The Emergence of Lyme Disease and Other Tick-Borne Diseases

Durland Fish, Ph.D.
Yale School of Public Health

Ticks: excellent vectors of disease agents

- Zoophilic feeding
- Prolonged host contact
- Pharmacologic saliva
- High pathogen prevalence

Tick vectors of Lyme disease

- *Ixodes scapularis* – Eastern North America
- *Ixodes pacificus* – Western North America
- *Ixodes ricinus* – Europe
- *Ixodes persulcatus* – Eurasia
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Established* and reported** distribution of the Lyme disease vectors Ixodes scapularis (I. dammini) and Ixodes pacificus, by county, United States, 1907-1996

Dennis et al. 1998 J. Med. Entomol 35: 629-638

Established* and reported** distribution of the Lyme disease vectors Ixodes scapularis (I. dammini) and Ixodes pacificus, by county, United States, 1907-1996

Distribution of Ixodes ricinus and Ixodes persulcatus


Ixodes scapularis

Three feeding stages
One feeding/stage
Slow feeding (3-7 days)
Dispersed in environment
Long lived (2 yrs)
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Ixodes scapularis life cycle

Collecting host-seeking ticks

Host seeking phenology

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#### Host seeking phenology

*lxodes scapularis*

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<th>Month</th>
<th>% Activity</th>
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#### Pathogen maintenance

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#### Synchronous host seeking of nymphs facilitates complete pathogen inventory

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LYME ARTHRITIS
AN EPIDEMIC OF OLIGOARTICULAR ARTHRITIS IN CHILDREN AND ADULTS IN THREE CONNECTICUT COMMUNITIES
ALDEN C. ELLIS, STEPHEN S. HALLAWEL, DAVID H. DISMAN, ROBERT H. SHORE, WARREN A. ANDREWS, MARTIN B. DOW, AND FRANCIS M. STEELE

1977 Arthritis and Rheumatism Vol. 20, No. 1

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Ixodes scapularis ticks were found to be much more abundant on the east side of the river, where most of the cases had occurred.
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Order: Spirochaetales
Genus: Borrelia

Relapsing Fever borrelia

Lyme Disease borrelia

Geographic distribution of Borrelia burgdorferi sensu lato

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- Three major pathogenic species:
  - *Borrelia burgdorferi* - North America and Europe
  - *Borrelia garinii* - Asia and Europe
  - *Borrelia afzelii* - Asia and Europe

*eBURST clonal complexes*

*Borrelia burgdorferi* in the U.S. originated in the northeast and spread westward
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Phylogeography of *Borrelia burgdorferi* in the eastern United States reflects multiple independent Lyme disease emergence events

Anna Guillamar-Ibanez,8,9, Elisha M. Margo5, Stephen L. Davis5, Nicola A. Dik-Scott,5 Alan I. Ginsberg,1,2 Ellen Netherwood,3,4, and Durland Fish7

PNAS | September 7, 2004 | vol. 101 | no. 35 | 15569-15573

B. burgdorferi infection in ticks

Re-forestation of the northeast

1900
Agriculture

1970
Forest succession
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Reforestation, deer and lyme disease in Connecticut

Ixodes scapularis relict populations (1960’s)
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Distribution of *Ixodes scapularis*
in northeastern US 2008

Source of infection for ticks
Eastern North America

White-footed mouse (*Peromyscus leucopus*)
reservoir host for *Borrelia burgdorferi*

Other reservoir hosts

- *Tamias striatus*
- *Sciurus carolinensis*
- *Turdus migratorius*
- *Procyon lotor*

50%

- *Borrelia burgdorferi*
- *Ixodes scapularis nymph*
- *Peromyscus leucopus*

50%
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Nymphal infection prevalence

Mean prevalence = 19.8%
1484 positive/7487 screened
From total of 92 sites
60 sites with >=11 ticks (shown)

Bowman et al., 2009 Veterinary Parasitology 160: 138-146

Canines with antibody to *Borrelia burgdorferi*
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Reported cases of lyme disease by year, United States, 1982-2007

Vectors a guild of five zoonotic pathogens
- Borrelia burgdorferi (lyme disease)
- Borrelia near miyamotoi
- Anaplasma phagocytophilum (human granulocytic ehrlichiosis)
- Babesia microti (human babesiosis)
- Flavivirus (DTV/POW encephalitis)

Ixodes scapularis

Pathogen prevalence Ixodes scapularis nymphs

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>N</th>
<th>%+</th>
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<tr>
<td>Borrelia burgdorferi (Northeast – Midwest US)</td>
<td>8,588</td>
<td>19.8</td>
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<tr>
<td>Anaplasma phagocytophilum (Northeast Coast)</td>
<td>4,674</td>
<td>4.2</td>
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<tr>
<td>Babesia microti (Block Island, RI)</td>
<td>231</td>
<td>14.7</td>
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<tr>
<td>Borrelia miyamotoi (Northeast – Midwest US)</td>
<td>8,588</td>
<td>1.9</td>
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<tr>
<td>Powassan/deer tick virus (Southern NY state)</td>
<td>286</td>
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Ixodes scapularis feeds on humans

Westchester Co., NY
Population 874,866 (1990)
178,889 bites/year
(20.4 per 100 person-years)

Campbell et al. 1998
American Journal of Epidemiology 148: 1018-1026

Emergence of human anaplasmosis

1987, First case of human infection with Ehrlichia canis, Detroit, MI, Maeda et al.
New England Journal of Medicine 316: 853-856
1994, Six cases of granulocytotrophic ehrlichiosis (2 fatal) Minnesota and Wisconsin, Chen et al., Journal of Clinical Microbiology
1998, Human granulocytic ehrlichiosis becomes a nationally reportable disease

Current phylogeny and taxonomic classification of genera in the family Anaplasmataceae

Dumler et al., 2005 Emerging Infectious Diseases 11: 12

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Anaplasma phagocytophilum prevalence in nymphal I. scapularis

Gatewood et al., 2009 Vector Borne and Zoonotic Diseases 9: 431-438

Number of Anaplasmosis cases reported to CDC by state health departments

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Canines with antibody to *Anaplasma phagocytophilum*

Bowman et al., 2009 Veterinary Parasitology 160: 138-148

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**Babesiosis emergence in Connecticut**

1989 Babesiosis in Eastern Connecticut, CDC MMWR 38: 649–50
2004 Babesiosis in Western Connecticut, Anderson & Magnarelli, *Emerging Infectious Diseases* 10: 545-546

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*Babesia microti*

Thin blood smear with Giemsa stain
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**Phylogenetic analysis of Babesia microti**
Bootstrap consensus tree of 18S rDNA

Goethert and Telford 2003 Parasitology 127: 301–309

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**Transfusion-transmitted babesiosis: a case report from a new endemic area**

E.D. Hurst, J.P. Acken, R.G. Cred, and J.L. McAllister

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**Emergence of powassan – deer tick virus**

1958 Powassan virus: isolation of virus from a fatal case of encephalitis, McLean et al., Can Med Assoc J 80: 708-11
1979 Powassan virus in Ixodes cookei and Mustelidae in New England, Main et al., J Wild Dis 15: 595–601
2009 First fatal case of deer tick virus reported from Westchester County, NY Tavolaki et al., NEJM 360: 2099-107

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Powassan virus
Vector
Reservoir
Ixodes scapularis
Mustelids

Phylogeny of North American powassan virus (POW)
Ebel 2010 Annu. Rev. Entomol. 55: 95–110

Deer Tick Virus Transmission Cycle
Powassan Virus Transmission Cycle
Ixodes scapularis
Ixodes cookei
Powassan Encephalitis

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Fatal Case of Deer Tick Virus Encephalitis
Norma P. Tennoi, Ph.D., Hong Wang, M.A., Michelle Dupade, B.Sc.,
Rene Hall, B.A., Gregory D. Evel, Sc.D., Emily J. Gilmore, M.D.,
and Phyllis L. Faust, M.D., Ph.D.

A Relapsing Fever Group Spirochete Transmitted
by Ixodes scapularis Ticks
Glen A. Schofield, Michele Pape, Lorenza Beat, and Durland Fish

Relapsing Fever Spirochetes
- B. ANSERNA
- B. CROCIDURAE
- B. DUTTONII
- B. RECURRENTIS
- B. HERMSII
- B. PARKERI
- B. TURICI
- B. LONESTAR
- B. MIYAMOTOI (Japan)
- B. MIYAMOTOI (US)
- B. TURDI
- B. ANDERSONI
- B. AFZELII
- B. VALASIANA
- B. LUSITANA
- B. JARIN
- B. DISSETI
- B. SURGOOPER (B31)
- B. SINCA

Lyme Disease Spirochetes
- B. BURGDORFERI (B31)
- B. SINCA

16s rDNA (1240 bp)

Scoles et al., 2001 Vector-Borne and Zoonotic Diseases 1: 21-34
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Spirochetes in SCID mouse blood
Geimsa stain

Prevalence of *B. miyamotoi* in host seeking *I. scapularis* nymphs

Reported cases of Lyme disease by year, United States, 1982-2007
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Summary

• Lyme disease is the most prevalent vector-borne disease in the US and Eurasia
• Other tick-borne pathogens are emerging (US):
  – Human babesiosis
  – Human anaplasmosis
  – Powassan viral encephalitis
  – Miyamotoi borreliosis?
• Emergence of these diseases is due primarily to environmental change caused by humans

Research team

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Jean Tsao, Ph.D.
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Ira Schwartz, Ph.D.
NY Med College
Gary Wormser, MD
NY Med College
Alan Barbour, MD
UC Irvine
Joseph Piesman, D.Sc.
CDC

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USDA
Boll Weevil Eradication
Great Smoky Mountains National Park
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