Tick Biology and Tick-borne Diseases: Overview and Trends

William L. Nicholson, PhD
Pathogen Biology and Disease Ecology
Rickettsial Zoonoses Branch,
Centers for Disease Control and Prevention

Introduction

- Summarize the diseases and pathogens transmitted by ticks in the United States
- Provide an update on newly recognized pathogens from the United States
- Discuss some newer findings in Rocky Mountain spotted fever
- Discuss prevention, management, and control measures

The views expressed in this presentation are those of the author and not necessarily those of the Centers for Disease Control and Prevention or Department of Health and Human Services

Emerging diseases

- Many emerging diseases are vector-borne and zoonotic diseases
- Reasons
  - increased international travel
  - insecticide resistance
  - drug resistance
  - ecologic/environmental changes
  - genetic changes in pathogens
  - increased awareness

Ticks and Tick-Borne Diseases

Tick-borne diseases are increasingly recognized in the United States
Geographic ranges of the vector ticks are expanding into new areas

Biology and Control of Vectors and Public Health Pests
Sacramento, CA – November 2011
Incredible diversity

- Over 850 species worldwide, about 80 species in the United States
- Three families:
  - Ixodidae (hard ticks)
  - Argasidae (soft ticks)
  - Nuttalliellidae

About 12 species of public health or veterinary importance in the US

Blood-feeding strategies

- Soft ticks attach for longer periods as larvae, but then use a feed-and-hide strategy (feed times 30 minutes or less)
- Ixodid ticks attach strongly for varying periods of time (multiple days)
- One-host, two-host, and three-host ixodid ticks
- Vary from host-specific to feeding on a broad range of vertebrate hosts
- Relevant to pathogen transmission

General Life Cycle of a Tick

- Dermacentor variabilis

Factors for Tick Survival

- Humidity
- Temperature
- Available hosts
- Hiding spots
- Predation
- Natural disease
- Pathogen-induced mortality

Biology and Control of Vectors and Public Health Pests
Sacramento, CA – November 2011
Effects of tick infestation

- Worry
- Blood loss
- Salivary toxicant
- Immune response
- Wounding (secondary pathogen entry)
- Pathogen transmission

Tick paralysis

- Progressive, flaccid, ascending paralysis
- Death can occur 24-48 hours after onset of symptoms
- Often due to undetected tick attachment along spine or base of skull
- Caused by many species of ticks
- Often a single tick can cause severe illness in a person
- Caused by different proteins in tick saliva

Tick Bite Allergies and Reactions

- Wide range of reactions
- Minor inflammatory reactions locally
- Severe systemic reactions (skin rash, fever, nausea, vomiting, diarrhea, shock, and death)
- Severe allergic reactions (edema, pain, erythema, tissue necrosis, ulceration, prolonged healing)
- Expanding erythematous lesions
- Anaphylactic shock

Maintenance of pathogen within tick populations

- Transovarial transmission: transfer from one generation to the next through the egg
  - Spotted fever group rickettsiae
  - Tick-borne encephalitis virus
  - Colorado tick fever virus
- Transstadial transmission: transfer from one life stage to the next stage
  - Lyme borreliae
  - Ehrlichia organisms
  - Anaplasma organisms
  - Babesia parasites
Ticks and their associated diseases are seasonally distributed

- Peak of disease activity corresponds with peak of tick activity (especially the life stage of tick most important for transmission).

Ticks and their associated diseases are focally distributed (clustered)

Diseases endemic to the USA
- Ehrlichiosis
- Anaplasmosis
- Rickettsioses
- Lyme disease and other borrelioses
- STARI
- Babesiosis
- Tularemia
- Colorado tick fever, Powassan encephalitis
- Bartonellosis, others

Classic Triad of Clinical Manifestations
Following tick bite:
- Fever
- Headache
- Rash

When to Suspect Tick-borne Illness
- Acute febrile illness without apparent cause (fever, malaise, lethargy + other symptoms)
- Onset during May-September (high tick activity)
- History of tick bite or exposure
- Persons at risk for tick bite
- History of travel to endemic areas (US and global travel)
- Thrombocytopenia, elevated liver enzymes
- Rash not always a feature

Borrelia burgdorferi
- Lyme disease is the most common vector-borne disease in US
- Caused by spirochete, *Borrelia burgdorferi*
- Transmitted by *Ixodes scapularis* and *Ixodes pacificus*
- Approximately 20,000 cases reported each year in United States
- Northeast, upper mid-Western United States
Relapsing fever borreliae

- *Borrelia hermsii, B. turicatae, B. parkeri*
- Uncommon (~25 cases/yr); 14 states
- Associated with stays in cabins infested with rodents, especially after rodent control has occurred
- Soft ticks (Family Argasidae) seek hosts in the absence of their normal rodent hosts

Francisella tularensis

- Tularemia
- Found in a number of ticks, but generally thought to be transmitted to humans by *Amblyomma americanum* or *Dermacentor variabilis*
- Several biotypes, other means of transmission
- Martha’s Vineyard focus (D.v.)
- Missouri-Arkansas focus (A.a.)
- Increase in cases in recent years (~200 cases/yr)

Babesia species

- First US case reported in 1966 from Nantucket Island, Mass.
- 25% of adults and 50% of children infected with babesiosis are asymptomatic and/or improve spontaneously without treatment.
- Less than 10% of patients with babesiosis have died in the United States, mostly composed of elderly or asplenic patients.
- Approximately 20% of patients with babesiosis are co-infected with Lyme disease. These patients experience more severe symptoms for a longer duration than those with either disease alone.

Babesia species

- *Babesia microti* (NE and upper Midwestern US)
- *Babesia duncanii* (WA-1; Washington state)
- *Babesia sp.* (MO-1; Missouri)
- *Babesia sp.* (CA-1; California)
- Most patients had their spleens removed surgically, and thus were immunocompromised
- Not commonly reported, increasing incidence
- Growing threat to donated blood supply
Colorado Tick Fever
- Transmitted to humans by the Rocky Mountain wood tick, *Dermacentor andersoni*
- Transstadial and transovarial transmission in ticks
- 777 cases (1987-2001)
- Rocky Mountain states

Powassan virus
- Widely distributed. Found in *Ixodes spinipalpis* and *Dermacentor andersoni* in the West and *Ixodes cookei* and *I. marxi* in the East
- Flavivirus related to TBE virus
- Groundhogs are one reservoir and good hosts for *Ixodes cookei*
- Causes neurologic disease in humans
- Not common (17 cases from 1999-2007)
- Incidence appears to be on the rise

Deer Tick Virus
- Described in 1997
- Subtype of Powassan virus, a flavivirus related to the tick-borne encephalitis virus complex
- 3-4% of white-footed mice (*Peromyscus leucopus*) in Massachusetts and Wisconsin are seropositive
- Detected in adult *Ixodes scapularis* ticks in those areas with seropositive mice
- Fatal encephalitis case described in 2009

STARI
- Southern Tick Associated Rash Illness
- Originally suspected to be due to “*Borrelia lonestari*” found in lone star ticks, but no good evidence for this
- Many bacteria and viruses extensively evaluated, but no real cause has been determined
- Need for further study
Anaplasma phagocytophilum

- Previously known as the human granulocytic ehrlichiosis (HGE) agent, Ehrlichia phagocytophila, Ehrlichia equi.
- Mainly distributed in the northeastern, upper midwestern, and western states, but also found in the southeast. Distribution of organism is wider than that of human cases.
- Reservoir: Rodents (Peromyscus, Neotoma); squirrels

Ixodes scapularis

In the eastern US, Anaplasma phagocytophilum is primarily transmitted by the blacklegged tick

Additional tick species (I. pacificus, I. spinipalpis) involved in western U.S. and in other parts of the world (I. ricinus, I. persulcatus, others)
**Ehrlichia chaffeensis**

- Disease: Human monocytic ehrlichiosis
- Primary vector: *Amblyomma americanum*
- Reservoirs may be dogs, wild canids, and deer

**Amblyomma americanum**

- Common name: Lone star tick
- Transstadial, but not transovarial transmission.
- Distributed throughout the southeastern U.S.

---

**Hypothetical Life Cycle**

United States

- Foxes, coyotes, and other wildlife
- White-tailed deer

**Ehrlichia ewingii**

- Organisms grow as clusters within the cytoplasm of certain types of white blood cells (neutrophils and eosinophils)
**Ehrlichia ewingii**

- Increasingly recognized as cause of human ehrlichiosis (first cases in humans from Missouri)
- Pathogen not yet cultured, so no specific serologic test was available, new recombinant antigen has been useful for veterinary studies
- Transmitted by *Amblyomma americanum*
- Found in ticks or dogs from several states thus far: Arkansas, Mississippi, Missouri, North Carolina, Oklahoma, Tennessee, Virginia

**Rickettsia rickettsii**

- Rocky Mountain spotted fever: the most severe rickettsial illness of humans
- Tropism for endothelial cells

**Hypothetical Life Cycle**

- United States
- *Ehrlichia ewingii*
- *Amblyomma americanum*
- White-tailed deer
- Wild and domestic animals (canids)
- Humans and their pet dogs

**When to suspect rickettsial infection**

- RMSF: Rash, especially macules on extremities
- Ehrlichiosis: rash not common in adults, but occasionally seen in children
- Anaplasmosis: no rash
- Don't wait for a rash to decide to treat!!!
- Fatal if not treated promptly

Biology and Control of Vectors and Public Health Pests
Sacramento, CA – November 2011
RMSF incidence

Rickettsia rickettsii
- Primary vectors in USA: Dermacentor variabilis, Dermacentor andersoni
- Other tick species may be involved in other areas (e.g. Rhipicephalus sanguineus)
- Transstadial and transovarial transmission in ticks

RMSF in Arizona
- High infestations of brown dog ticks, Rhipicephalus sanguineus (all stages)
- Many confirmed bites by nymphs (usually behind ears or back of neck)

For the population size, incidence of RMSF in this area was 300x that of rest of country

Rhipicephalus sanguineus Infestation
Vegetation in surrounding areas increased moisture levels under houses on piers.
“Shady places where dogs lie”
Voids in the concrete piers contained ticks of all stages. Larvae and nymphs quested from the surface.

Up to 1000 ticks per hour on dry ice traps.

Mattresses discarded or stored under houses provided dog resting sites and tick hiding spots. Over 150 ticks were removed from this single mattress. (Adults, nymphs, and nymphs molting into adults)

RMSF in Arizona

• Now seen in four widely separated tribal lands. From 2002-2009, we identified 95 cases
• 527 cases per million persons/yr
• Fatal Cases
  • N = 9
  • Case fatality rate = 9.5%

Mexicali Outbreak

• Initial report: 4 Sept. 2008 to 19 Feb. 2009, eight deaths reported from Los Santorales area of Mexicali, Baja California, Mexico
• Additional 52 cases, 2 deaths in early 2009
• CDC assisted local and federal health officials in confirming these as due to *Rickettsia rickettsii*
• Large numbers of ticks on dogs and in environment (earlier studies had shown 50-79% of dogs infested with a seroprevalence of 17% to *R. rickettsii*)

*Cases continue in multiple states*
Brown dog tick
- Found worldwide, primarily feeding on dogs as preferred host
- Larval and nymphal ticks occasionally feed on humans, especially when tick populations are high
- Transmit spotted fever rickettsiae in other parts of the world

Rhipicephalus sanguineus

R. rickettsii Transmission
- Rhipicephalus sanguineus was shown to be a vector of *Rickettsia rickettsii* in at least 4 states in Mexico in the 1940s (work by Bustemante, Varela, and Marriote)
- Rocky Mtn Labs: R.R. Parker conducted laboratory studies to show that *R. sanguineus* was effectively maintained through successive stages to the second generation
- Role of this tick species in the United States had been discounted for decades due to the perception of this species not feeding on humans. Yet a number of studies document human feeding in the U.S. and elsewhere.

R. rickettsii and Rhipicephalus
- Labruna and associates (2008) showed that *R. sanguineus* was readily infected by *R. rickettsii* (89-100% infected) and mortality did not differ from uninfected vs. infected ticks (8-21% died)
- Naturally infected ticks found in Sao Paulo, Brazil (Moraes-Filho et al. 2008) and southern California (Wikswo et al.)

Incredible Reproductive Capacity
- Brown dog ticks can complete their life cycle in as little as 93 days.
- Each engorged female can lay 3000-4000 eggs.
- Ticks can be transported to new locations as dogs move around from house-to-house. It takes a very short time to re-colonize an area after dogs have been removed or control efforts have been conducted.
Biology and Control of Vectors and Public Health Pests
Sacramento, CA – November 2011

Biological Features
- Ticks move among hosts during high tick activity (interrupted feeding may shorten transmission time to second host)
- Nocturnal detachment of nymphal and adult engorged ticks concentrates ticks and facilitates host contact
- Increased height of questing and human biting rate with elevated temperature (Melendez et al. 1995; Parola et al. 2008)
- Survives temperatures and humidities that other ticks cannot (Yoder et al. 2006a,b): 90% survival at 40°C and 33% survival at 50°C

Rickettsia parkeri
- Most recently recognized tick-borne pathogen
- Mild spotted fever with eschar, a skin lesion with a necrotic center
- First case identified in Tidewater, Virginia; now have about 30-40 cases identified
- Organism known for >60 years before recognized as a human pathogen

Rickettsia parkeri has been specifically identified in Amblyomma maculatum ticks from Alabama, Georgia, Mississippi, Virginia, and Texas (and wider)

Cutaneous lesions (Rickettsia parkeri)
A: Diffuse, pink, macular rash involving the abdomen
B: Small pustule on hand
C: Eschar on right lower leg
D: Eschar on left lower leg

Amblyomma maculatum
Hypothetical Life Cycle

Amblyomma maculatum

Humans

Rodents (?) Birds (?)

Amblyomma maculatum

“Rickettsia philipii” (serotype 364D)

- 1966: First isolated from a Pacific Coast tick, *Dermacentor occidentalis*, collected in Ventura Co., California
- Serologically distinct from other SFGR
- Found in a high proportion of *Dermacentor occidentalis* ticks in nature
- Suspected as cause of spotted fever infections in California since the early 1980s.

“Rickettsia philipii” (serotype 364D)

- Now known to be a cause of mild spotted fever with eschar as primary feature
- Molecular and serologic evidence for cases in northern California
- Eschar is primary site of rickettsial concentration resulting in necrotic center.

Ehrlichia muris-like agent

- Discovery (2009)
  - Mayo Clinic
  - 20 year old male from Wisconsin
  - County of residence along the border of MN/WI
  - Post-kidney transplant, treated with immunosuppressive drugs
  - Presented with fever, malaise, and headache
  - Lymphopenia and mildly elevated AST/ALT
  - Peripheral blood smear was negative for babesia
  - Serologic panel for babesiosis, anaplasmosis, and ehrlichiosis was negative
  - Tick-borne disease PCR panel was performed

Biology and Control of Vectors and Public Health Pests
Sacramento, CA – November 2011
**Ehrlichia muris-like agent**

- **Epidemiology**
  - All patients had documented history of tick exposure
  - <30 human cases have been identified thus far
  - All from Minnesota and Wisconsin
  - Some had history of organ transplant
  - Investigations underway among Mayo, MN and WI DOH, US Army, and CDC

- **Field studies**
  - *Ixodes scapularis* ticks were collected from areas of suspected tick exposure of the patients in Wisconsin
  - 1/100 pools were positive (*I. scapularis* nymphs)

**Serologic assays**

- One of the patients had antibodies that reacted with *Ehrlichia chaffeensis* antigens in an IFA
- Reliability of the use of surrogate antigens is unknown
- Cultivation achieved by Mayo Clinic
- Specific antigen has been produced by CDC
- Serum samples from patients with suspected ehrlichiosis due to EML were banked by the Wisconsin Department of Health and will be tested against the EML antigen in an IFA study

---

**“Rickettsia amblyommii”**

- Found in a high proportion of *Amblyoma americanum*, lone star ticks
- Thought to be a cause of less severe human spotted fever
- Serologic evidence exists, but may be crossreactivity.
- More work needs to be done

---

**Potential and emerging pathogens**

- *Rickettsia massiliae*
- Found in multiple countries; known from Arizona and California
- Cause of human illness in Argentina and Sicily
- Not yet found to cause disease in humans in the USA
Imported rickettsial diseases

- Travel-associated
- Usually recognized as acute illness in 2-4 weeks following return from travel
- *Rickettsia conorii*-Mediterranean SF
- *Rickettsia africae*-Tick bite fever
- *Rickettsia typhi*-Murine typhus
- Others

Red meat allergy

- IgE to mammalian oligosaccharide: galactose-alpha-1,3-galactose
- Allergy is more prevalent in the south-central and southeastern states where *Amblyomma americanum* is distributed.
- Study followed only 3 patients, but interest is growing.

Prevention

- Clothing adjustment & access prevention measures (e.g., pants in sock, double-stick tape)
- Use of repellents
- Avoidance of tick habitat
- Body checks after spending time in tick habitat

Prevention

- Routine tick check and removal
  - Transmission unlikely to occur if promptly removed (grace period varies)
  - Use fine-tipped tweezers
  - Mirrors help
  - Record date/save tick
**Prevention**

- Proper Use of EPA-approved Products
- Skin Applications
  - DEET
  - Picaridin
  - Oil of Eucalyptus
  - BioUD
- Clothing Applications
  - Permethrin (Permanone)
  - BioUD

**Tick Control and Management**

- Management of habitat
  - Decreasing humidity
  - Decreasing harborage
- Management of free-living ticks
- Management of parasitic ticks
- Management of host population

**Surveillance for ticks**

- Carbon dioxide (dry ice) trap
- Flagging
- Dragging
- Host exam
- Limitations to each method

**Tools for management**

- Biological/Mechanical
  - Soaps
  - Dessicants
  - Fungal pathogens
  - Pheromone attractants
- Chemical
  - Many registered products in various formulations (spray, granules, dust)
  - Topicals and impregnated collars for animals
Effective tick control targets all life stages

- Target areas where ticks are located
- Target timing of acaricide application to coincide with optimal numbers and life stage for best control
- Target repeat applications to maximize effectiveness and minimize waste.

Targeted approach

- Egg
- Free-living stages
- Parasitic stages

Hosts

- Reduce host contact with vector
  - Self-applicator bait stations
  - Topicals/collars
- Reduce vector contact with pathogen
  - Host vaccination strategy (against pathogen, tick)
  - Host treatment with long-acting tetracyclines
- Reduce overall host numbers
  - Exclusion
  - Active removal or relocation
  - Modification of habitat

Responsibility

- Governmental
  - Federal, state, county, tribal
- Community
- Individual
AZ: Potential for control

- Tick species strongly prefers one host (dog) in all life stages
- Ticks primarily located in a limited peridomestic environment
- Demonstrated effective methods

AZ: Challenges for control

- Magnitude of the stray dog problem and lack of animal control (est. 25,000 dogs with 2500 removals/year)
- Limited political will and sustained effort for community-wide control
- Difficulty in treating individual animals
- Retreatment, identification, logistics
- Sustainability: Long-term control requires a coordinated integrated approach
- Ongoing effort in community education, habitat modification, and chemical management
- Ongoing efforts to educate health care professionals

Trends in Tick-borne Diseases

- Increasing recognition of novel organisms and recognition as human pathogens
- Increasing incidence of tick-borne diseases worldwide (attributed to social and environmental changes)
- Decreasing expertise in vector biology and control

Trends in Tick-borne Diseases

- Increasingly mobile society (and pets)
- Increasingly "green" society
- Increasingly sophisticated diagnostics
- Decrease in medical awareness or suspicion for many TBD (it’s not all Lyme)
Contact Information

William L. Nicholson
Pathogen Biology and Disease Ecology
Rickettsial Zoonoses Branch
Mail Stop G-13, CDC, 1600 Clifton Rd.,
Atlanta, GA
wnicholson@cdc.gov
Tel: 404-639-1095; 1090 lab
Fax: 404-639-4436

THANKS!