3 families, 2 of medical importance**

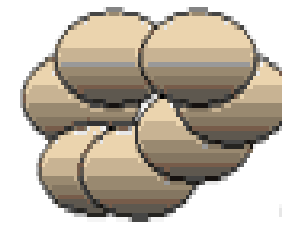
→ **Ixodidae (hard ticks): over 650 species**

→ **Argasidae (soft ticks): over 170 species**



**Female**

Feeds on large and medium sized mammals  
and humans

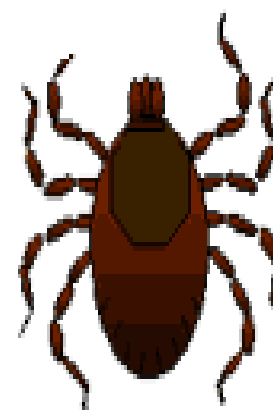


**Eggs**



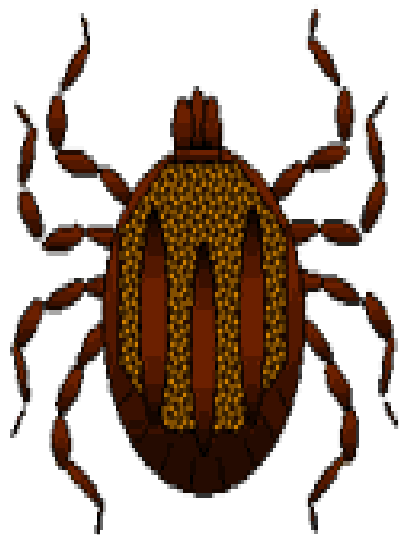
**Larva**

Feeds on small  
mammals



**Nymph**

Feeds on small and medium sized  
mammals



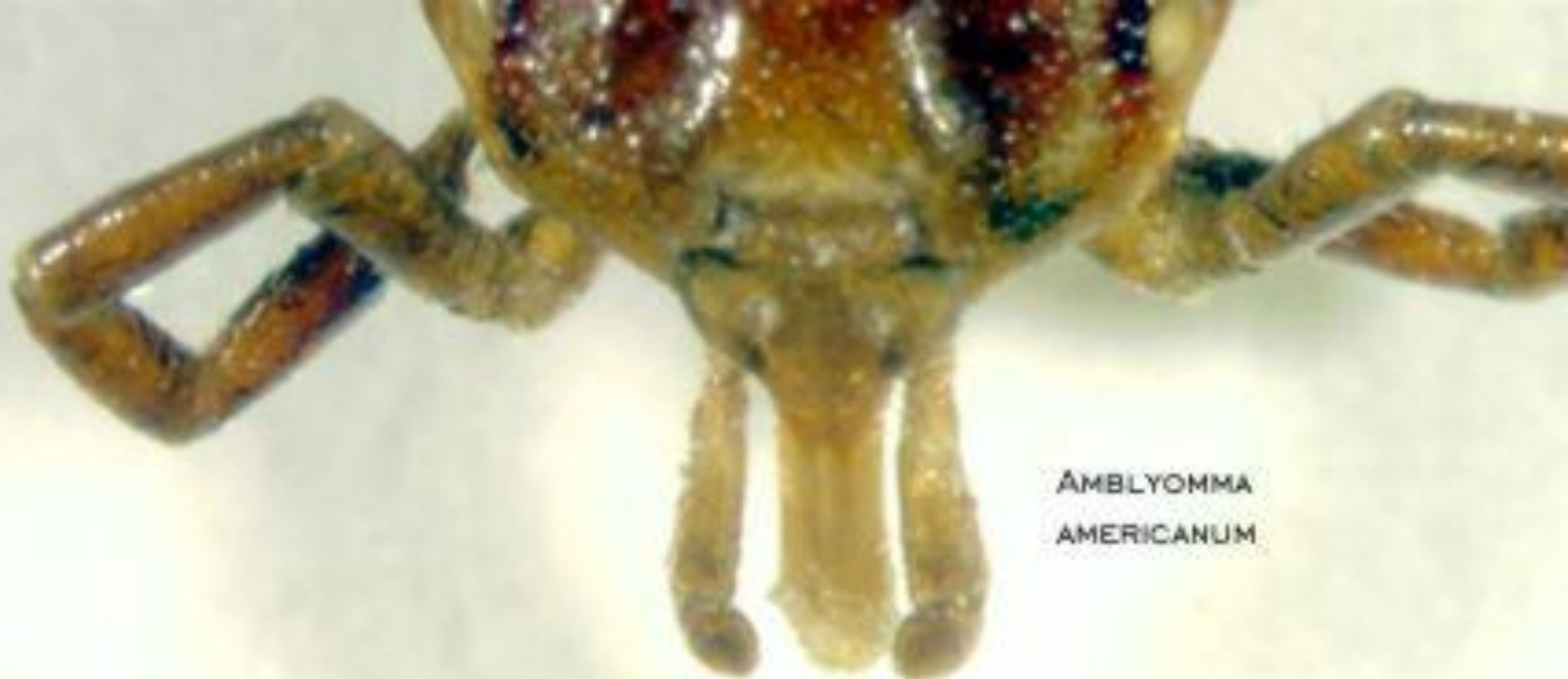
**Male**



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# How Ticks Transmit Disease

- Pathogens are harbored in the midgut
- Prostaglandins in tick saliva are passed to the skin at attachment
- Decrease in host IL-1, IL-2, TNF-alpha and interferon gamma
- Apyrase and coagulation inhibitors



AMBLYOMMA  
AMERICANUM



DERMACENTOR  
VARIABILIS



# Tick-borne Infections

## Bacteria

Ehrlichiosis

Lyme disease

Q fever

Rocky Mountain Spotted  
Fever

Tularemia

Southern Tick Associated  
Rash Illness

*Rickettsia parkeri*

## Viruses

Colorado tick fever

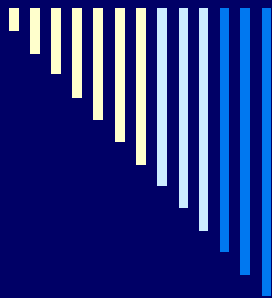
Hemorrhagic fever

Encephalitis

## Parasites

## Toxins

Tick paralysis



# MMWR™

## Morbidity and Mortality Weekly Report

Recommendations and Reports

March 31, 2006 / Vol. 55 / No. RR-4

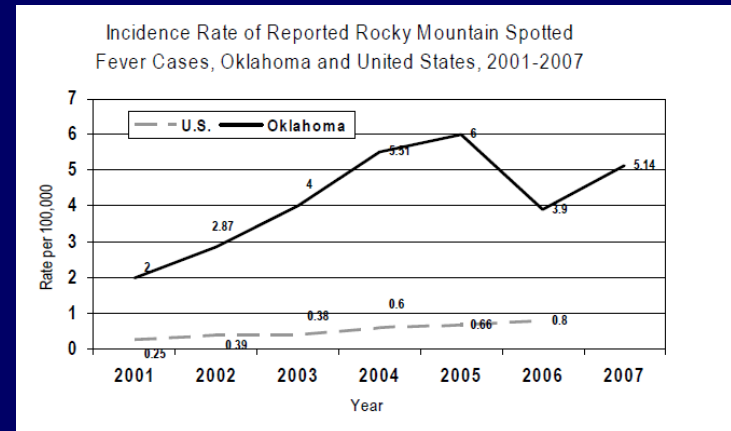
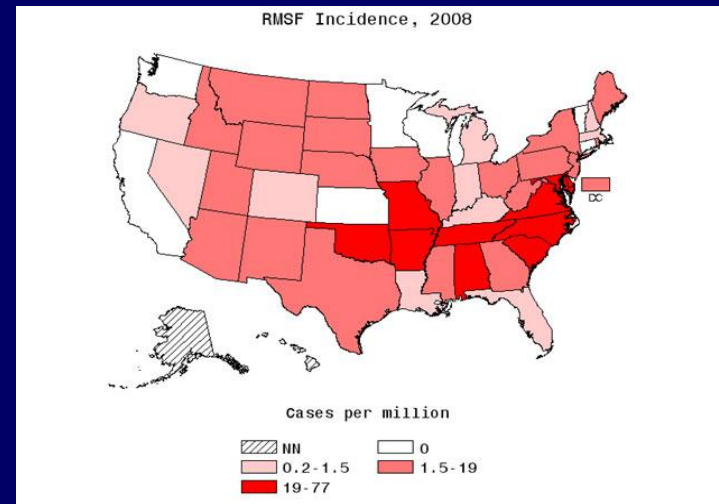
### **Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever, Ehrlichioses, and Anaplasmosis — United States**

**A Practical Guide for Physicians and Other  
Health-Care and Public Health Professionals**



# Rocky Mountain Spotted Fever

- Most common rickettsial disease in US
- 250-2500 cases/year
- 342 cases in OK 2010

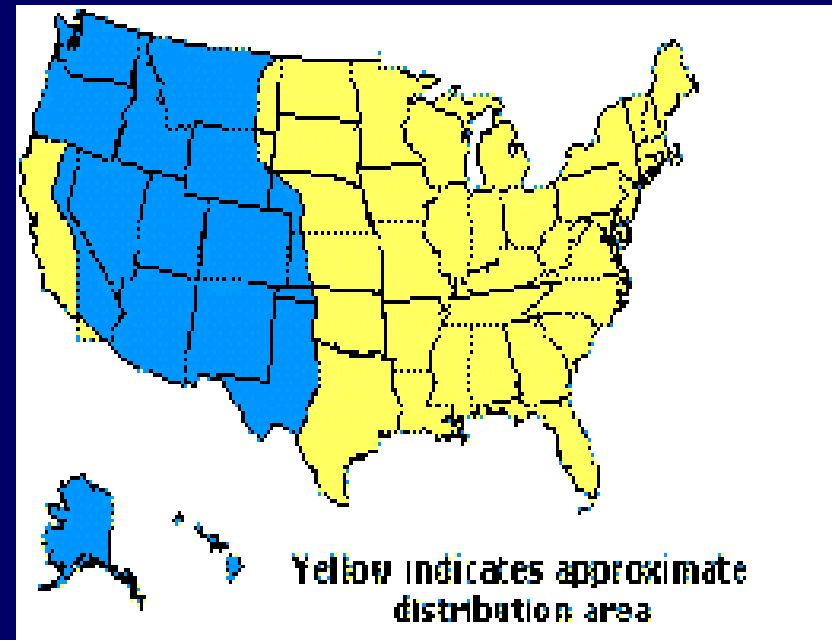


# RMSF

- Etiologic agent: *Rickettsia rickettsii*
- Vectors: *Dermacentor variabilis* (dog tick), *D. andersoni* (wood tick), *Amblyomma americanum* (lone star tick)



*D. variabilis*





# Clinical Presentation

- ❑ Incubation period: ~ 7 days (2-14)
- ❑ Abrupt onset severe HA, F/C, prostration, myalgias, nonproductive cough (later)
- ❑ GI manifestations very common
- ❑ CNS: meningitis, meningoencephalitis
- ❑ Death: 1-2 weeks after symptom onset in 4-8% (untreated)

# RMSF Rash



- ❑ Macular rash develops day 2-6 (90%): wrists, ankles, palms, & soles then centrally
- ❑ Lesions become petechial, hemorrhagic
- ❑ Vasculitis

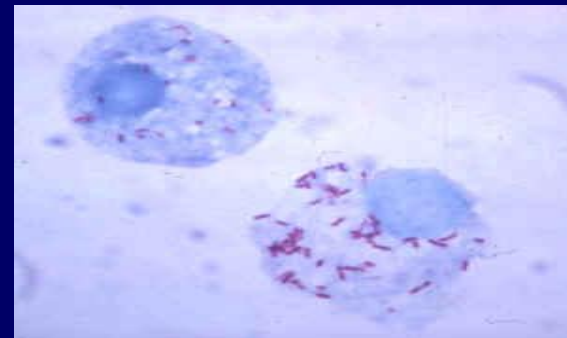
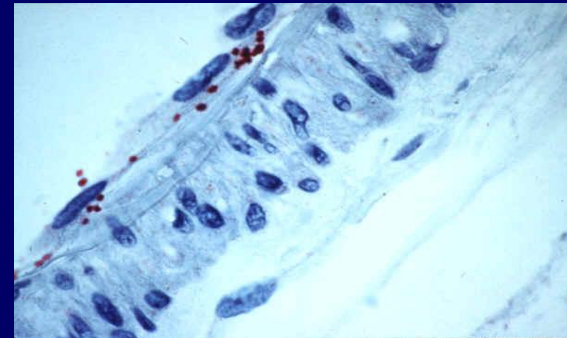
# RMSF Rash



# Diagnosis

- Clinical & epidemiologic
- Nonspecific lab findings: anemia, ↓Na, azotemia, ↓plts, ↑AST
- RMSF PCR from rash site is now preferred
- IFA: IgM +: 1-2 w but may be false +  
IgG +: 4-6 w

- Immunostaining: skin biopsy prior to therapy





# Diagnosis

- Confirmed: Clinically compatible case that is laboratory confirmed.
- Probable: Clinically compatible that has supportive laboratory results
- Suspect: Lab evidence of past or present infection but no clinical information available



# Treatment

- *Begin treatment for presumptive diagnosis*
- Doxycycline 100 mg every 12 hrs is very effective
- Chloramphenicol
- Levofloxacin is an alternative
- Duration: 7-14 days

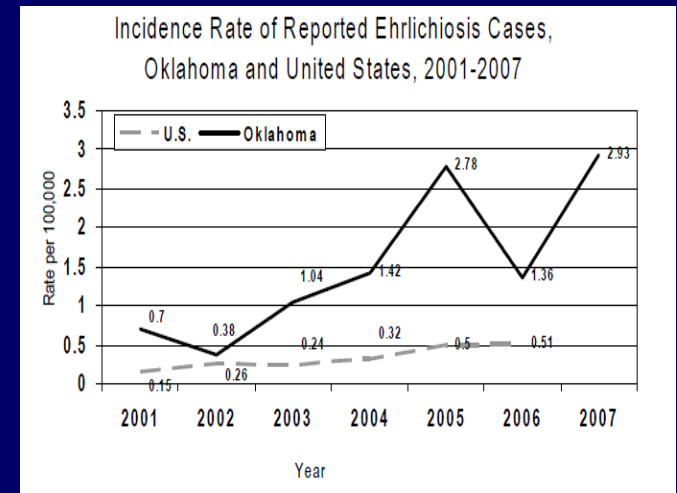
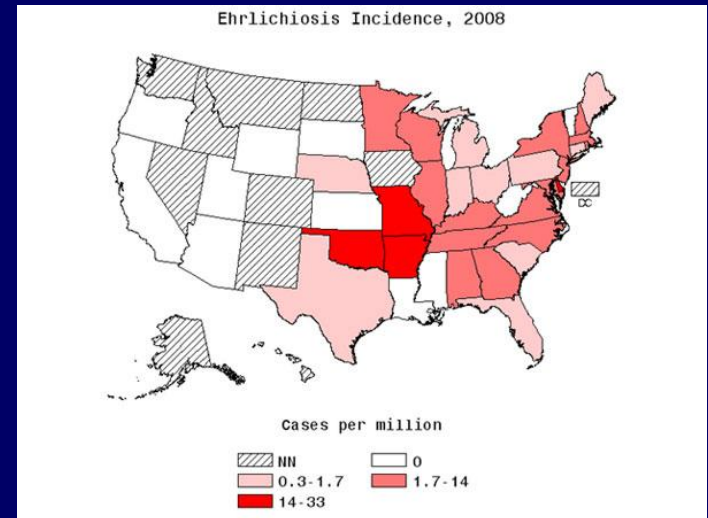


# Ehrlichiosis

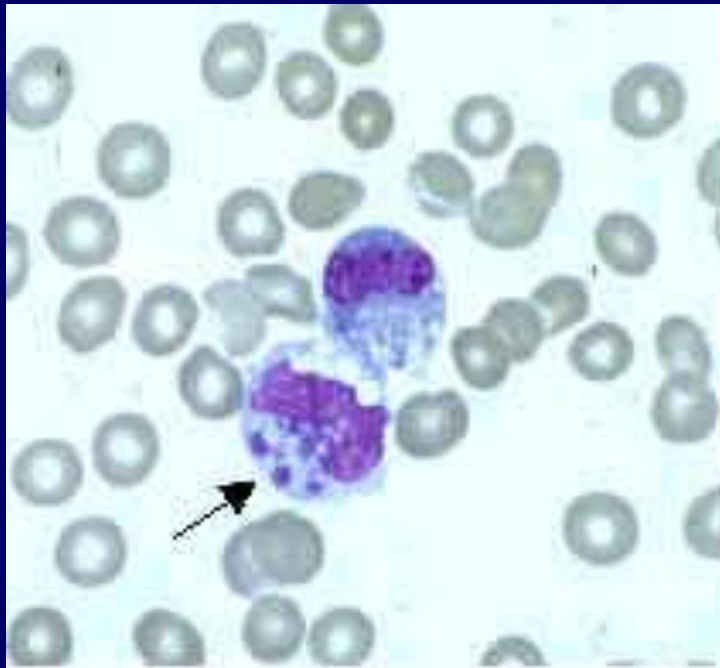
- Obligate intracellular bacteria form distinct microcolonies called morulae
- 3 diseases:
  - **Human Monocytic Ehrlichiosis**
  - **Human Granulocytic Anaplasmosis**
  - ***E. ewingii***
- “Rocky Mountain Spotless Fever”

# Ehrlichiosis

- ~215 cases HME/year
- 47 cases in OK in 2006
- 106 cases in OK in 2007
- 147 cases in OK in 2009 (most recent)



# Human Monocytic Ehrlichiosis (HME)



- Pathogen: *E. chaffeensis*
- Vector: *A. americanum*, *D. variabilis*
- 90% recall tick bite
- Symptoms begin 7-21 days after bite

# Distribution of *Amblyomma americanum*





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## ***Ehrlichia ewingii***

- **Canine granulocytic ehrlichiosis**
- **Vector: *A. americanum***
- **Antigenic similarity to *E. chaffeensis* and *E. canis***
- **First 4 cases of human infection reported July, 1999 (NEJM 341:148-55)**



# Clinical Findings

<u><i>Sign or Symptom</i></u>	<u><i>% Abnormal</i></u>
Fever	97-100
Chills/rigors	65-85
Malaise	85-95
Myalgias	65-95
Headache	60-85



# Laboratory

<u><i>Finding</i></u>	<u><i>% Abnormal</i></u>
Leukopenia	50-60
Thrombocytopenia	60-90
Elevated AST	60-80
Elevated ALT	60-90
Anemia	50
Elevated BUN & creatinine	30-70



# Diagnosis

## Serology (IFA)

- Minimum peak of 1:80
- Fourfold change
- Positive: week 3
- Peak: week 6
- Cross-reactivity

## Morulae

HME: ~7%

HGE: 20-80%

*E. ewingii* ??

## Culture

- ## Species-specific PCR



# Treatment

- Doxycycline 100 mg twice daily for 7-10 days for adults  
4.4 mg/kg in 2 divided doses for children <45.4 kg (100 lbs)
- Prompt response to therapy

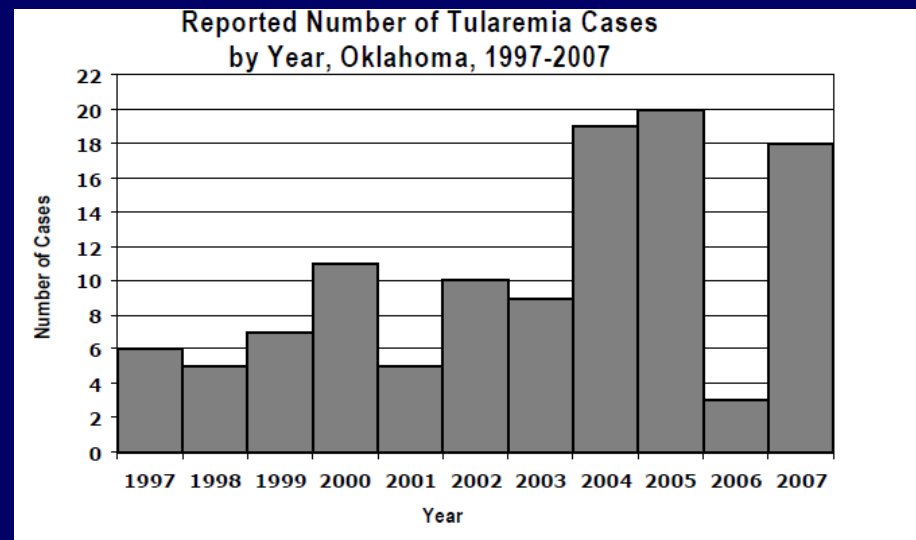
# Tularemia

- Causative agent: *Francisella tularensis*
- Small, gram-negative coccobacillus
- Tick bites account for > 50% cases
- Vectors: *A. americanum*, *D. variabilis* and *D. andersoni*



# Natural Epidemiology

- Worldwide distribution
- Arkansas, Missouri, and Oklahoma reported 53% of all cases from 1990-94
- OK reported 20 cases in 2005
- 8 cases in 2008



# Arthropod Vectors

- Mosquitoes
- > 12 tick species
- Deer flies





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# Natural Epidemiology

- Tick and deer fly bites are common modes of transmission
- Arthropod-borne disease accounts for most cases between June and September
- A second smaller peak in December results from hunting-associated acquisition



# Pathogenesis

- Infection occurs through skin, lungs, GI tract, or mucous membranes
- *Person to person transmission does not occur*
- Infectious dose is dependent on the portal of entry
- Papule forms at the cutaneous inoculation site 3-5 days after insult
- Bacteria multiply locally, spread to regional lymph nodes then disseminate
- Lesions become granulomatous and can caseate

# Clinical Manifestations

6 forms of disease,  
often with  
significant  
overlap

Ulceroglandular  
Typhoidal  
Oculoglandular  
Glandular  
Oropharyngeal  
Pneumonic

## Ulceroglandular





# Diagnosis

- Exposure history and high index of suspicion
- Nonspecific laboratory findings:
  - leukocytosis
  - thrombocytopenia
  - elevated sedimentation rate
  - elevated ALT/AST
  - sterile pyuria in 20-35%
- Organism may be cultured from blood, sputum, gastric aspirates, lymph nodes



# Diagnosis

- ELISA, microagglutinin, hemoagglutinin
- Tube agglutinins develop by day 10-14
- Peak at 4-6 weeks
- Initial titer of 1:160 or greater is diagnostic
- Fourfold rise between acute and convalescent titers
- Because of its extreme infectivity, *laboratory personnel must be informed of the possibility of tularemia*
- Biosafety Level 3 precautions



# Treatment

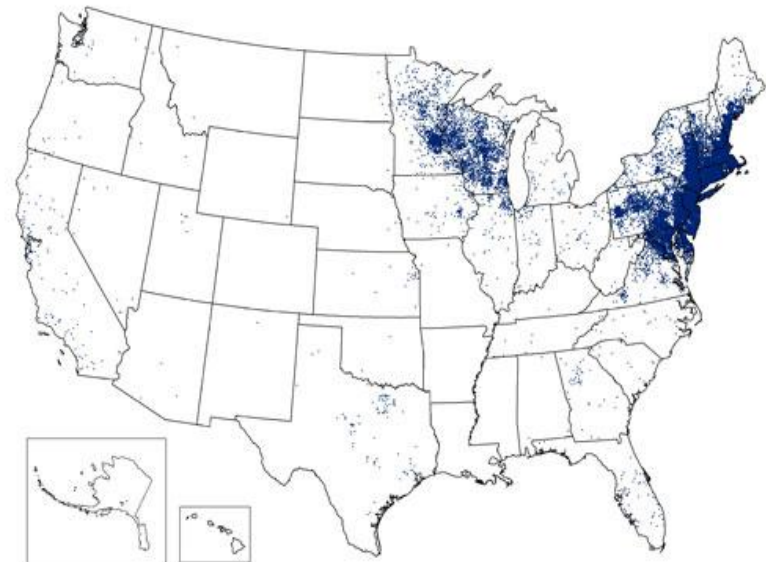
- Historically, streptomycin has been the treatment of choice (7.5-10 mg/kg IM q12h for adults)
- Streptomycin-resistant strains exist
- Primary alternative regimens (adult):  
gentamicin 3-5 mg/kg IV qd  
*or*  
ciprofloxacin 750 mg PO or 400 mg IV q12h

# Lyme Disease

**Most common tick-borne disease in North America**

- ◆ ~16,000 cases/year in the US
- ◆ 90% cases occur in 12 states
- Tick vectors: *Ixodes scapularis*, *I. pacificus*

Reported Cases of Lyme Disease -- United States, 2009



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

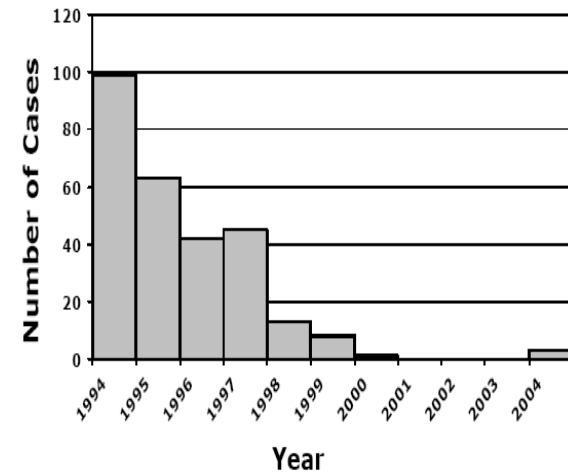
# Lyme Disease in OK

□ 0 cases 2001-2003

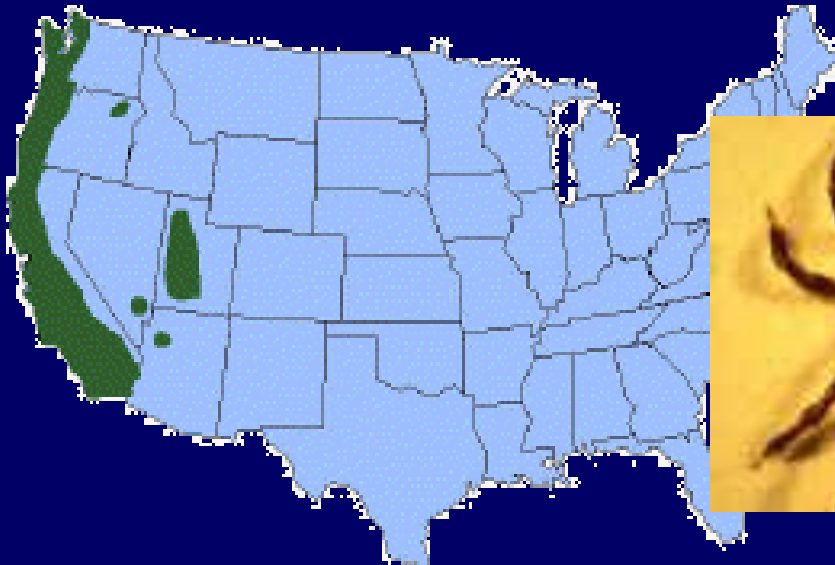
□ 3 cases in 2004...

□ 0 cases in 2005

Reported Number of Lyme Disease Cases by Year, Oklahoma, 1994-2004



***I. scapularis***



***I. pacificus***

# Causative Agent



## *Borrelia burgdorferi*

- ◆ spirochete
- ◆ can be cultured from EM lesion
- ◆ culture requires special medium



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# Lyme Disease

- **Seasonal (April-September)**
- **Low risk of disease if tick attached <36 hrs**
- **Signs/symptoms begin 7-10 days after bite (range 3-30 days)**
- **Clinical manifestations: asymptomatic-rarely fatal**

# Stage 1: Localized Infection



## Erythema migrans

- ◆ **occurs in ~90%**
- ◆ **begins 7-10 days after tick bite**
- ◆ **expands over days to weeks**
- ◆ **central clearing occurs in minority**
- ◆ **constitutional sx**



# Lyme Disease

## Stage 2

- ◆ may develop multiple 2<sup>o</sup> skin lesions
- ◆ generalized lymphadenopathy
- ◆ malaise, fatigue, HA , F/C
- ◆ meningeal irritation, facial palsy
- ◆ 5% develop cardiac involvement
- ◆ musculoskeletal pain

## Stage 3

- ◆ 60% develop joint swelling
- ◆ lasts weeks-months (intermittent)
- ◆ neurologic: memory, mood, sleep disturbances
- ◆ peripheral sensory symptoms



# Diagnosis

- **Characteristic clinical picture**
- **Serology: 2-step**
  - 1) **ELISA: 60-70% positive by wk 4**  
if equivocal or + →
  - 2) **Western blot (IgG): requires 5 of 10 bands**
- **Culture: low yield**



# Treatment

- **Early**

doxycycline,  
amoxicillin,  
cefuroxime for 21-28  
days

- **Arthritis** doxycycline,  
amox, ceftriaxone,  
PCN

- **Neurologic**

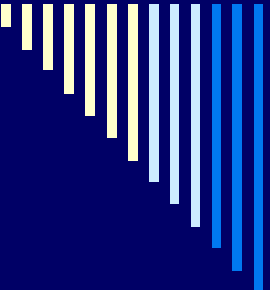
ceftriaxone or PCN  
(IV) 14-30 days

- **Facial palsy**

oral regimen ~OK

- **Cardiac**

1st AVB: oral  
high-degree: IV



# Southern Tick-Associated Rash Illness (STARI)

- Seronegative Lyme disease
- Southern Lyme disease
- Master's disease
- “One of the more obtuse diseases...at CDC”



## Remember...

- 95% of cases of Lyme Disease are found in 12 states
- Established tick vectors are *Ixodes scapularis* and *Ixodes pacificus*
- The characteristic erythema migrans (EM) skin lesion occurs in early Lyme disease
- *Borrelia burgdorferi* can be readily cultured from ~80%

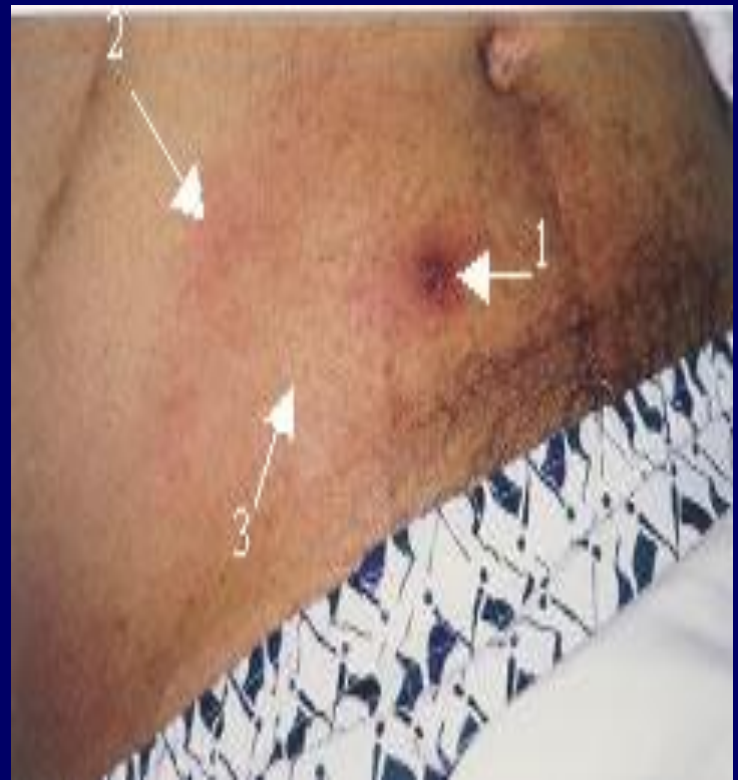


# The Mystery

- Persons from southcentral and southern US have developed tick-bite associated EM-like lesions
- *Amblyomma americanum* (Lone Star) tick most commonly bites human in this area
- *B. burdorferi* has not been isolated from clinical specimens
- Serology rarely indicates exposure

# Cutaneous Manifestations

- 1. Site of tick bite
- 2. Red, radial, expanding edge
- 3. Central clearing



# STARI





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## After More than Ten Years...

- STARI is indistinguishable from early Lyme disease
- Tick vector is *A. americanum*
- Etiologic agent remains unknown
- Management and natural history remain unclear
- Further studies required

# An Ounce of Prevention...

- Light-colored clothing
- Tuck pants into shoes
- DEET-containing repellent
- Permethrin-containing insecticide
- Remove tick(s) within 24 hrs of attachment

