

# Tickborne Rickettsial Diseases

Rachel Radcliffe, DVM, MPH

CDC Career Epidemiology Field Officer

Division of Infectious Disease Epidemiology

# Objectives

- **Describe the epidemiologic characteristics of tickborne rickettsial diseases**
- **Review the clinical symptoms, diagnosis, and treatment of tickborne rickettsial diseases**
- **Explain how the case definitions are used to classify reported cases of tickborne rickettsial diseases**

# Tickborne Rickettsial Diseases (TBRD)

- **Group of clinically similar but epidemiologically and etiologically distinct illnesses**
  - **Rocky Mountain Spotted Fever**
    - *Rickettsia rickettsii*
  - **Ehrlichiosis**
    - *Ehrlichia chaffeensis* and *E. ewingii*
  - **Anaplasmosis**
    - *Anaplasma phagocytophilum*
- **Incidence of these diseases increasing in US**

# Epidemiology of TBRD

- **Maintained in natural cycles involving wild mammals and ixodid ticks**
- **90%–93% of cases are reported during April–September**
- **Males appear at higher risk for all TBRD**
- **Age incidence varies among diseases**



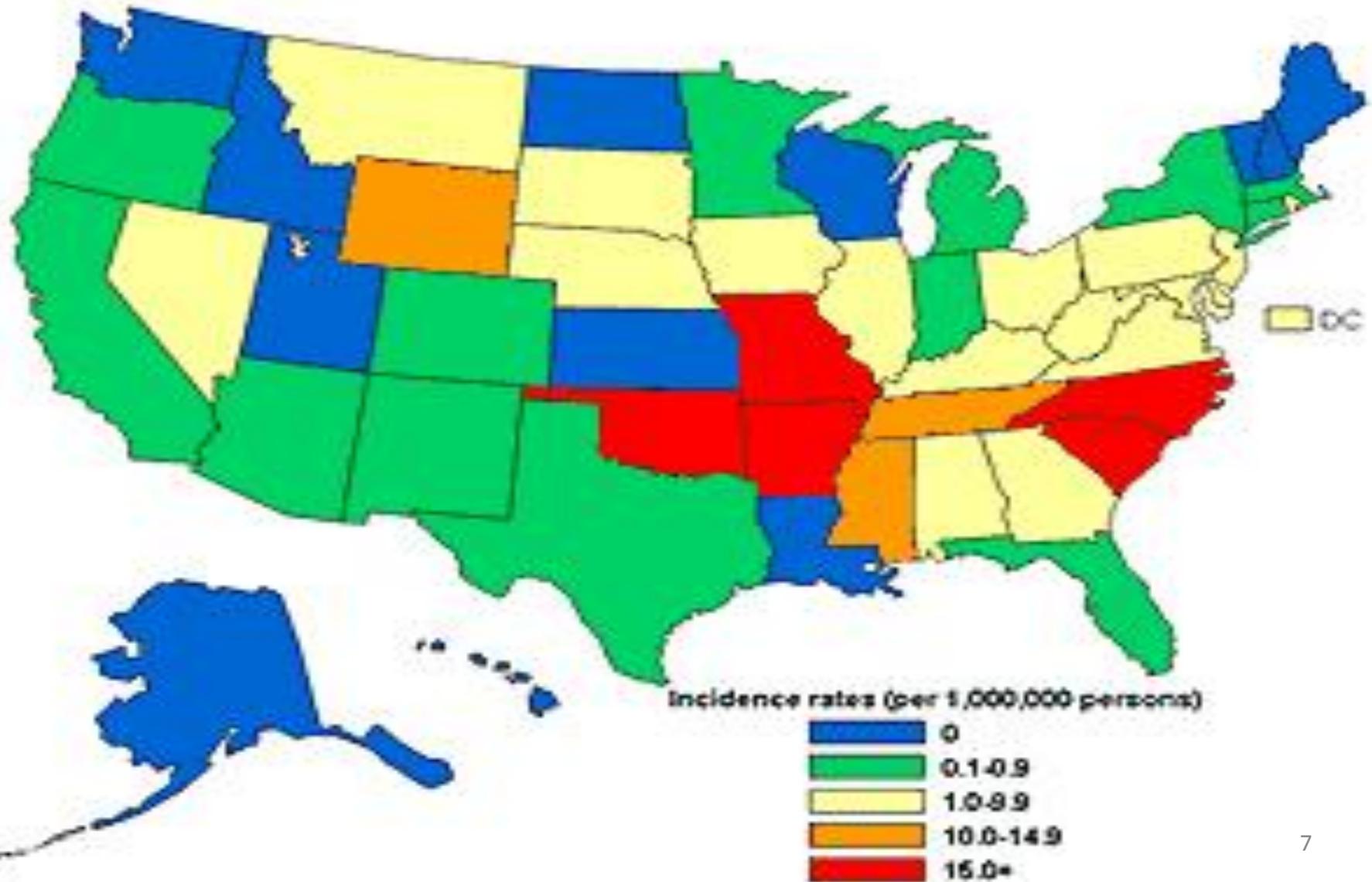
# Rocky Mountain Spotted Fever

- Disease in the spotted fever rickettsiosis group
- Most severe tickborne illness in US
- Transmitted by several tick species in US
  - American dog tick (*Dermacentor variabilis*)
  - Rocky Mountain wood tick (*D. andersoni*)
  - Brown dog tick (*Rhipicephalus sanguineus*)
- Affects dogs
  - Can develop disease with other human household members

# RMSF Epidemiology

- **1997–2002**
  - **Estimated US average annual incidence was 2.2 cases per million**
  - **56% of cases from five states**
    - **TN, NC, SC, OK, AR**
- **Highest incidence among persons <15 years**
  - **Peak age 5–9 years**
- **Household clusters of disease reported**

# RMSF Annual Incidence – US, 2002



# Ehrlichiosis



- ***Ehrlichia chaffeensis* most common**
  - **Human monocytotropic ehrlichiosis (HME)**
- ***E. ewingii* has also been identified**
- **Transmitted by lone star tick (*Amblyomma americanum*)**
- **White-tailed deer major host for tick species and natural reservoir for bacteria**
- **Infections in coyotes, dogs, and goats have been documented**

# Ehrlichiosis Epidemiology

- **2001–2002**
  - **HME Average US annual incidence was 0.7 cases per million population**
  - **Incidence varied by state**
    - **Most commonly reported from MO, OK, TN, AR, MD**
- **Highest incidence among persons >60 years**
- **HME clusters have been reported**



# Anaplasmosis

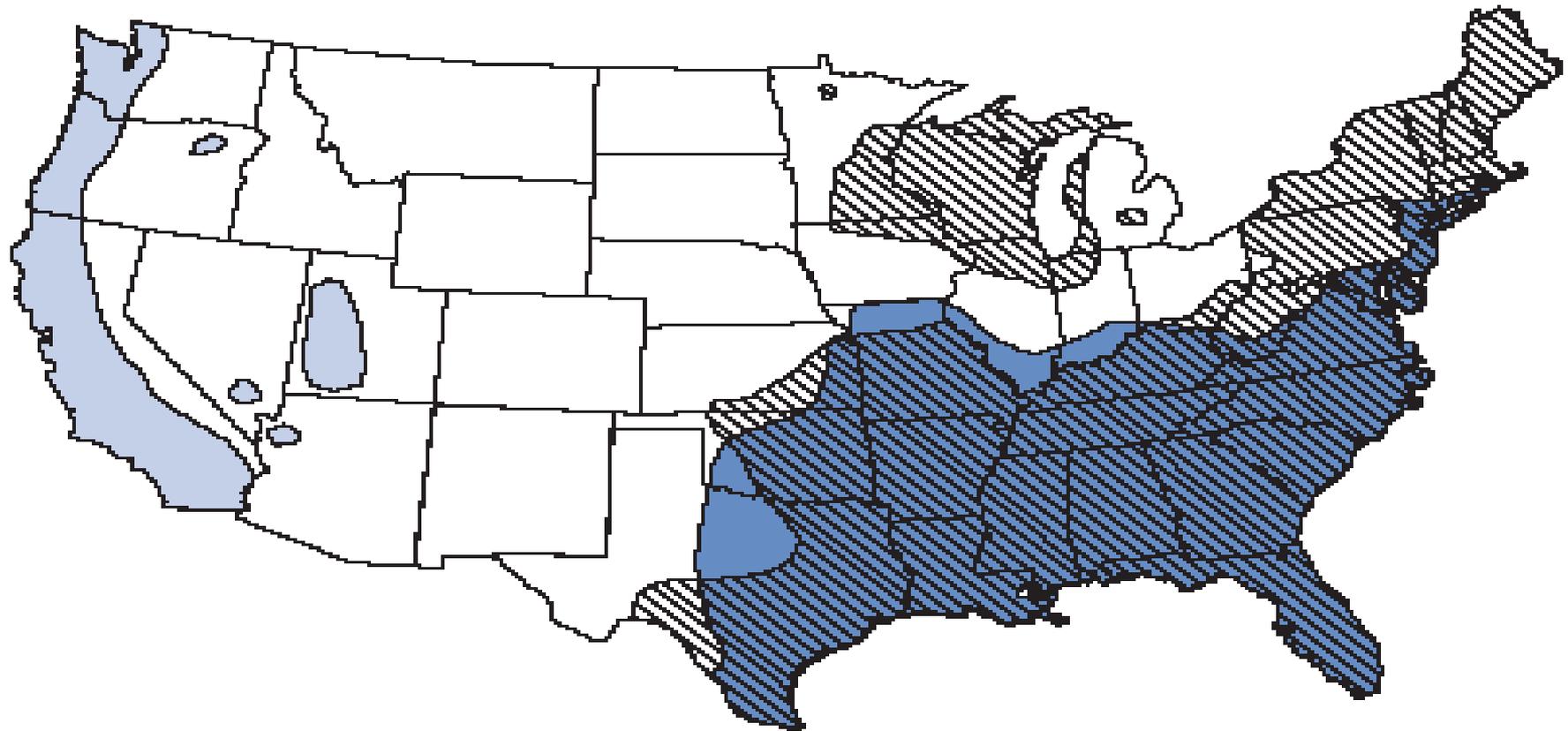


- **Human granulocytotropic anaplasmosis (HGA)**
- **Transmitted by blacklegged tick (*Ixodes scapularis*) and western blacklegged tick (*I. pacificus*)**
  - **Same vectors as Lyme disease**
  - **Coinfections have been reported**
- **Deer, elk, and wild rodents are reservoirs**

# Anaplasmosis Epidemiology

- **2001–2002**
  - **Average US annual incidence was 1.6 cases per million population**
  - **Highest incidence in RI, MN, CT, NY, MD, possibly WI**
- **Highest incidence among persons >60 years**

# Geographic Distribution of Tick Species for HME and HGA



-  *Ixodes scapularis* distribution
-  *Ixodes pacificus* distribution
-  *Amblyomma americanum* distribution
-  Overlapping distribution (*I. scapularis* and *A. americanum*)

# Summary of TBRD Epidemiology

- **RMSF and HME most commonly reported in southeastern and south central US**
- **HGA most commonly reported in New England, north central states, and focal areas of West Coast**
- **RMSF has highest incidence among children <15 years**
- **HME and HGA have highest incidence among adults >60 years**

# TBRD Clinical Signs and Symptoms

- **Early signs of TBRD may be non-specific**
- **Overlap in initial clinical presentation of TBRD**
  - **Sudden onset of fever**
  - **Chills**
  - **Headache**
  - **Malaise**
  - **Myalgia**
  - **Nausea, vomiting, anorexia**

# RMSF Clinical Information

- **Onset occurs about 5–10 days after tick bite**
- **Infects endothelial cells**
- **Small vessel vasculitis**
  - **Maculopapular or petechial rash**
  - **Vasculitis in organs can be life-threatening**
- **Rash typically appears 2–4 days after onset of fever**

# RMSF Rash Appearance

- **Occurs earlier in children than adults**
- **~90% of children will get rash**
- **Small, blanching, pink macules on ankles, wrists, or forearms**
- **Evolves to maculopapules or petechiae**
- **Can include palms and soles**
- **Limited presentation on face**



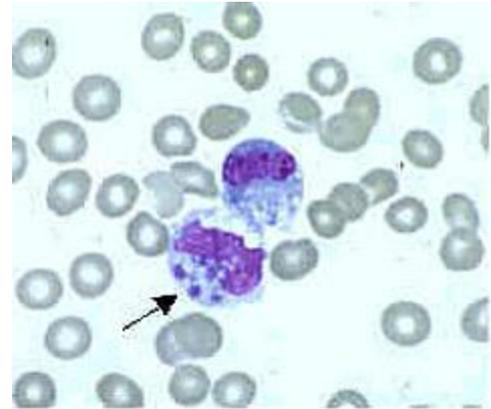
Photo/G.S. Marshall, University of Louisville School of Medicine,  
Louisville, KY



**Photo/CDC**

# Ehrlichiosis Clinical Information

- Onset occurs 5–10 days after tick bite
- Infects leukocytes
  - *E. chaffeensis* prefers monocytes
  - *E. ewingii* prefers granulocytes
  - Morulae can be identified
- Rash observed ~33% of patients with HME
  - Vary from petechial or maculopapular to diffuse erythema
  - Occurs later in disease
- Rash rarely seen with *E. ewingii* infections



# Anaplasmosis Clinical Information

- Onset occurs about 3 weeks after tick bite
- Infects leukocytes
  - Prefers granulocytes
  - Morulae can be identified
- Rash rarely seen

# TBRD Treatment

- **All agents of TBRD susceptible to tetracycline-class antibiotics**
  - **Doxycycline is drug of choice for children and adults**
- **RMSF and HME**
  - **Treat for 3 days after fever subsides**
  - **Standard duration of 5–10 days**
- **HGA**
  - **Treat for 10–14 days**

# TBRD Diagnosis

- **Clinical symptoms**
- **History of tick bite or tick exposure**
  - **Recreational or occupational exposures**
  - **Recent travel**
- **Similar illness in family members, coworkers, pet dogs**
- **Laboratory tests**
  - **CBC, metabolic panel**
- **Diagnostic tests**

# Laboratory Findings

- **Common to all TBRD**
  - **Thrombocytopenia**
  - **Elevated hepatic transaminases**
- **RMSF**
  - **Hyponatremia**
- **Ehrlichiosis and Anaplasmosis**
  - **Leukopenia**

# Diagnostic Tests — General

- **Rapid confirmatory tests not commonly available**
- **Laboratory confirmation**
  - **Retrospectively validates clinical diagnosis**
  - **Important to understanding epidemiology and public health impact**
- **Treatment should not be delayed**

# Diagnostic Tests

- **Blood Smear Microscopy**
  - Identify morulae in circulating cells
  - Not useful for RMSF
- **Nucleic acid detection or PCR**
  - Skin biopsy or autopsy tissue
- **Immunohistochemical (IHC) staining**
  - Skin biopsy or autopsy tissue
- **Cell culture**
  - RMSF is Biosafety Level-3 (BSL-3) agent

# Serologic Testing

- **Principle diagnostic tool for TBRD**
- **Paired serum samples 2–3 weeks apart is most appropriate approach for TBRD confirmation**
- **Indirect immunofluorescence (IFA) assay**
  - **Gold standard of serologic testing**
  - **Sensitivity depends on timing of specimen collection**
- **ELISA also used but cannot monitor changes in antibody titer**

# RMSF Testing

- **Serologic testing with IFA available at CAMC for free**
  - **Providers should call DIDE for approval**
  - **Clinically appropriate specimens**
    - **Have clinical evidence of infection**
  - **Paired serum samples needed to confirm diagnosis**

# CAMC Testing Criteria

- **Specimens taken  $<7$  days from illness onset will be held for 45 days**
  - **Will not be tested if convalescent specimen not received within 45 days**
- **Specimens taken  $\geq 7$  days will be tested immediately**
  - **Strongly recommend convalescent specimen sent for testing**

# TBRD Surveillance

- **All TBRD are nationally notifiable diseases**
  - **RMSF – 1989**
  - **Ehrlichiosis and Anaplasmosis – 1998**
- **West Virginia surveillance**
  - **All TBRD are reportable to LHD in 1 week**
- **TBRD case definitions**
  - **Clinical evidence**
  - **Laboratory criteria**

# **RMSF Case Definition — Clinical Evidence**

- **Any reported fever and one or more of the following:**
  - **Eschar**
  - **Rash**
  - **Headache**
  - **Myalgia**
  - **Anemia**
  - **Thrombocytopenia**
  - **Hepatic transaminase elevation**

# RMSF Case Definition — Laboratory Criteria

- **Confirmed**
  - Serological evidence of fourfold change in IgG by IFA among paired serum specimens
  - *R. rickettsii* DNA detected by PCR assay
  - *R. rickettsii* antigen by IHC in biopsy or autopsy specimen
  - Isolation of *R. rickettsii* in cell culture
- **Supportive**
  - Increased serum IgG or IgM by IFA, ELISA, or latex agglutination

# RMSF Case Definition

- **Confirmed**
  - **Clinical evidence and confirmatory laboratory results**
- **Probable**
  - **Clinical evidence and supportive laboratory results**
- **Suspect**
  - **Laboratory results but no clinical information**

# Four Sub-Categories of Ehrlichiosis/Anaplasmosis

- ***Ehrlichia chaffeensis* infection (HME)**
- ***Ehrlichia ewingii* infection**
- ***Anaplasma phagocytophilum* infection (HGA)**
- **Ehrlichiosis/Anaplasmosis, human, undetermined**

# Ehrlichiosis Case Definition — Clinical Evidence

- **Any reported fever and one or more of the following**
  - **Headache**
  - **Myalgia**
  - **Anemia**
  - **Leukopenia**
  - **Thrombocytopenia**
  - **Any hepatic transaminase elevation**

# ***E. Chaffeensis* Laboratory Criteria**

- **Confirmed**
  - **Fourfold change in IgG by IFA in paired serum samples**
  - **Detection of DNA by PCR**
  - **Demonstration of antigen by IHC in biopsy or autopsys sample**
  - **Isolation of bacteria by cell culture**
- **Supportive**
  - **Elevated IgG or IgM by IFA, ELISA, dot-ELISA or other formats**
  - **Morulae identification by blood smear microscopic examination**

# ***E. chaffeensis* Case Definition**

- **Confirmed**
  - **Clinical evidence and confirmatory laboratory results**
- **Probable**
  - **Clinical evidence and supportive laboratory results**
- **Suspected**
  - **Laboratory evidence but no clinical information available**

# ***E. ewingii* Laboratory Criteria**

- **Confirmed**
  - **Only diagnosed by molecular detection methods**
  - ***E. ewingii* DNA detected by PCR**
- **Supportive**
  - **Not applicable**

# ***E. ewingii* Case Definition**

- **Confirmed**
  - **Clinical evidence and confirmatory laboratory results**
- **Probable**
  - **Not applicable**
- **Suspected**
  - **Not applicable**

# **Anaplasmosis Case Definition — Clinical Evidence**

- **Any reported fever and one or more of the following**
  - **Headache**
  - **Myalgia**
  - **Anemia**
  - **Leukopenia**
  - **Thrombocytopenia**
  - **Any hepatic transaminase elevation**

# **Anaplasmosis Case Definition — Laboratory Criteria**

- **Confirmed**
  - **Fourfold change in IgG by IFA in paired serum samples**
  - **Detection of DNA by PCR**
  - **Demonstration of antigen by IHC in biopsy or autopsy sample**
  - **Isolation of bacteria by cell culture**
- **Supportive**
  - **Elevated IgG or IgM by IFA, ELISA, dot-ELISA or other formats**
  - **Morulae identification by blood smear microscopic examination**

# Anaplasmosis Case Definition

- **Confirmed**
  - **Clinical evidence and confirmatory laboratory results**
- **Probable**
  - **Clinical evidence and supportive laboratory results**
- **Suspected**
  - **Laboratory evidence but no clinical information available**

# **Ehrlichiosis/Anaplasmosis, Undetermined**

- **Cases can only be reported as probable**
  - **Weakly supported by laboratory results**
- **Cases have clinical evidence with laboratory evidence of Ehrlichia/Anaplasmosis**
  - **Cannot be definitively placed in one of the previously described categories**

# Summary of TBRD

- **Numerous tick species that transmit TBRD**
- **Some differences among TBRD in incidence, geographic distribution, and clinical appearance**
- **Treatment is similar for TBRD**
- **Diagnosis can be difficult**
  - **Patient history important**
- **Serologic testing is most appropriate method to diagnose TBRD**
- **TBRD reportable nationally and in WV**