Borrelia burgdorferi Complex

Lyme disease

BC Centre for Disease Control
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Muhammad Morshed, PhD, SCCM
Program Head, BCCDC Public Health Laboratory
Clinical Professor, Path & Lab Med; UBC
Vancouver, British Columbia

Zoonotic & vector-borne workshop, Ellensberg, WA, Sept. 22nd , 2016

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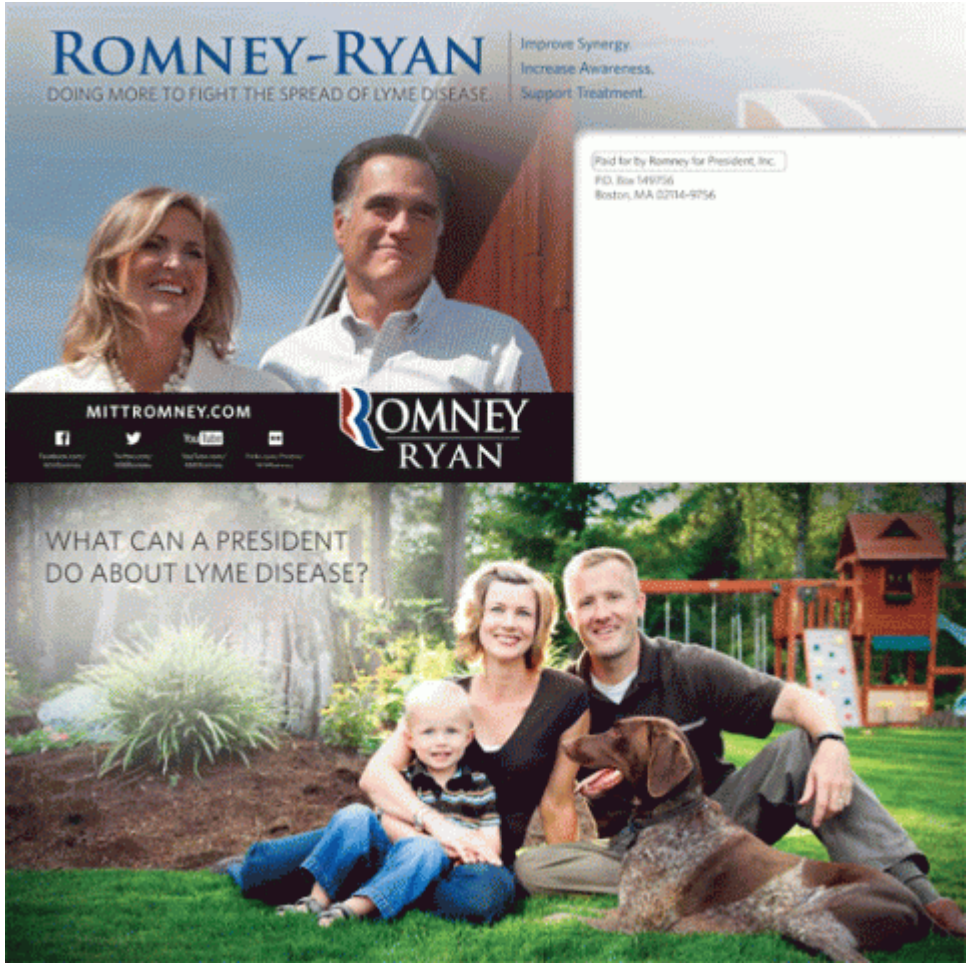
Disclosure

Obtained honorarium for giving a presentation to Bayer Inc.'s continuing education for Veterinarians in BC

No other disclosure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WHAT CAN A PRESIDENT
DO ABOUT LYME DISEASE?

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2 News Leader Wed., August 12, 1998

Lyme disease suspected on Burnaby Mountain

Health officials believe a second case of Lyme disease has been diagnosed at Simon Fraser University's Burnaby Mountain campus.

On Aug. 6, a nine-year-old girl attending a summer sports camp at SFU developed a bull's eye rash which is a common presenting sign of Lyme disease. On July 24, SFU health services reported that a female undergraduate student had been confirmed by laboratory tests as having contracted Lyme disease several weeks earlier.

Lyme disease is an infection caused by Borrelia burgdorferi bacteria which are spread in BC by the I. pacificus tick. These ticks are found in many locations throughout the Lower Mainland, Gulf Island and southern Vancouver Island. Mice are the most common host for the I. pacificus tick.

Lyme disease is relatively uncommon in BC, with only a few confirmed cases reported each year. Officials estimate that only one out of every 1,000 tick bites of humans will result in transmission of the Lyme disease bacteria.

The most common early sign of Lyme disease is the spreading, bull's eye-shaped rash, though this is only present in 50 to 60 per cent of Lyme disease cases. Other common symptoms include headache, muscle and joint pains, fatigue and weakness.

Diagnosed in its early stages, Lyme disease is treated with antibiotics. If not diagnosed and left untreated, it can, at times, lead to arthritis, heart or neurological problems.

Dr. Rob Parker, deputy health officer of the Simon Health Region, says: "Since ti mice in outdoor areas will li ways be with us, it's best to tak simple precautions when parti in outdoor activities on B Mountain or elsewhere in the Mainland." He recommends lowing:

- Wear light-coloured clothi long sleeves and with long tucked into socks.
- Avoid long grass or areas, or alternatively, stay on trails and paths.
- Use insect repellent co DEET on clothing, and spari exposed skin and with caus young children.

Lyme disease suspected in Okanagan area

■ Disease is transmitted by ticks

By Okanagan Sunday Staff

KELOWNA — The Okanagan may become part of a national study into Lyme disease, which is suspected in the death Kelowna's Kimberley Brown last month.

Dr. Muhammad Morshed of the

said Morshed.

Three cases of Lyme disease w reported in 2001, bringing the n ber of reported cases since 1991 t

Lyme disease often starts wit five-cm (two-inch) red circular pa on the skin with a central clear a that looks like a bulls-eye.

The disease can be cured with tibiotics but, if left untreated, it affect a person's heart, nervous

Monday, July 26, 1999

Health

Danger of Lyme disease on the rise

More ticks around, thanks to the mild B.C. winters

By Hardip Johal
Staff Reporter

If you go out in the woods this summer, be aware that the British Columbia Centre for Disease Control has identified 26 areas in B.C. as being home to deer ticks, the ugly, nasty bugs that infect people with Lyme disease.

"The tick population is on the rise and spreading," says Dr. Muhammed Moshed, head of the vector-borne diseases laboratory at the B.C. Centre for Disease Control, which tests thousands of ticks for the Lyme bacteria each year.

Moshed says there have been 60 confirmed cases of Lyme disease in B.C. over the last 10 years but he believes many cases go unreported.

He cites climate changes — warmer overall temperatures — as the major reason for the growing tick population in B.C.

"The tick needs a very humid environment and a mild winter," says Moshed.

"It gets the environment it needs here — and the length of this environment is increasing."

Moshed says people can protect themselves by taking the following precautions when out in the bush and other high-risk areas: Avoid long grasses, walk in the middle of a trail, wear long sleeves and pants, tuck in shirts and spray a tick repellent on clothes and exposed skin.

Areas in B.C. where ticks have been found:

Belcarra Regional Park, Bowen Island, Burnaby Mountain, Campbell River, Cranbrook, Cultus Lake, Duncan, Galiano Island, Harrison, Hope, Kitsilano, Langford, Langley, Lighthouse Park, Lions Bay, Matsqui, Metchosin, Mount Finlayson, Mundi Point, Nanoose, Powell River, Quadra Island, Saltspring Island, Sechelt, Squamish, White Rock.

What is Lyme disease?

Lyme disease is an infection caused by the bacteria Borrelia burgdorferi, transmitted by one of two species of ticks, both commonly referred to as deer ticks. In addition to deer, the ticks feed on humans, dogs, cats, horses, birds and several other animals.

Early symptoms include a slowly expanding red rash at the site of the tick bite. Sometimes there are also multiple, secondary skin rashes. Other common symptoms are fl including fatigue, headach neck stiffness, jaw discom pain or stiffness in muscl joints, slight fever, swolle glands or reddening of the If untreated, Lyme disease become far more serious.

Friday, June 26, 1998

Lyme Disease

e reported

dical health officer
nance of contracting
s locally is very low

Douan

The tick TIMEBOMB

Lyme disease remains a rarity Ontario but for th suffering from th bug-borne illness life is a living hell

He says that if anything, Lyme is overdiagnosed, even in Canada where the numbers are

Tuesday, June 15, 1993 The Province ★A5

Lyme disease found in B.C.

6 persons infected here could be 'tip of iceberg'

By Holly Horwood
Staff Reporter

Scientists say Lyme disease has arrived in B.C. and "thousands" may be unknowingly infected with it — or a mysterious twin ailment.

Twenty-three British Columbians have been diagnosed with the potentially fatal, multisystemic disease, which is transmitted by ticks.

And for the first time, at a press conference yesterday, specialists confirmed that six persons — including a two-year-old child — were infected in B.C.

"We have to accept the fact the disease is here," said University of B.C. microbiologist Satyendra Banerjee, who heads a new, five-year, $1-million government research project into the disease.

But experts fear there may be many more individuals who show antibodies indicating an almost identical Lyme-like disease who have never been diagnosed, or have been wrongly diagnosed.

"There are thousands, perhaps, who have never appeared to the physicians," said Banerjee. "It could be the tip of the iceberg."

Caused by a spiral-shaped bacterium (spirochete), Lyme disease has reached epidemic levels in the northeast and north-central U.S.

Its early symptoms include flu-like malaise, fever, headache, stiff neck and joints.

It is treatable with antibiotics.

But if undetected, the symptoms can become chronic.

Rarely, death can occur from respiratory or heart failure.

Experts stress the likelihood of encountering an infected tick is still very small. Only one per cent of ticks tested in the past few years have been found to be infected.

"It's a very low-risk situation at this time," said Ron Zapp of the B.C. Centre for Disease Control.

But that's little consolation for West Vancouver nurse Diane Kindree, who was infected while gardening in 1988.

Her arthritic-like symptoms weren't properly diagnosed for 10 months. Though treated, she still has residual arthritic problems.

"Do not give up, do not give in," Kindree told others struggling to find research dollars to unravel the "great mystery of Lyme."

NEWS Friday, August 7, 1998

Lyme disease makes its way to Island

Bay Wake
Weekend Edition staff

Ticks carrying Lyme disease are crossing the U.S. border, and settling in Canada.

And if global warming continues, some researchers say Canadians could find themselves threatened at an increasing rate by ticks — even on Vancouver Island.

"That I agree with," says Dr. Muhammad Morshed, head of vector borne disease at the B.C. Centre for Disease Control.

While Canadians used to contract Lyme disease only by trav-

The tick that carries Lyme disease discovered locally

tick move, and we aren't sure that it's going to stop."

Morshed, who examines the ticks collected from patients by doctors in B.C., says he sees about 300 ticks a year — a num-

ing adult.

With more ticks, Morshed says, the chances of rodents being infected with Lyme disease increases — and the chance of rodents passing the disease

tem abnormalities and arthritis. Early symptoms include a red-ringed expanding rash, fatigue, headaches, achiness and fever, which can progress to severe headaches and stiffness, light sensitivity, facial paralysis, heart problems and memory lapses. Eventually, it can lead to arthritis in the large joints and inflammation of the brain.

In the U.S., there an estimated 10,000 cases annually making it the most serious arthropod-borne disease in the country.

Ticks — which are about two-mm in length — search for

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Taxonomy of Borrelia

- Kingdom: Bacteria
- Phylum: Spirochaetae
- Class: Spirochaetes
- Order: Spirochaetales
- Family: Sprochaetaceae
- Genus: Borrelia

Borrelia burgdoreferi Complex

↓

Borrelia burgdoreferi sensu Lato

↓

Borrelia burgdoreferi sensu stricto

↓

Lyme disease

↓

Western Pacific Coast Situation

Variants of phrases using the word *sensu*

Base phrase	Comparative	Superlative	Meanings
sensu stricto	*sensu strictiore*	*sensu strictissimo*	in the strict/stricter/strictest sense
sensu lato	*sensu latiore*	*sensu latissimo*	in the broad/broader/broadest sense
sensu amplo	*sensu ampliore*	*sensu amplissimo*	in a relaxed/more relaxed/most relaxed sense

Wikipedia

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Currently known spirochete species from the *Borrelia burgdorferi* sensu lato complex.

Borrelia species	Vector	Hosts/reservoirs	Geographical distribution	Reference
B. afzelii	*I. ricinus I. persulcatus*	Rodents	Asia, Europe	Canica et al. (1993)
B. americana	*I. pacificus, I. minor*	Birds	United States	Rudenko et al. (2009c)
B. andersonii	*I. dentatus*	Cotton tail rabbit	United States	Marconi et al. (1995)
B. bavariensis	*I. ricinus*	Rodents	Europe	Margos et al. (2009)
B. bissettii	*I. ricinus, I. scapularis, I. pacificus, I. minor*	Rodents	Europe, United States	Postic et al. (1998)
B. burgdorferi sensu stricto	*I. ricinus, I. scapularis, I. pacificus*	Rodents, birds, lizards, big mammals	Europe, United States	Baranton et al. (1992)
B. californiensis	*I. pacificus, I. jellisonii, I. spinipalpis*	Kangaroo rat, mule deer	United States	Postic et al. (2007)
B. carolinensis	*I. minor*	Rodents, birds	United States	Rudenko et al. (2009b)
B. garinii	*I. ricinus, I. persulcatus, I. hexagonus, I. nipponensis*	Birds, lizards, rodents	Asia, Europe	Baranton et al. (1992)
B. japonica	*I. ovatus*	Rodents	Japan	Kawabata et al. (1993)
B. kurtenbachii	*I. scapularis*	Rodents	Europe, United States	Margos et al. (2010)
B. lusitaniae	*I. ricinus*	Rodents, lizards	Europe, North Africa	LeFleche et al. (1997)
B. sinica	*I. ovatus*	Rodents	China	Masuzawa et al. (2001)
B. tanukii	*I. tanuki*	Unknown (possibly dogs and cats)	Japan	Fukunaga et al. (1996)
B. turdi	*I. turdus*	Birds	Japan	Fukunaga et al. (1996)
B. spielmanii	*I. ricinus*	Rodents	Europe	Richter et al. (2006)
B. valaisiana	*I. ricinus, I. granulatus*	Birds, lizards	Asia, Europe	Wang et al. (1997)
B. yangtze	*Haemaphysalis longicornis, I. granulatus*	Rodents	China	Chu et al. (2008)
Genomospecies 2	*I. pacificus*	Unknown	United States	Postic et al. (2007)
B. miyamotoi			United States	Pritt et al (2015)
B. mayonii			United States	Pritt et al (2016)

Ticks tic Borne Dis. 2011. 2930 123-128

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Association of Borrelia spp with Human Disease

No	Not Isolated from Human	Pathogenic Potential in Human	Mostly Found on Human
1	*B americana*	*B afzeli*	*B afzeli*
2	*B andersonii*	*B bavariensis*	*B burgdoreferi (ss)*
3	*B californianiensis*	*B bissettii*	*B garinii*
4	*B carollinensis*	*B burgdorferi (ss)*	
5	*B japonica*	*B garinii*	
6	*B tanuki*	*B kurtenbachii*	
7	*B turdi*	*B mayonii*	
8	*B sinica*	*B miyamotoi*	
9	*B yangtze*	*B lusitaniae*	
10		*B spelmanii*	
11		*B valisiana*	

Ticks tic Borne Dis. 2011. 2930 123-128

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Borrelia-Vcetor-Host Association

Bridge Vector	Maintenance Vector
Ixodes scapularis	*Amplyomma americanum;*
I pacificus	*I minor; I affinis; I dentatus; I spinapalpis;*
I angustus	*I hexanus; I uriae; I turdus; I tanuki;*
I ricinus	*I ovatus; I columnae; I nipponensis*
I persulcatus	*Many more Ixodes species……..*
	Darmacentor variabilis; D albipictus;
	Hemophysalis longicornis, h concinna; H bispinosa

Ticks tic Borne Dis. 2011. 2930 123-128

Conclusions

- There are 21 Borrelia species under *Borrelia burgdorferi* senu lato ……more to come
- 9 of them usually do not found on human
- 3 of them are responsible for over 99% cases in Eurasia and NA

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Lyme Disease Symptoms

Stage	System	Manifestation
Early localized disease (< 30 days)*	Skin	Erythema migrans (note: must be > 5 cm in diameter, painless and slowly expanding)
	Systemic	Fever
		Arthralgias
		Headache
Early disseminated disease (< 3 months)*	Skin	Multiple erythema migrans
	Systemic	Fever
		Arthralgias
		Headache
		Lymphadenophathy
	Heart	Atrioventricular block
		Tachyarrhythmias
		Myopericarditis
		Myocardial dysfunction
	CNS	Aseptic meningitis
		Cranial neuropathy (especially facial nerve palsy)
	Ocular	Conjunctivitis (rare)
Late disseminated disease (> 3 months)*	MSK	Oligoarticular arthritis
	CNS	Encephalopathy
		Axonal polyradiculoneuropathy
		Chronic encephalomyelitis
	Ocular	Retinitis (rare)

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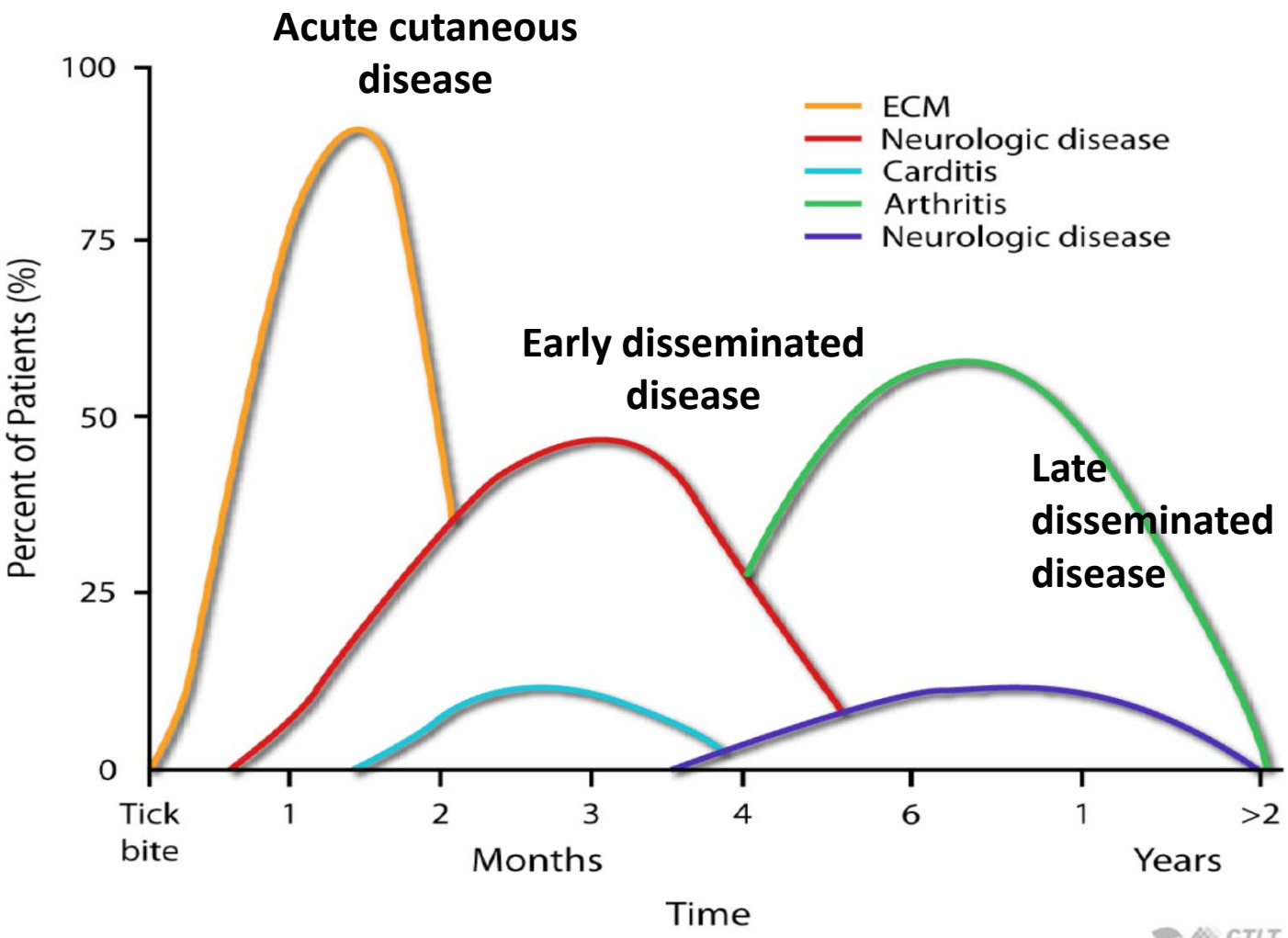
Lyme Disease Clinical Course



CTLT
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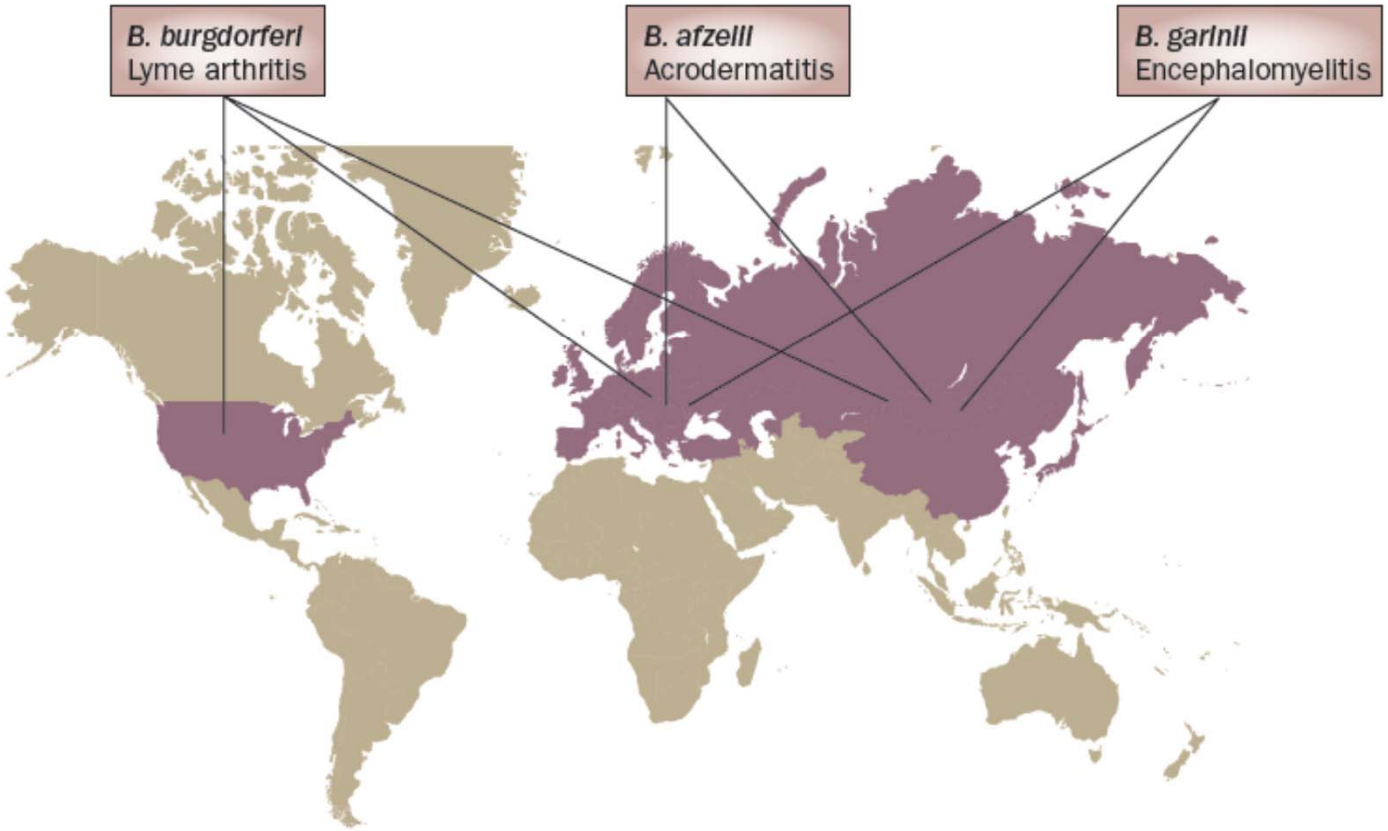
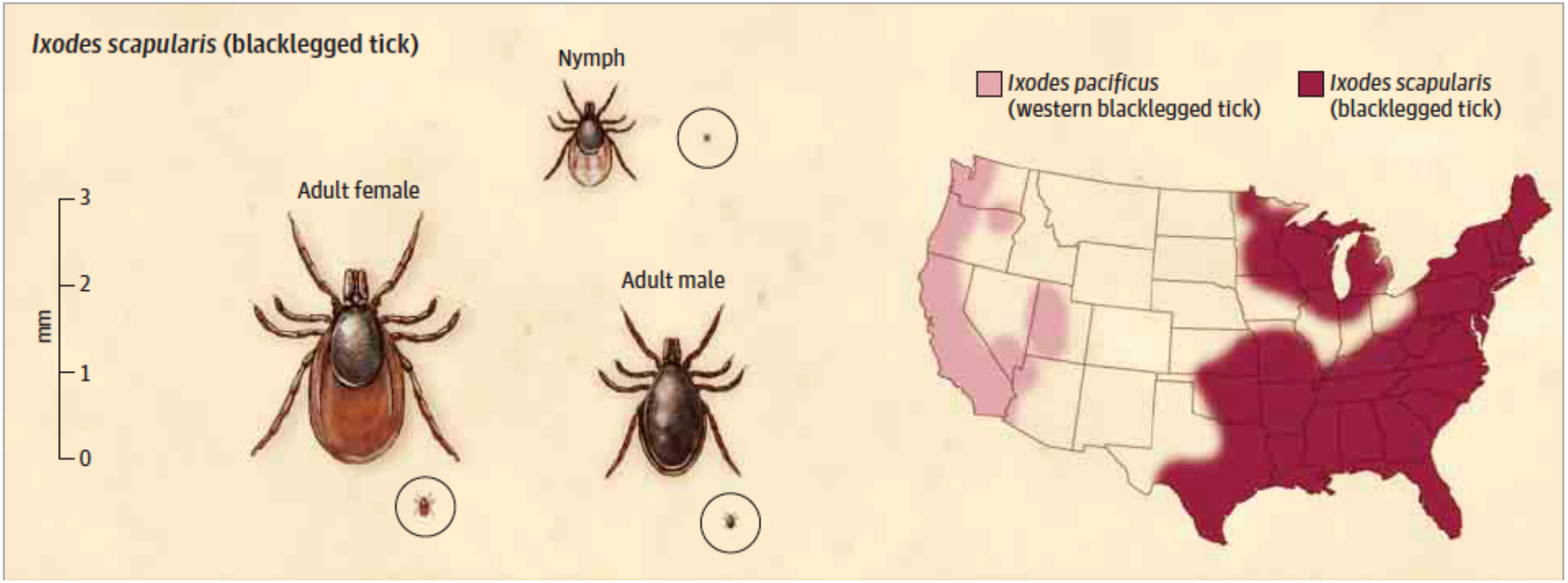
Distribution of *Borrelia* spp causing disease in humans

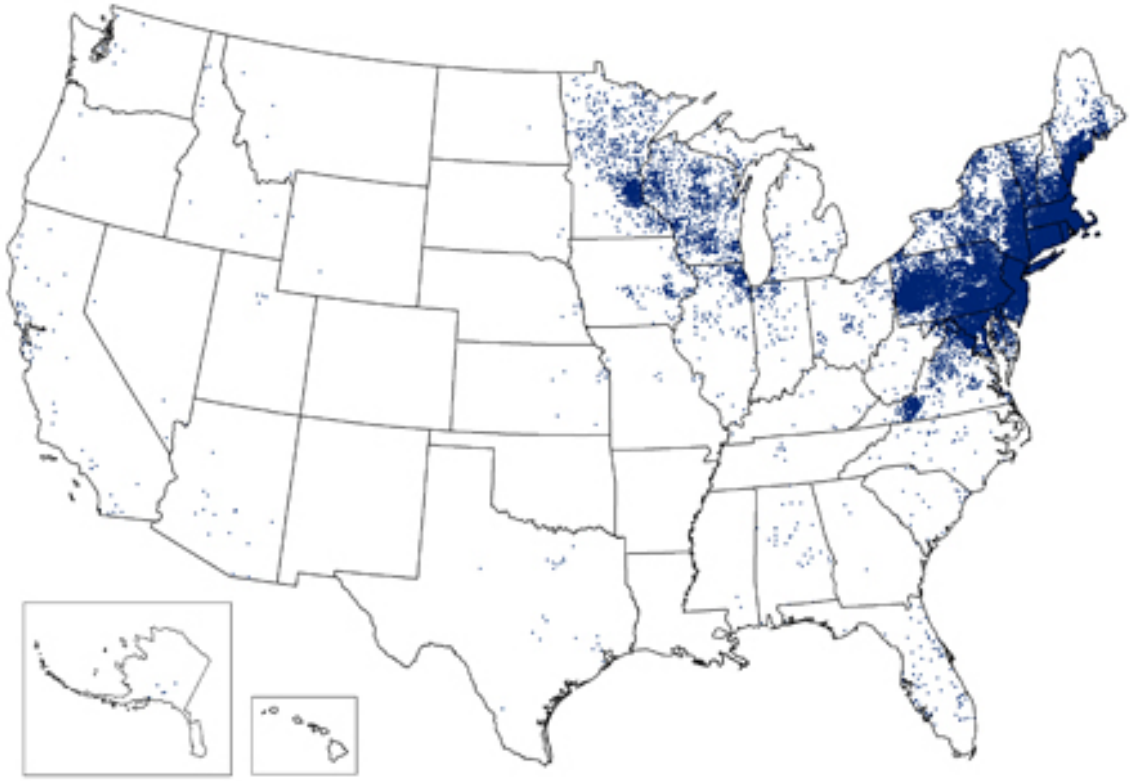




Ixodes Ticks and Their Geographic Distributions in the United States. *Ixodes scapularis* nymphal and adult ticks (ticks in black circles are shown at actual size). The nymphs and adult females can *transmit Borrelia burgdorferi*, *Anaplasma phagocytophilum*, and *Babesia microti*; adult males may attach but do not feed and thus do not transmit these pathogens. Map showing distribution of *Ixodes scaularis* in the eastern part and *I pacificus* in the western part

JAMA. 2016;315(16):1767-1777. doi:10.1001/jama.2016.2884

Reported Cases of Lyme Disease -- United States, 2014



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

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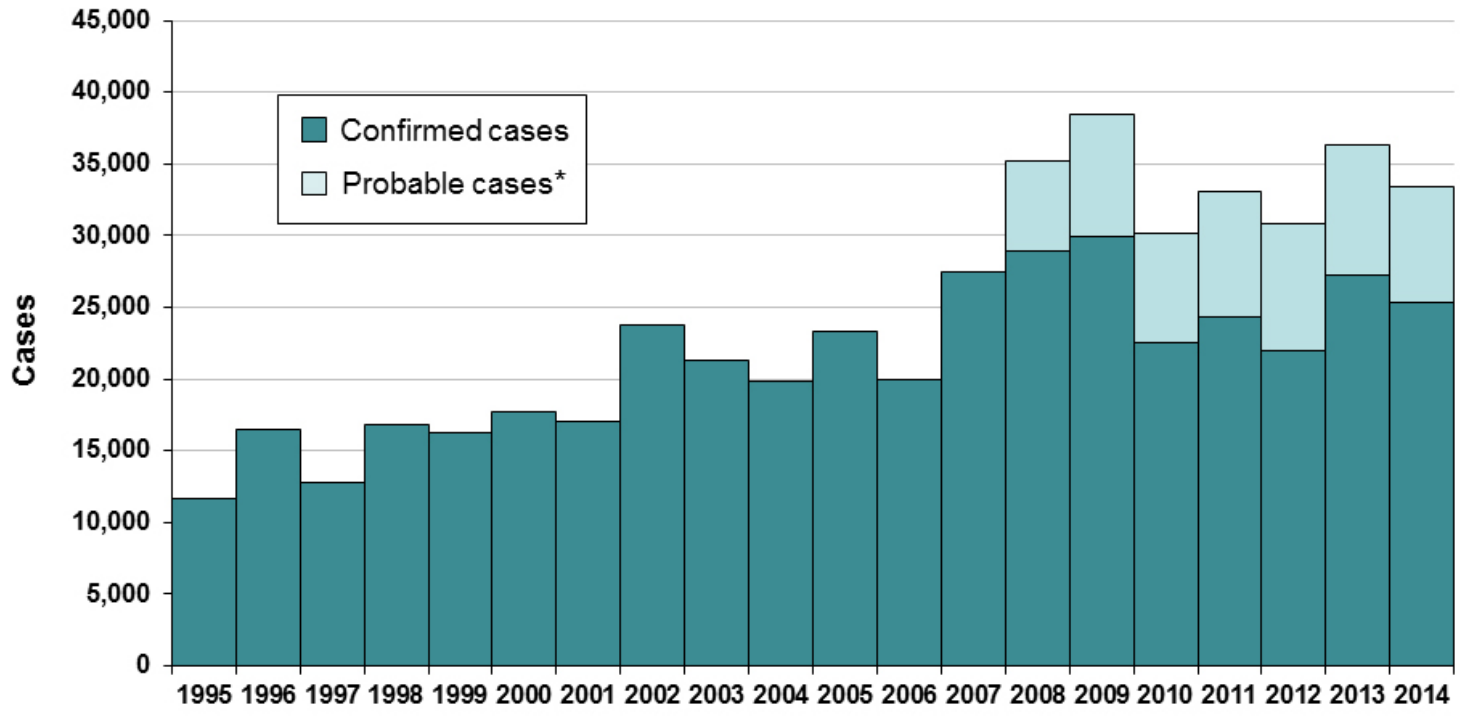
Reported Cases of Lyme Disease in US



CDC

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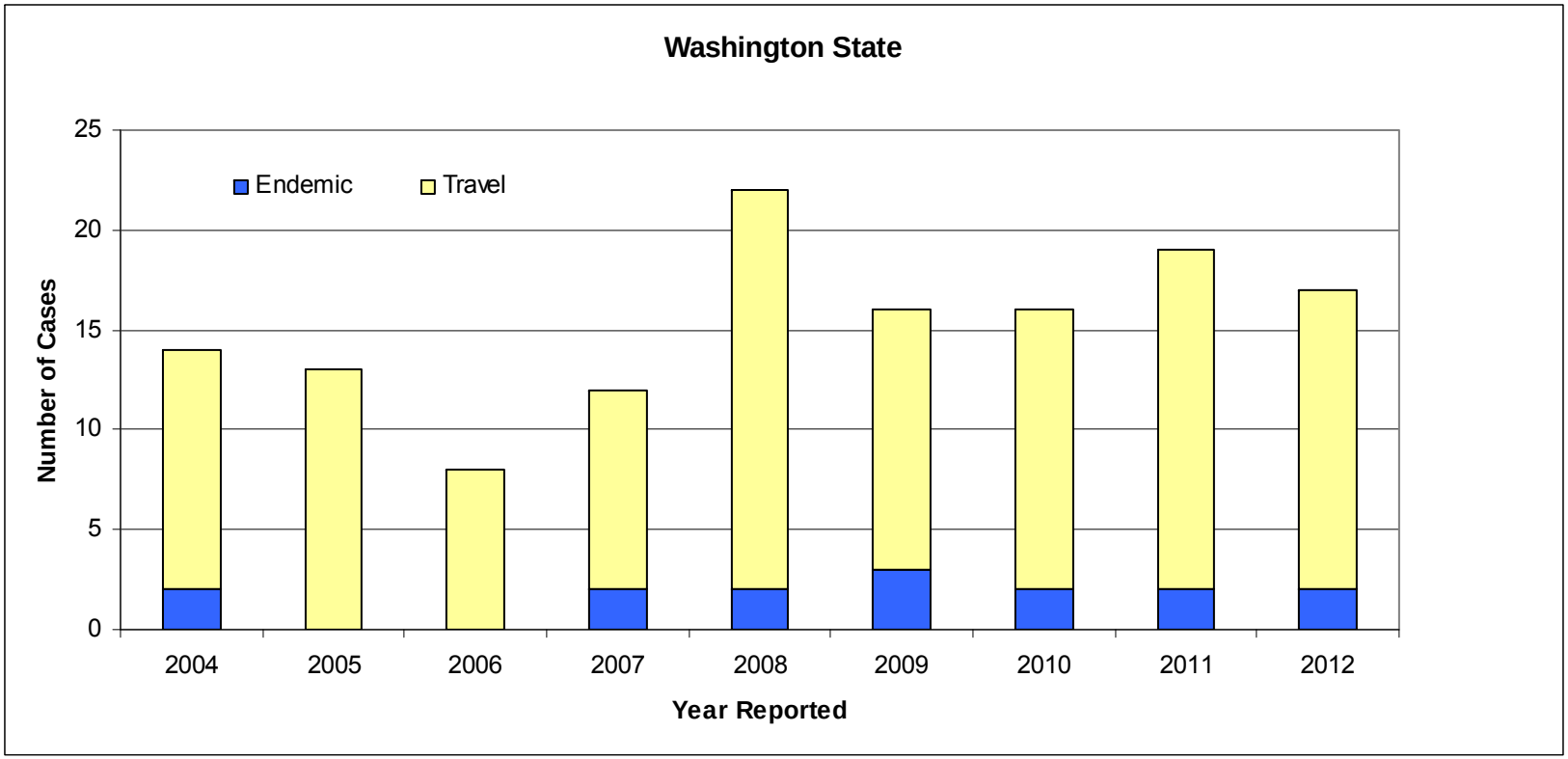
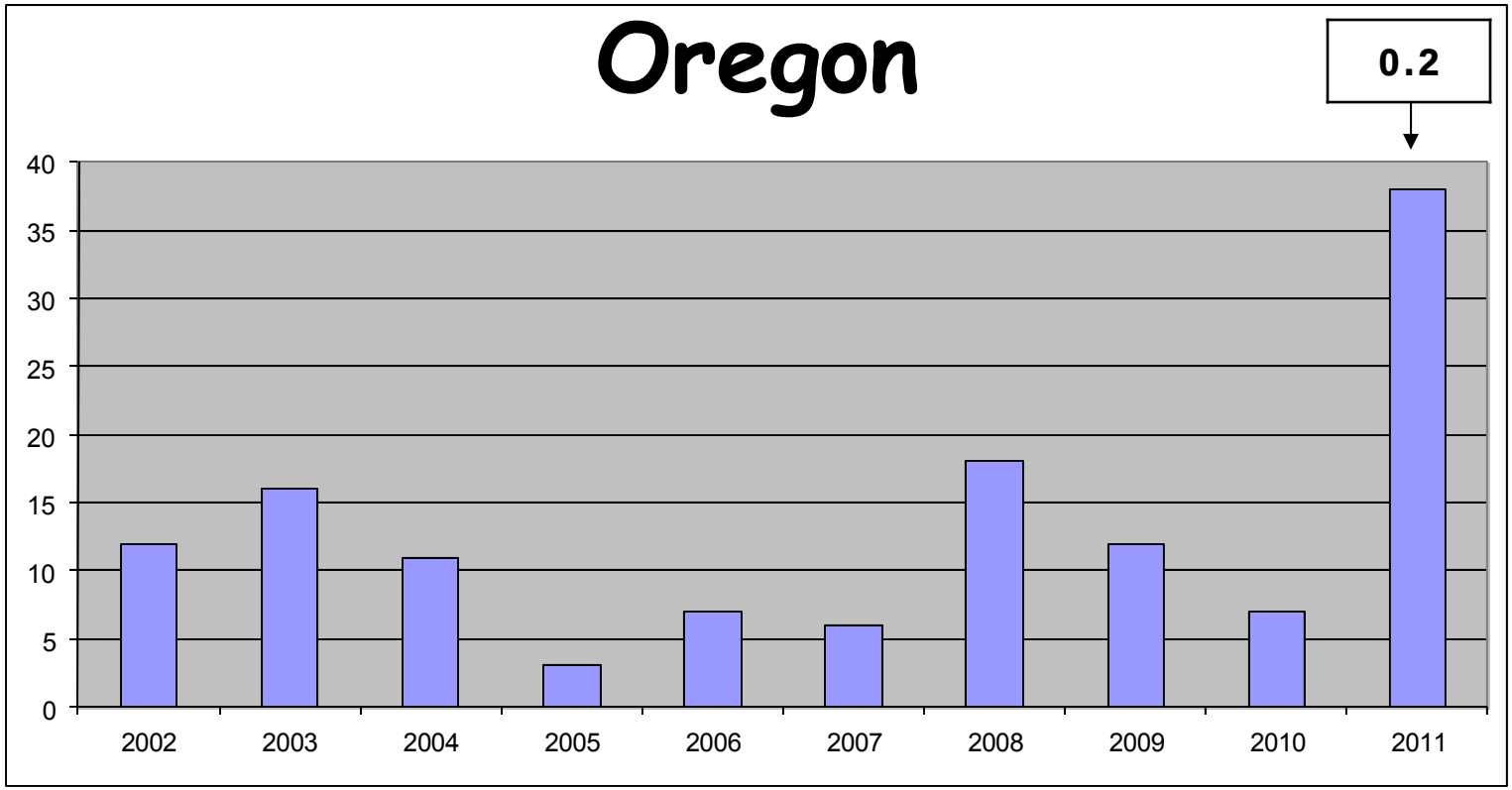
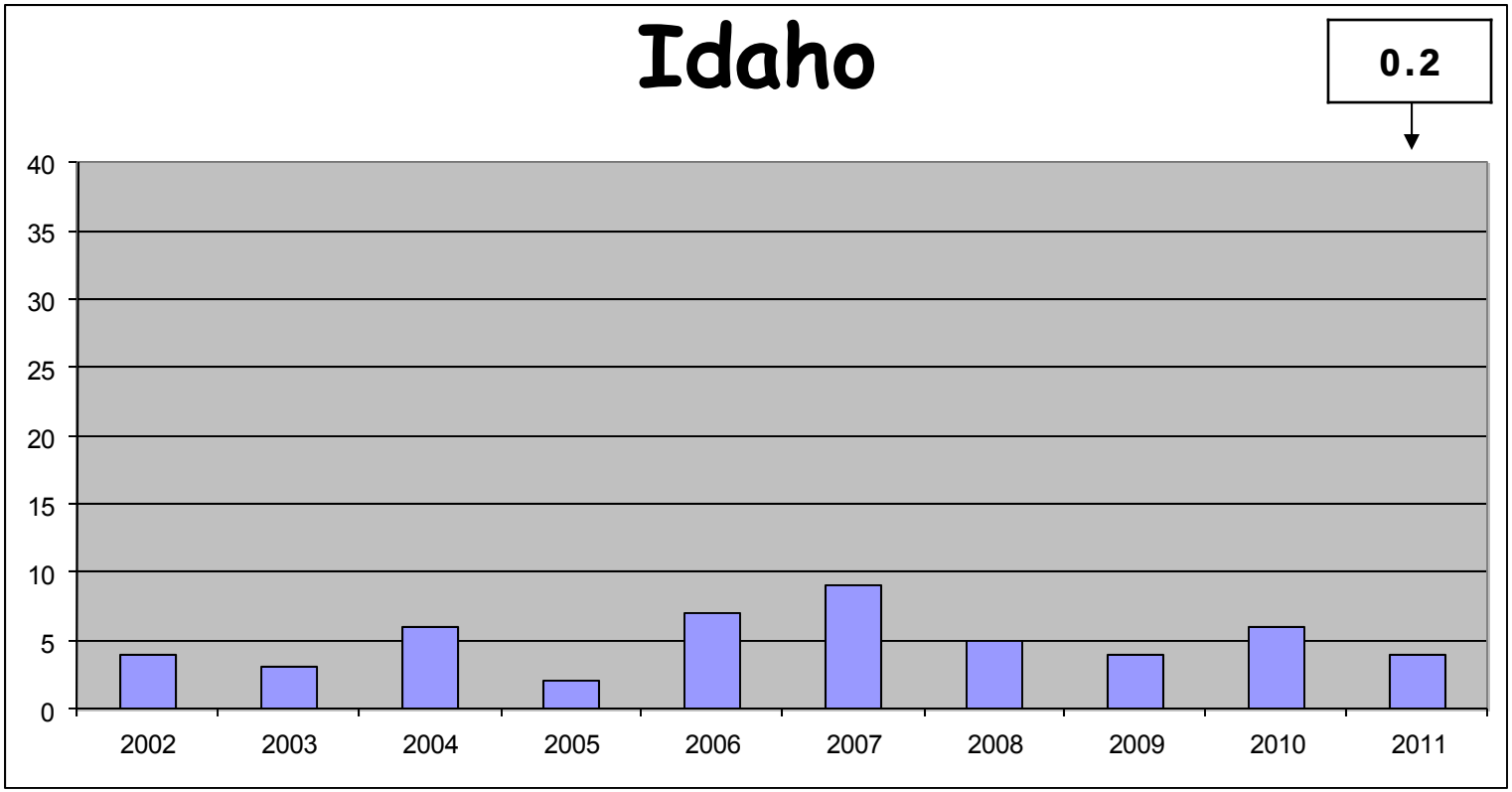
Endemic and travel-related cases of Lyme diseases in Washington State between 2004-2012





Source: CDC USA



Source: CDC USA

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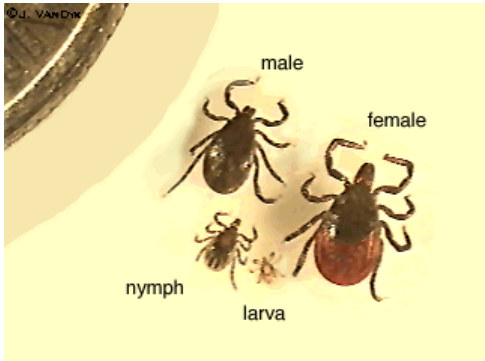
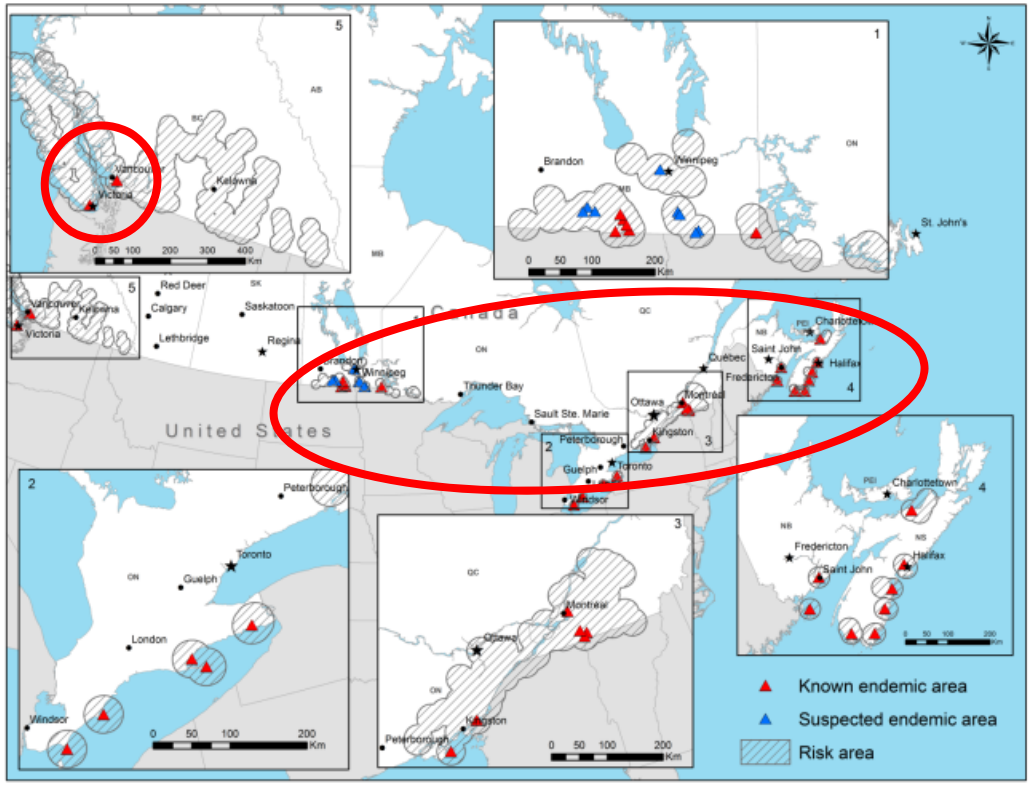
Distribution of Lyme Disease Ticks in Canada





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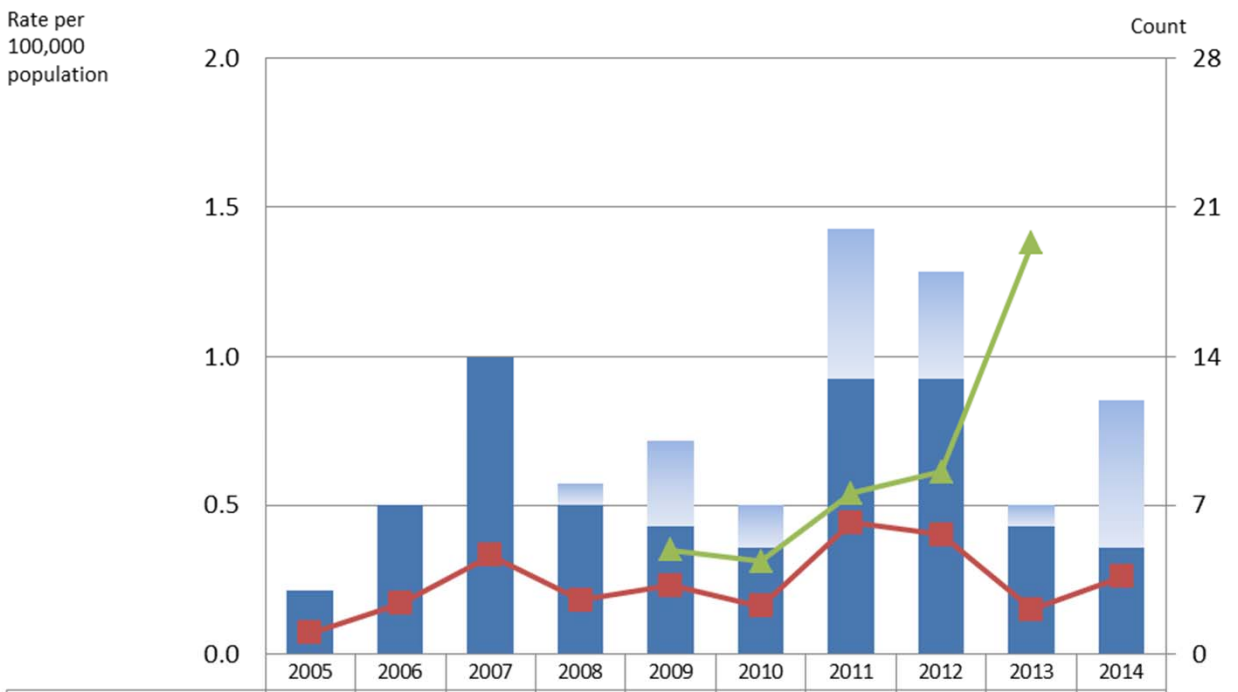
Lyme disease in BC: 2005-2014



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
BC Lyme Probable	0	0	0	1	4	2	7	5	1	7
BC Lyme Confirmed	3	7	14	7	6	5	13	13	6	5
BC Lyme Rate	0.1	0.2	0.3	0.2	0.2	0.2	0.4	0.4	0.2	0.3
Canadian Lyme Rate					0.4	0.3	0.5	0.6	1.4	

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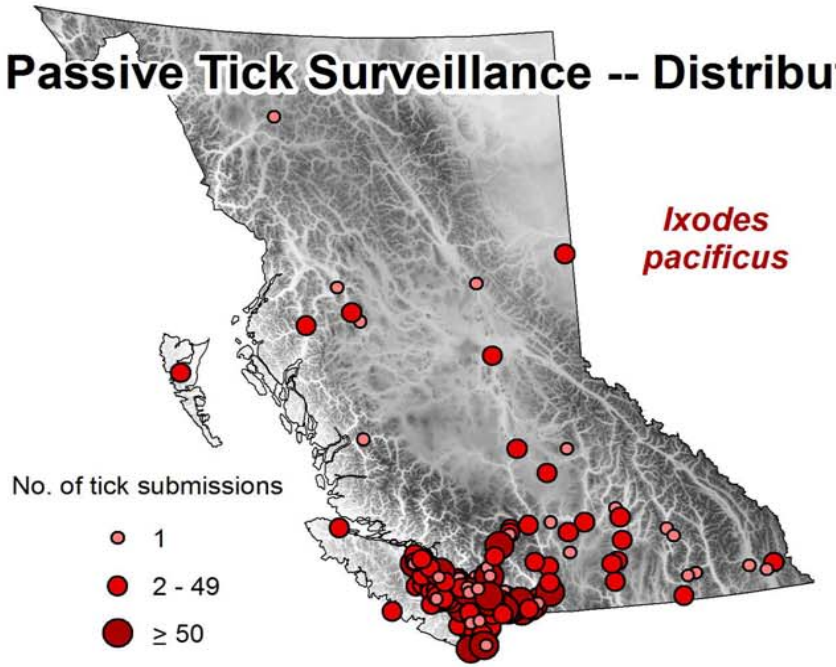
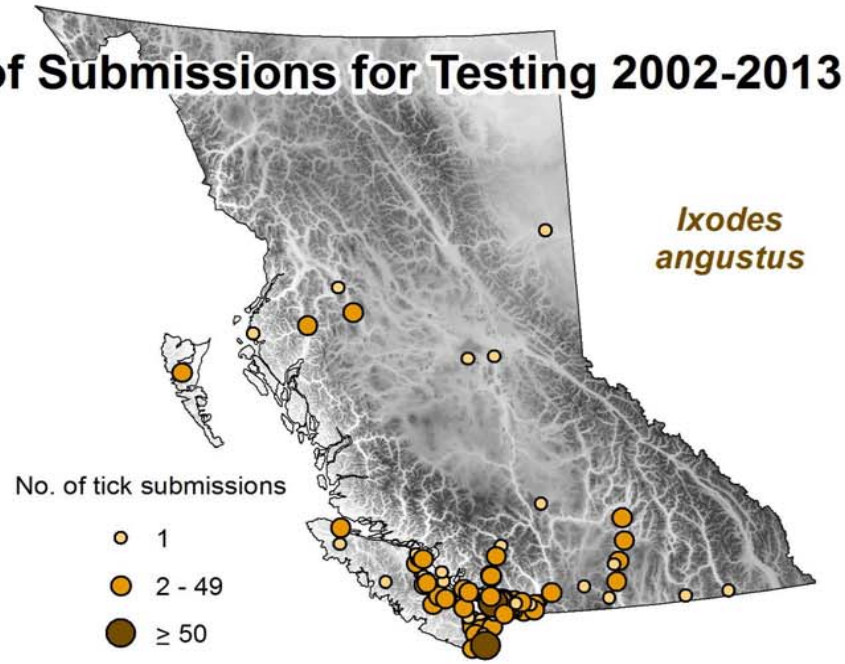
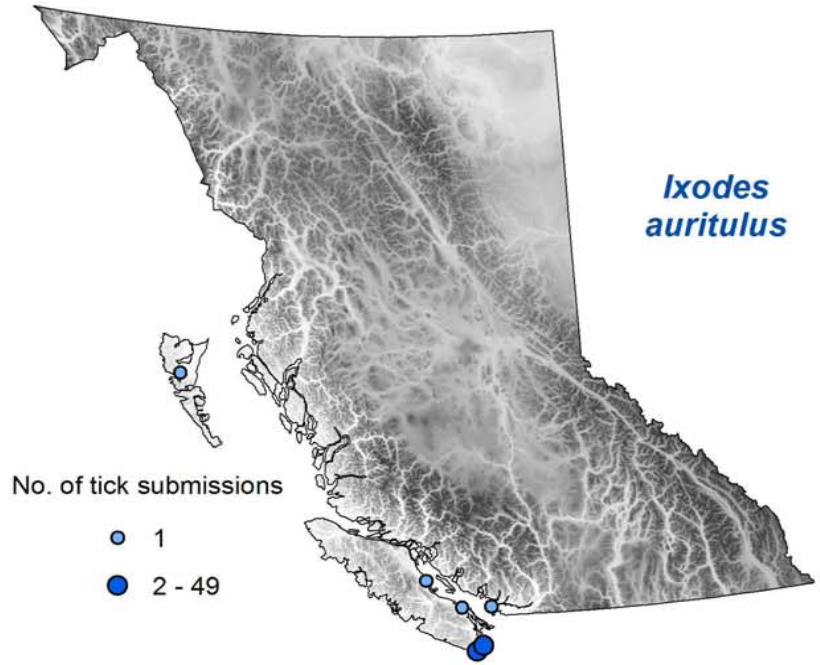
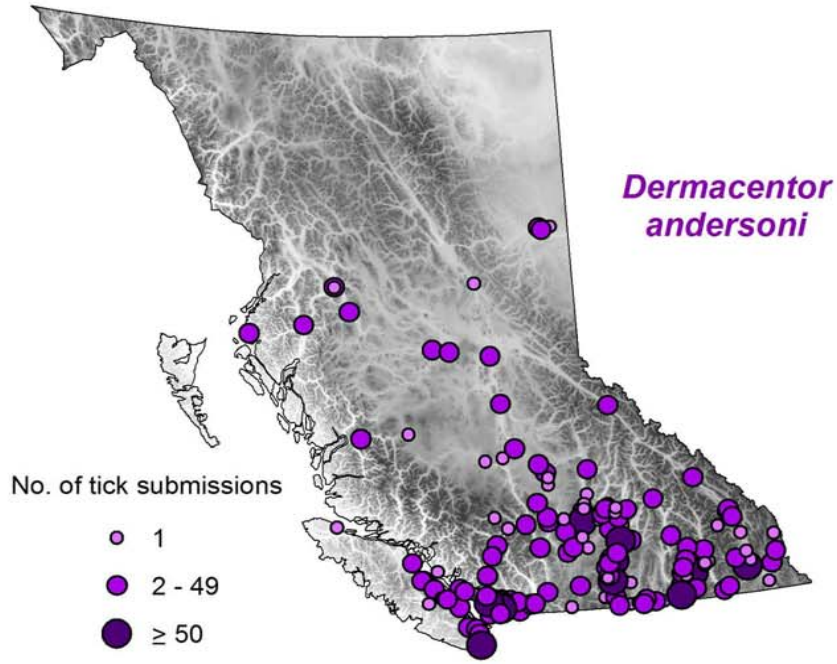
Passive Tick Surveillance -- Distribution of Submissions for Testing 2002-2013









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Rate of Lyme Disease In the Pacific Northwest

* Rate per 100,000	2009	2010	2011	2012	2013	2014	2015
British Columbia	0.2	0.2	0.4	0.4			
Washington	0.2	0.2	0.2	0.2	0.2	0.1	
Oregon	0.3	0.2	0.2	0.1	0.3	0.1	
Idaho	0.3	0.4	0.2	0.0	0.9	0.5	
California	0.3	0.4	0.0	0.2	0.2	0.2	
U.S.A.	9.8	7.3	7.8	7.0	8.6	7.9	

*Eastern US states such as ME, VT, NH, MA, NY, CT, RI observe an average rate of 40-50 cases per 100,000 annually!

Source: Centers for Disease Control and Prevention:
Lyme Disease Incidence Rates by State, 2009-2015

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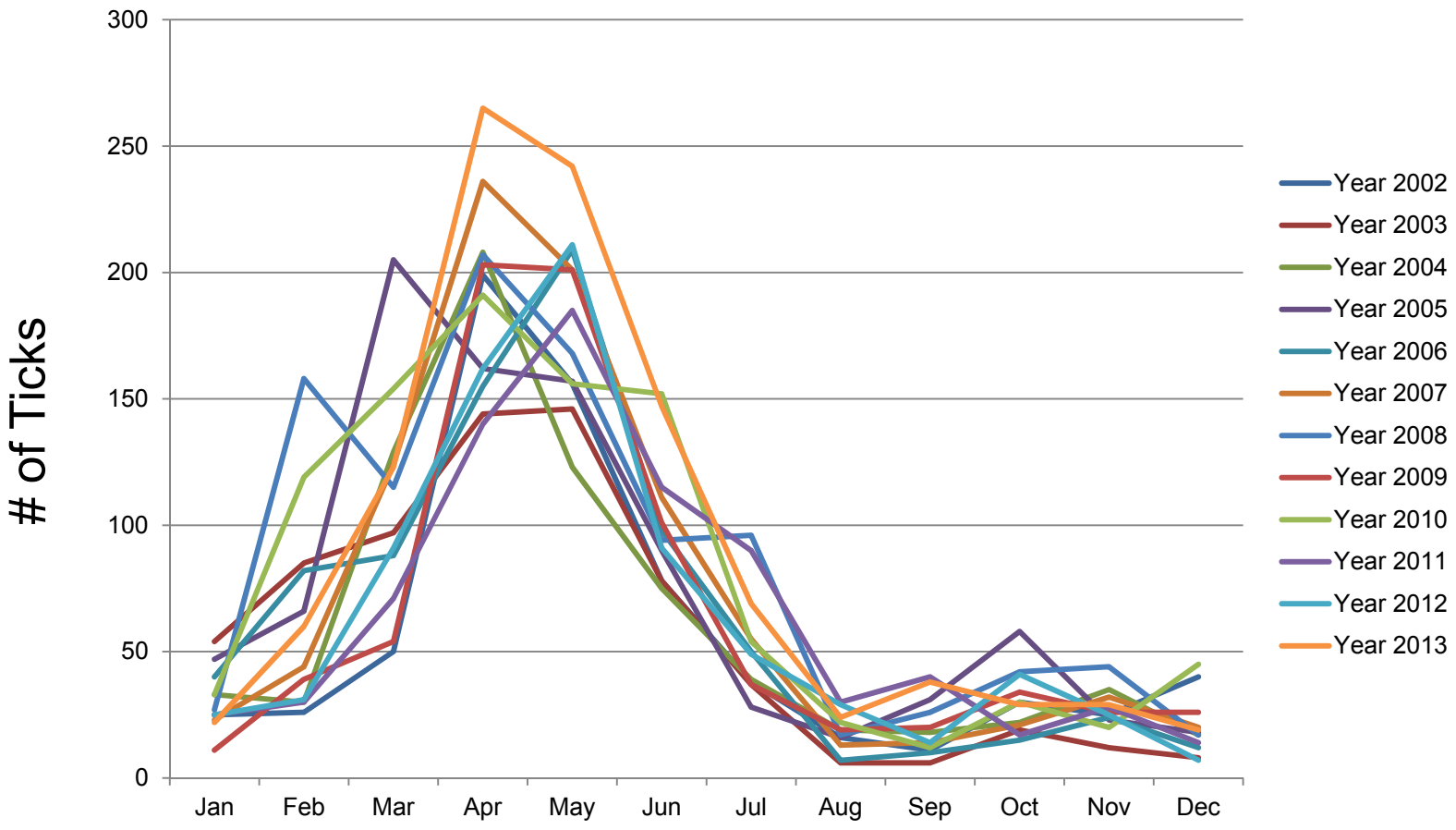
Seasonal Distribution of Ticks in BC



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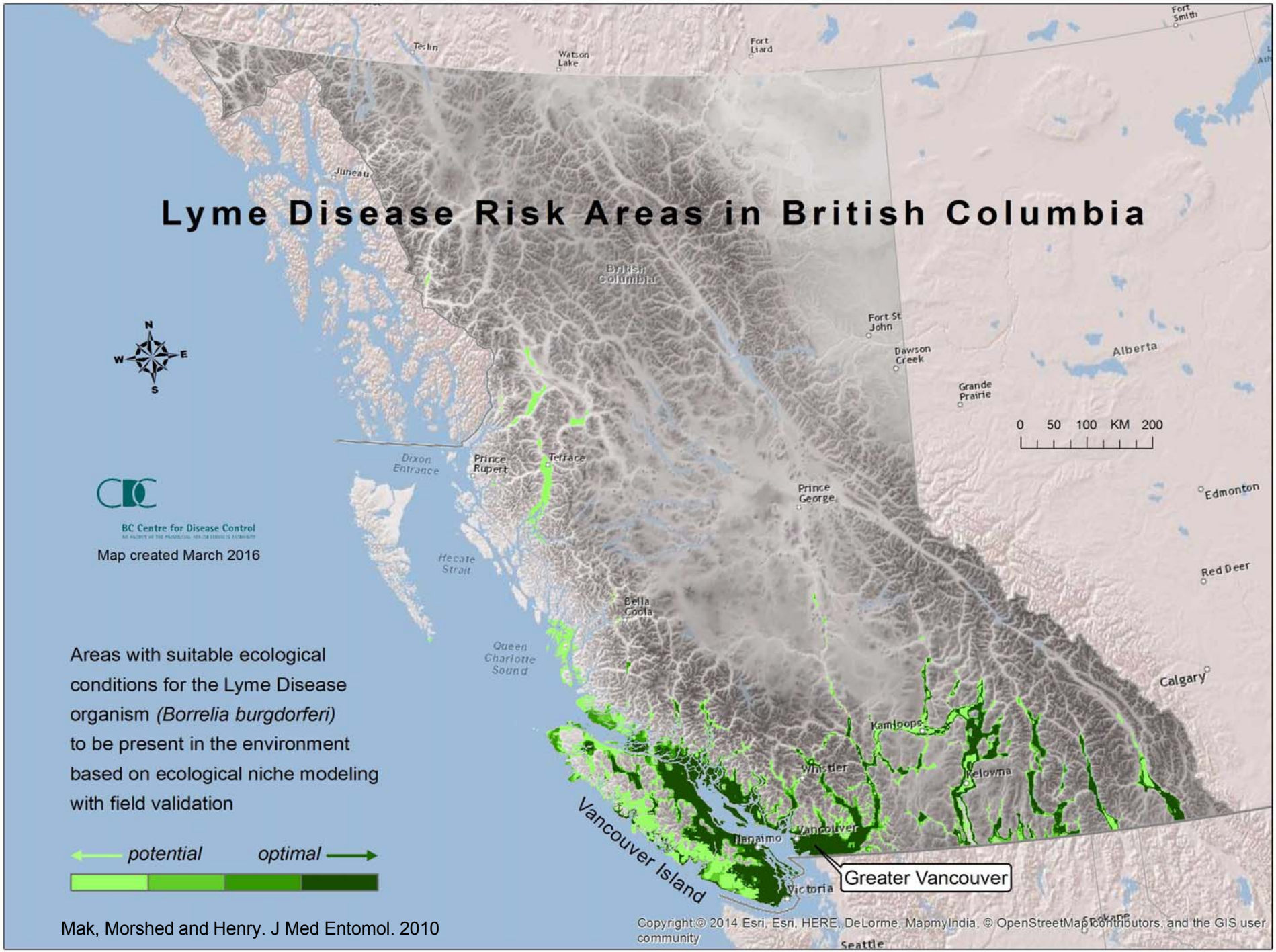
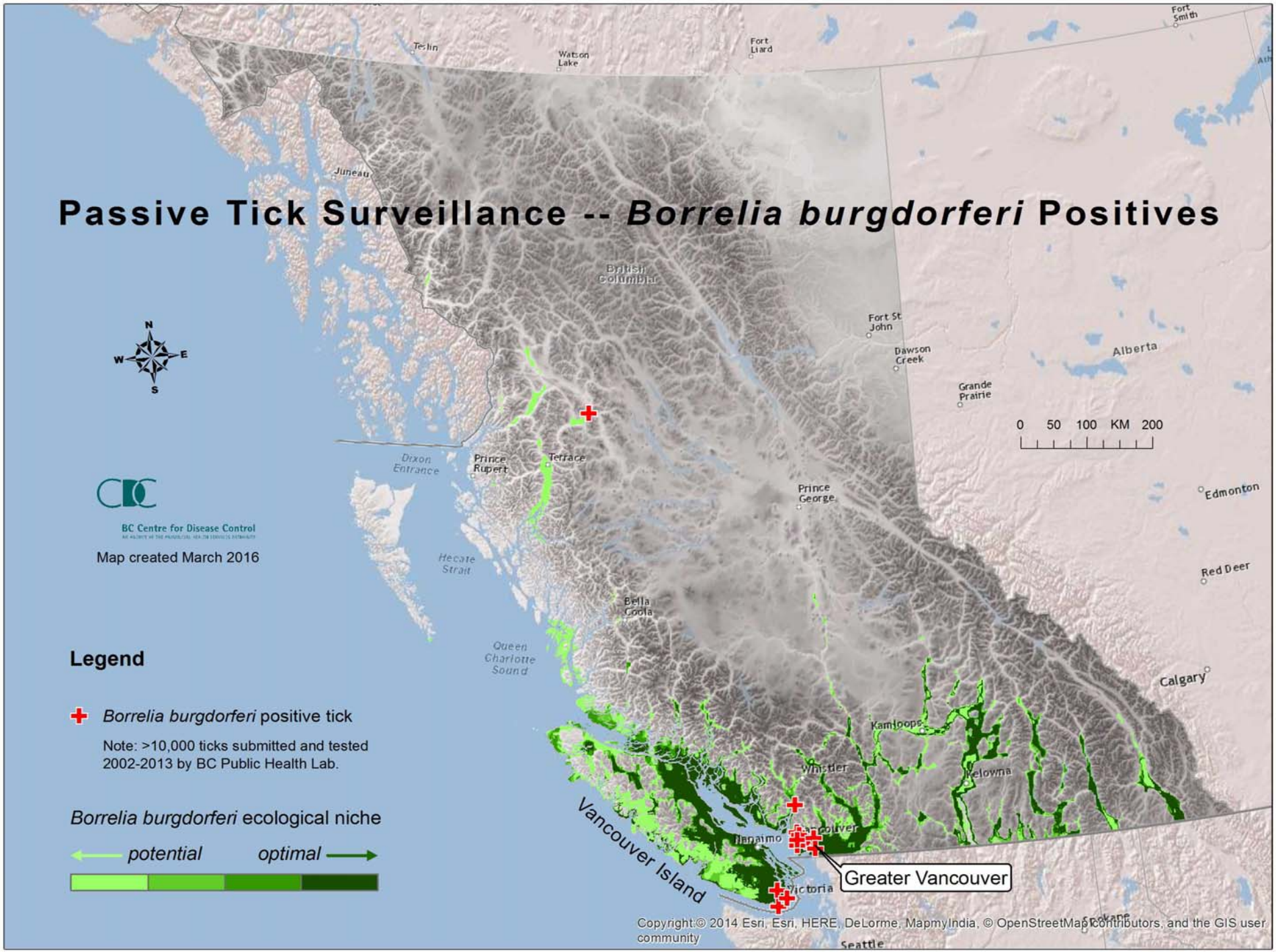


Mak, Morshed and Henry. J Med Entomol. 2010


Passive Tick Surveillance -- Borrelia burgdorferi Positives
N
W
E
S
BC Centre for Disease Control
Map created March 2016
Legend
Borrelia burgdorferi positive tick
Note: >10,000 ticks submitted and tested 2002-2013 by BC Public Health Lab.
Borrelia burgdorferi ecological niche
potential
optimal
0 50 100 KM 200
Teslin
Watson Lake
Fort Liard
Fort Smith
Juneau
British Columbia
Fort St John
Dawson Creek
Alberta
Grande Prairie
Dixon Entrance
Prince Rupert
Terrace
Prince George
Edmonton
Hecate Strait
Red Deer
Bella Coola
Queen Charlotte Sound
Calgary
Kamloops
Whistler
Kelowna
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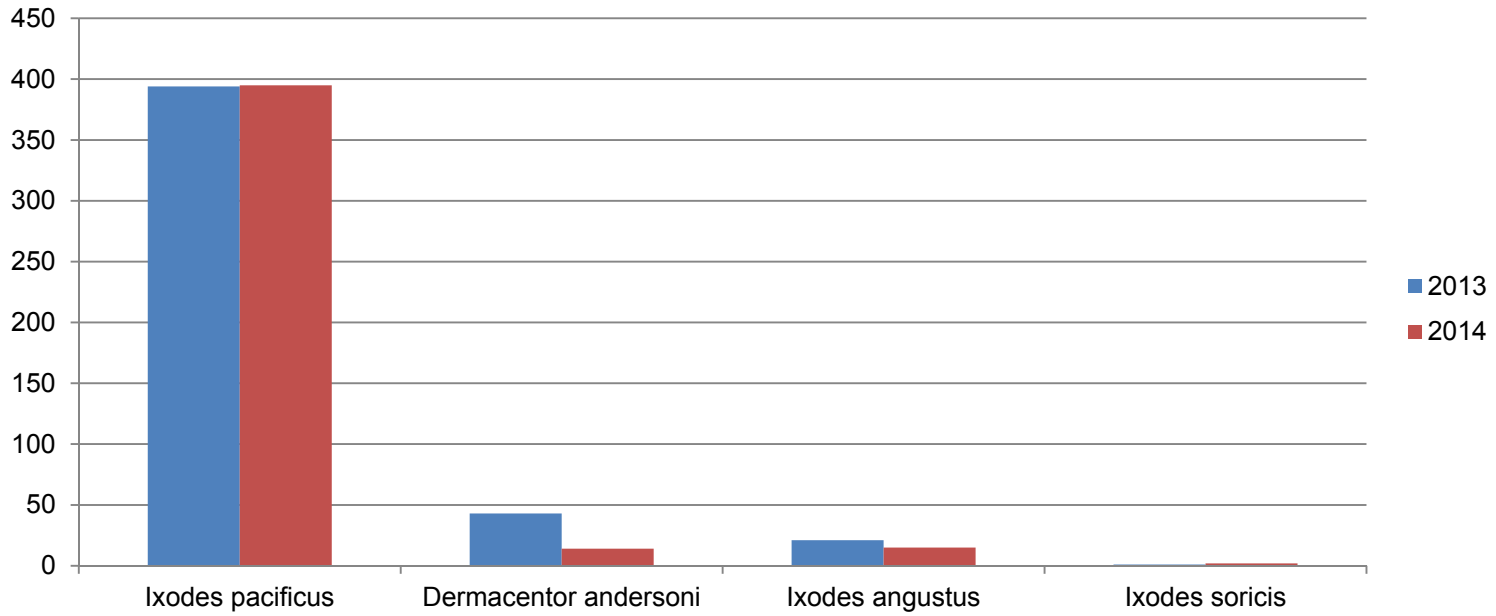
Ticks Retrieved from Mice

Yearly Comparison of Species



Species	2013		2014	
	Sample Size	Positives	Sample Size	Positives
Ixodes pacificus	394	**3 (0.76%)**	395	**2 (0.51%)**
Ixodes angustus	21	0 (0.0%)	15	0 (0.0%)
Ixodes soricis	1	0 (0.0%)	2	0 (0.0%)

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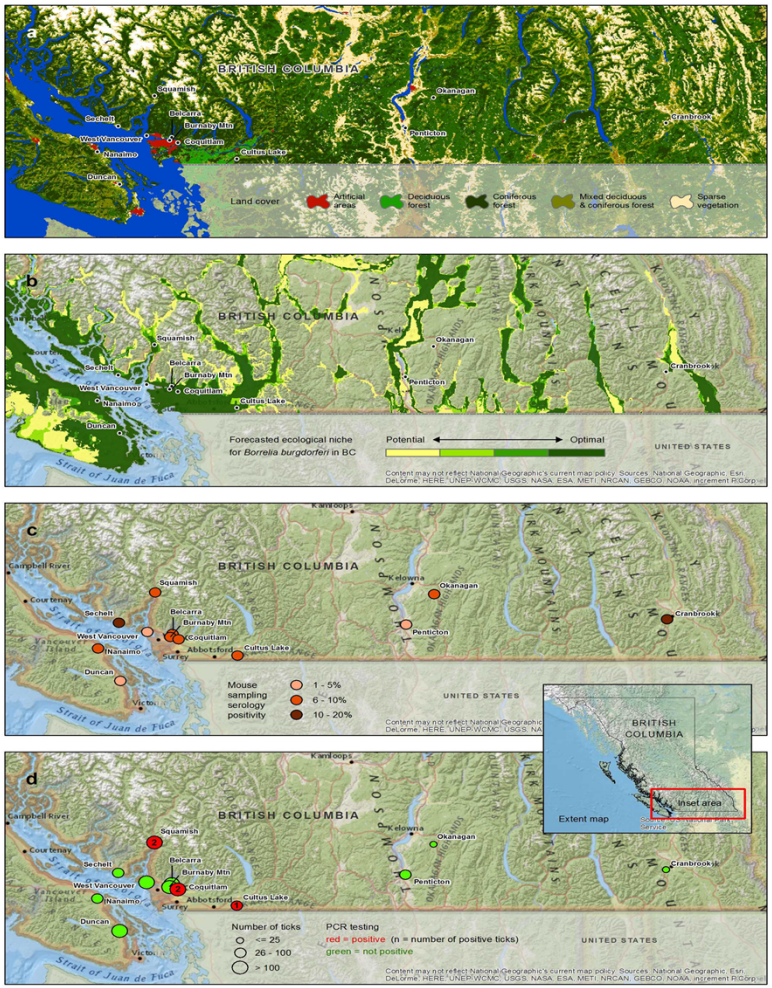
A

B

C

D



Map of *Borrelia burgdorferi* surveillance in ticks and mice in British Columbia. Land cover type (A), ecological niche model for *B. burgdorferi* (B), mice (C) and ticks (D) captured from study locations.

Morshed et al, Vector Borne Zoonotic Dis. 2015

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First isolation of Lyme disease spirochete, Borrelia burgdorferi, from blacklegged tick, Ixodes - Microsoft Internet Explorer

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Public Health Agency of Canada (PHAC)

Canada Communicable Disease Report — CCDR

Volume 25-18
15 September 1999

[Table of Contents]

FIRST ISOLATION OF LYME DISEASE SPIROCHETE, *BORRELIA BURGDORFERI*, FROM BLACKLEGGED TICK, *IXODES SCAPULARIS*, REMOVED FROM A BIRD IN NOVA SCOTIA, CANADA

The Lyme disease spirochete, *Borrelia burgdorferi,* has been isolated from a blacklegged tick, *Ixodes scapularis*, removed from a songbird in Canada. On 28 May 1999, this engorged blacklegged tick nymph was removed from a common yellowthroat, *Geothlypis trichas,* collected during bird banding on Bon Portage Island, Nova Scotia.

The Atlantic Bird Observatory participated in collecting attached ticks from passerine birds banded on Seal Island and Bon Portage Island off the southwest tip of Nova Scotia. During spring migration, 21 ticks were collected from 12 individual birds (4 species) from 14 to 29 May 1999. These immature (larva, nymph) ticks on birds included the rabbit tick, *Haemaphysalis leporispalustris*, and *I. scapularis* (Table 1).

As part of a monitoring program of ticks on birds in southern Canada, these engorged ticks were forwarded for identification, and then sent by courier to the British Columbia Centre for Disease Control Society (BCCDCS) for spirochetal analysis. At the BCCDCS, the tick identifications were confirmed and the ticks were surface sterilized using 10% hydrogen peroxide followed by 70% isopropyl alcohol, and transferred to sterile tissue to remove excess water. Dead ticks underwent DNA analysis directly using polymerase chain reaction (PCR) testing. For live ticks, the midgut contents were cultured in Barbour-Stoenner-Kelly (BSK) II medium at 34° C, and cultures were checked weekly by dark-field microscopy. Within 10 days, characteristic motile

Done Internet

Start Inbox - Microsoft Outl... Inbox - Outlook Express Microsoft PowerPoint -... First isolation of Ly... 3:06 PM

Morshed et al,

Can Commun Dis Rep. 2000

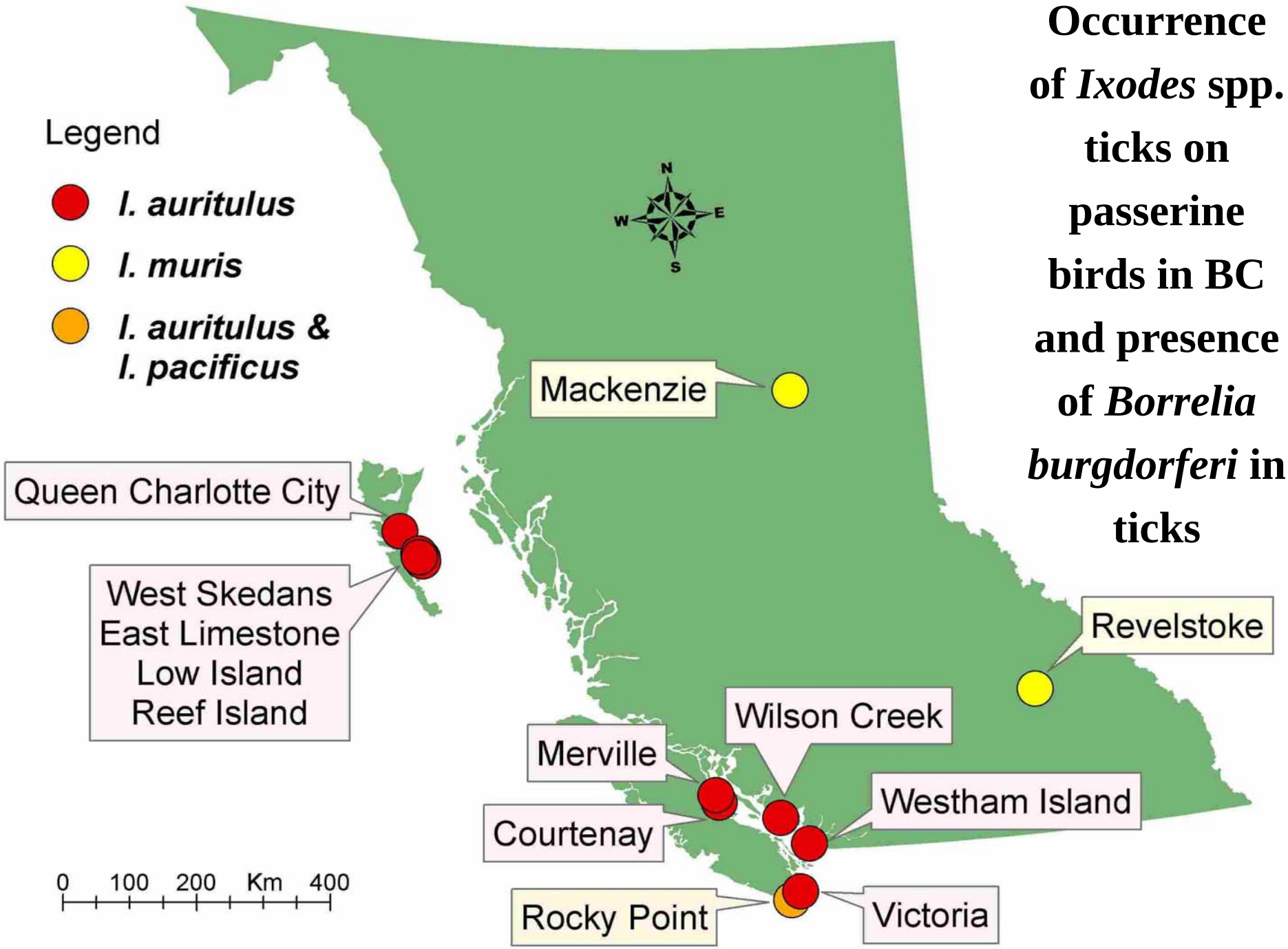
BIRD TICK STUDY

Swainson's thrush
Catharus ustulatus

American robin
Turdus migratorius

Fox sparrow
Passerella iliaca

Occurrence of *Ixodes* spp. ticks on passerine birds in BC and presence of *Borrelia burgdorferi* in ticks



Conclusions

- *Borrelia burgdorferi* originated from Europe
- Only few species of *B burgdoreferi* sensu lato is responsible for causing Lyme disease in human and animals.
- *B. Burgdorferi* activities is much higher in the Eastern NA compare to the Pacific West Coast.
- Lyme disease Case numbers in the Pacific West Coast are much lower than Eastern part of USA
- Tick activities are seasonal
- Bird may carry ticks from long distance. More studies are needed on their establishment

Diagnosis

Laboratory Based Diagnostic Options

- **Serology**

  Most common and widely accepted

- **PCR**

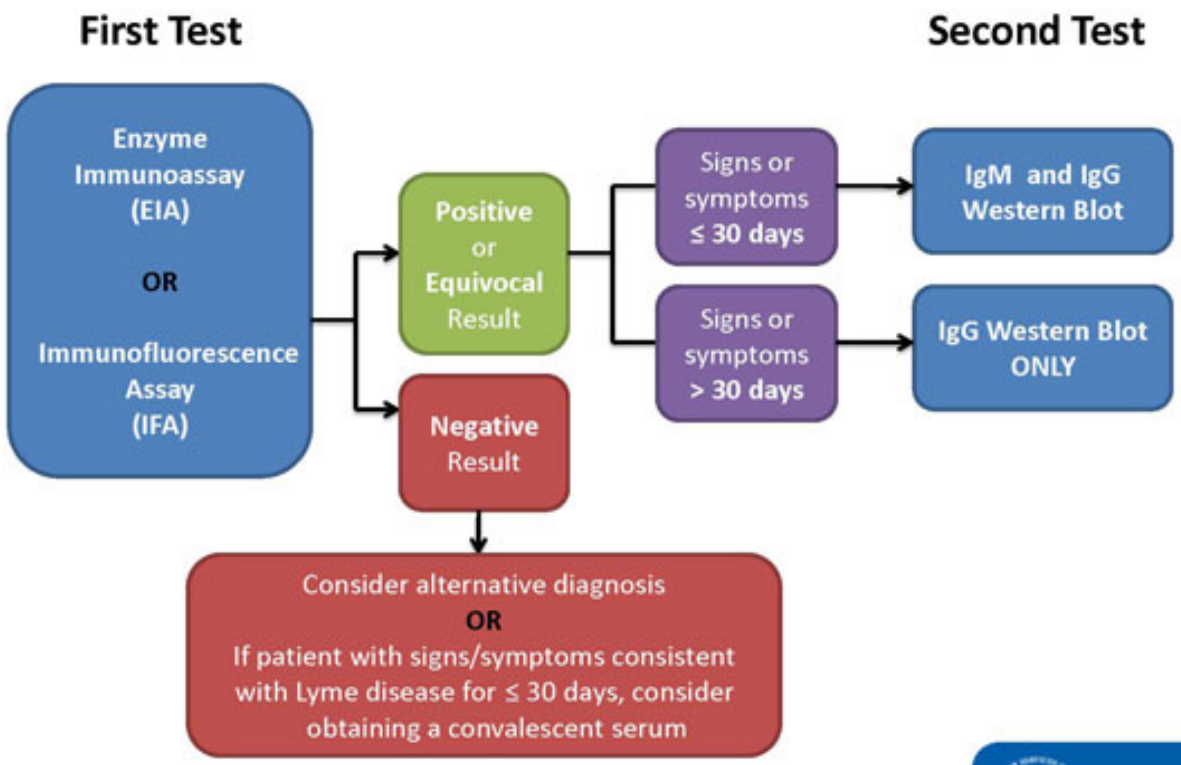
  Work best on synovial fluid if patients has not been given any antibiotics

- **Culture**

  For special cases only, take weeks, sensitivity low and not recommended for routine diagnosis

Test Algorithms

Two-Tiered Testing for Lyme Disease



National Center for Emerging and Zoonotic Infectious Diseases
Division of Vector Borne Diseases | Bacterial Diseases Branch

Western blots can not be used independent of EIAs

- EIAs are quantitative, blots are subjective
- IgM western blots have poor specificity. Only diagnostic if used in first 6 weeks of infection
- European species can be falsely negative on NA WB

Aguero-Rosenfeld and Wormser, 2015. Exprt Rev Mol Diagn 15:1-4
DeBiasi. 2014. Curr Infect Dis Rep 16:450-455

Prospective Study of Serologic Tests for Lyme Disease

Allen C. Steere, Gail McHugh, Nitin Damle, and Vijay K. Sikand

Center for Immunology and Inflammatory Diseases, Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Harvard Medical School, Boston

1999-2001 East Lyme Connecticut

76 patients who had culture confirmed EM

147 with late Lyme or other illnesses

- **objective clinical findings and positive serology**

PLD (Post LD or Chronic LD)

- **pain or neurocognitive or fatigue < 6 months after appropriate ABX Rx**

Controls

CID 2008 47:188-195

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CID 2008 47:188-195 Contd….

Disease State	C6 EIA	EIA IgM WB	EIA IgG WB	EIA IgM or IgG WB
Acute (stage 1)	19-38%	11-38%	6-15%	17-43%
Convalescent after antibiotics	47-63%	39-70%	17-20%	53-75%
Disseminated infection (acute neurologic or arthritis) (stage 2)	**100%**	85%	85%	**100%**
Persistent infection (stage 3)	**100%**	23%	100%	**100%**
Not Lyme (n=75) (CFS, FM,MS,RA)	1%	0%	0%	0%
Healthy (endemic area) (n=86)	5%	1%	1%	2%
Healthy (non-endemic area) (n=50)	2%	0%	0%	0%

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Performance characteristics of serological assay

Sample category (n^a)	No. (%) positive by method					
		WB[c]		Two-tiered testing		
	WCS EIA (Vidas)[b]	IgM	IgG	Vidas-WB IgM[d]	Vidas-WB IgG	Standard[e]
Lyme disease, total patients = 86						
Early Lyme disease with EM						
Acute phase (40)	27 (68)	14 (35)	8 (20)	12 (30)	8 (20)	16 (40)
Convalescent phase (38)	34 (89)	20 (53)	14 (37)	20 (53)	13 (34)	23 (61)
Early Lyme disease with Lyme neuroborreliosis or Lyme carditis						
Lyme neuroborreliosis (10)	9 (90)	10 (100)	3 (30)	9 (90.0)	3 (30)	9 (90)
Lyme carditis (7)	7 (100)	4 (57)	4 (57)	4 (57)	4 (57)	6 (86)
Late Lyme diseases						
Lyme arthritis (29)	29 (100)	9 (31)	29 (100)	9 (31)	29 (100)	29 (100)
Look-alike diseases, total patients = 144						
Fibromyalgia (31)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)
Severe periodontitis (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Rheumatoid arthritis (21)	2 (10)	1 (5)	0 (0)	1 (5)	0 (0)	0 (0)
Syphilis (20)	17 (85)	2 (10)	0 (0)	2 (10)	0 (0)	1 (5)
Multiple sclerosis (22)	4 (18)	2 (9)	0 (0)	1 (5)	0 (0)	0 (0)
Infectious mononucleosis (30)	16 (53)	5 (17)	0 (0)	3 (10)	0 (0)	3 (10)
Healthy controls, total donors = 203						
Area of disease endemicity (101)	9 (9)	2 (2)	2 (2)	1 (1)	2 (2)	2 (2)
Area of disease nonendemicity (102)	5 (5)	2 (2)	0 (0)	0 (0)	0 (0)	0 (0)

Molins et al 2014 JCM 52:10

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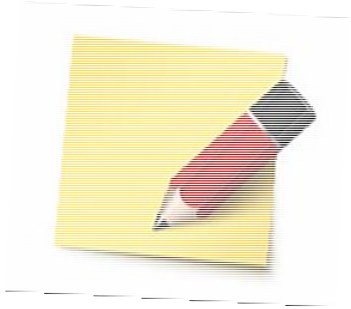
Conclusions



- **Serological test is good for** detecting early disseminated (>1M) and late disseminated or persistent (>3M) infections
- **Refractory symptoms may persist in 10-20% patients**
- **Long term treatment may do harm to patients**

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In acute stage, EM rash itself is diagnostic, no Lab confirmation is needed for diagnosing acute Lyme disease. So physician should treat at this stage on suspicion of infection.

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Bull's-Eye and Non-target Skin Lesions of Lyme Disease: An Internet Survey of Identification of Erythema Migrans

John Hopkins Univ. Maryland

42,068
Visits or page clicks to the website

3,902
Opened the link to the rash survey

3,104
Answered every question

2,543
Definitively responded to the classic target EM question with "I am sure this is a Lyme disease rash" or "I am sure this is not a Lyme disease rash"

342
Definitively responded to every question with "I am sure this is a Lyme disease rash" or "I am sure this is not a Lyme disease rash"

Aucott et al, Dermatol Res Pract. 2012

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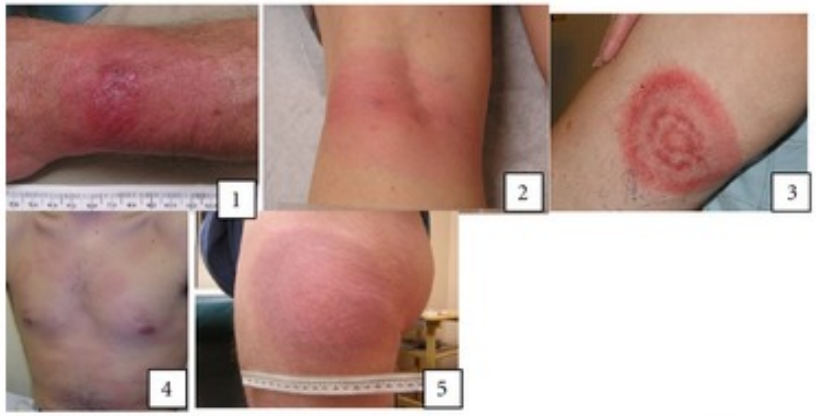
Bull's-Eye and Nontarget Skin Lesions of Lyme Disease: An Internet Survey of Identification of Erythema Migrans

Rashes caused by Lyme disease (1–5)



Rashes not caused by Lyme disease (6–12)

Aucott et al, Dermatol Res Pract. 2012

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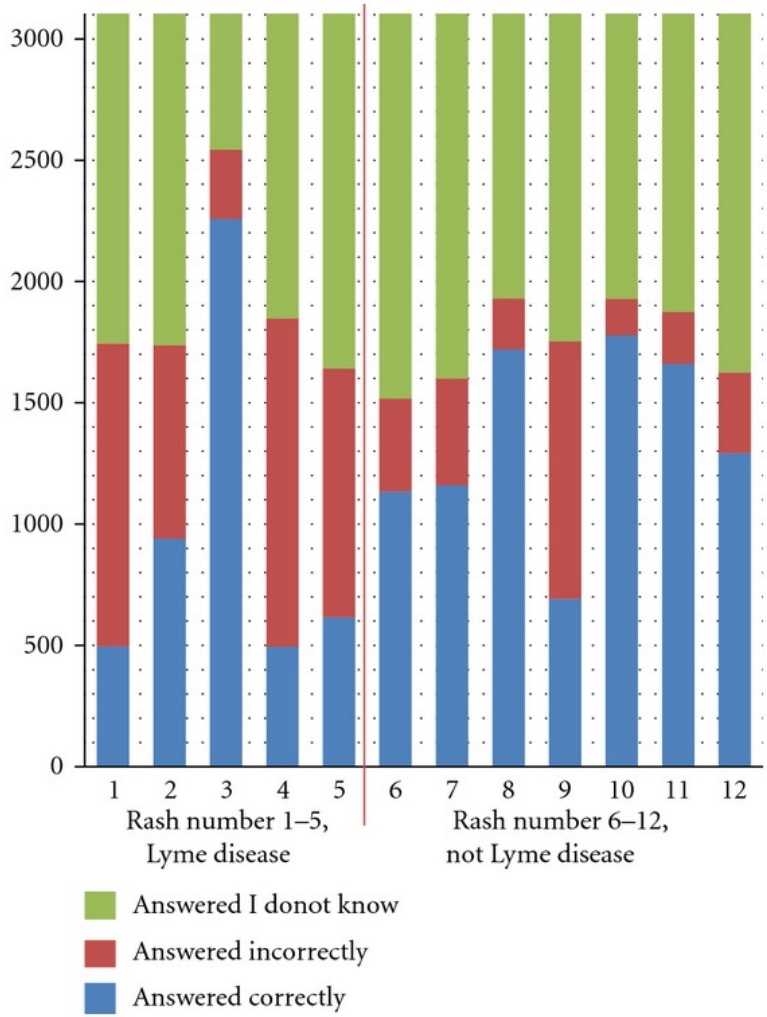
Bull's-Eye and Non-target Skin Lesions of Lyme Disease: An Internet Survey of Identification of Erythema Migrans

John Hopkins Univ. Maryland



Aucott et al, Dermatol Res Pract. 2012

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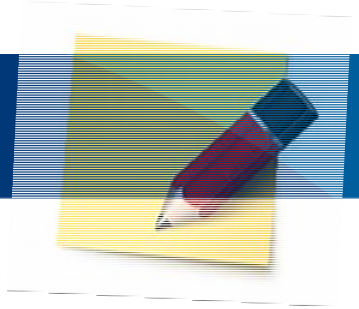
Conclusions



- **Early treatment of this disease has much better outcome than late disseminated disease BUT…**
  - **Tick exposure history is very important and also need to know tick and Borrelia endemicity around that area.**
  - **In a low endemic areas, physicians should be careful about judging EM rashes. Many rashes are simply could be bite mark or due to other reasons. If it's a bite mark and no other symptoms, wait for 3 weeks and do Lyme serology testing before giving antibiotics.**

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How about diagnosing

B. miayamotoi; B Mayonii, B americana ?

Diagnostic test available for other Borrelia strains

- PCR can detect if acutely infected-window period is very short
- Current serology can't distinguish new species
- Approx. over 99.9 percent cases are due to Bb
  - Dr Pritt tested over 100,00 sample and found 6 Lyme positive cases due to *B mayonii*

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Complains

- BCCDC test is not good
- US “X” lab gave me positive results

THE X LAB

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Fallon et al., 2014. Clin Infect Dis 59(12):1705–10

Table 2. Number and Percentage of False-Positive Serologic Test Results and Discordant Pairs for 40 Medically Healthy Controls (University Reference Laboratory Versus Commercial and Lyme Specialty Laboratories)

	University Reference Laboratory	Commercial Laboratory			Specialty Laboratory A			Specialty Laboratory B		
Test	No. Positive[a] (%)	No. Positive[a] (%)	*P* Value	Disc Pairs	No. Positive[a] (%)	*P* Value	Disc Pairs	No. Positive[a] (%)	*P* Value	Disc Pairs
?/+ ELISA	5 (12.5)	3 (7.5)	.683	6	1 (2.5)	.125	4	3 (7.5)	.683	6
C6 ELISA	. . .	. . .	. . .	. . .	0	. . .	. . .	0	. . .	. . .
WB IgM (CDC)	5 (12.5)	0	.074	5	1 (2.5)	.125	4	8 (20.0)	.505	9
WB IgM (laboratory)	. . .	. . .	. . .	. . .	1 (2.5)	.125[b]	4	15 (37.5)	.024	16[b]
WB IgG (CDC)	1 (2.5)	0	1.00	1	0	1.00	1	3 (7.5)	.480	2
WB IgG (laboratory)	. . .	. . .	. . .	. . .	0	1.00[b]	1	11 (27.5)	.004	10[b]
2-tier: ?/+ ELISA & WB IgG	0	0	. . .	0	0	. . .	0	1 (2.5)	1.000	1
2-tier: C6 ELISA & WB IgG	. . .	. . .	. . .	. . .	0	. . .	. . .	0	. . .	. . .
2-tier: ?/+ ELISA & C6 ELISA	. . .	. . .	. . .	. . .	0	. . .	. . .	0	. . .	. . .
+ WB IgM or IgG (CDC)	5 (12.5)	0	.074	5	1 (2.5)	.133	4	10 (25.0)	.182	9
+WB IgM or IgG (laboratory)					1 (2.5)	.133	4	23 (57.5)	<.001	22

Abbreviations: ?/+, indeterminate/positive; CDC, Centers for Disease Control and Prevention; Disc pairs, discordant pairs; ELISA, enzyme-linked immunosorbent assay; IgG, immunoglobulin G; IgM, immunoglobulin M; WB, Western blot.

[a] Criteria for a positive test are given in Table 1.

[b] Results using in-house criteria at Specialty Laboratories A and B were compared with results using CDC criteria at the university-based reference laboratory.

In-house laboratory criteria for a positive IgM WB at Specialty Laboratory B were ≥2 of the following bands: 23–25, 31, 34, 39, 41, 83/93. Criteria for a positive IgG WB were ≥2 of the following bands: 23–25, 31, 34, 39, 41, 83/93.

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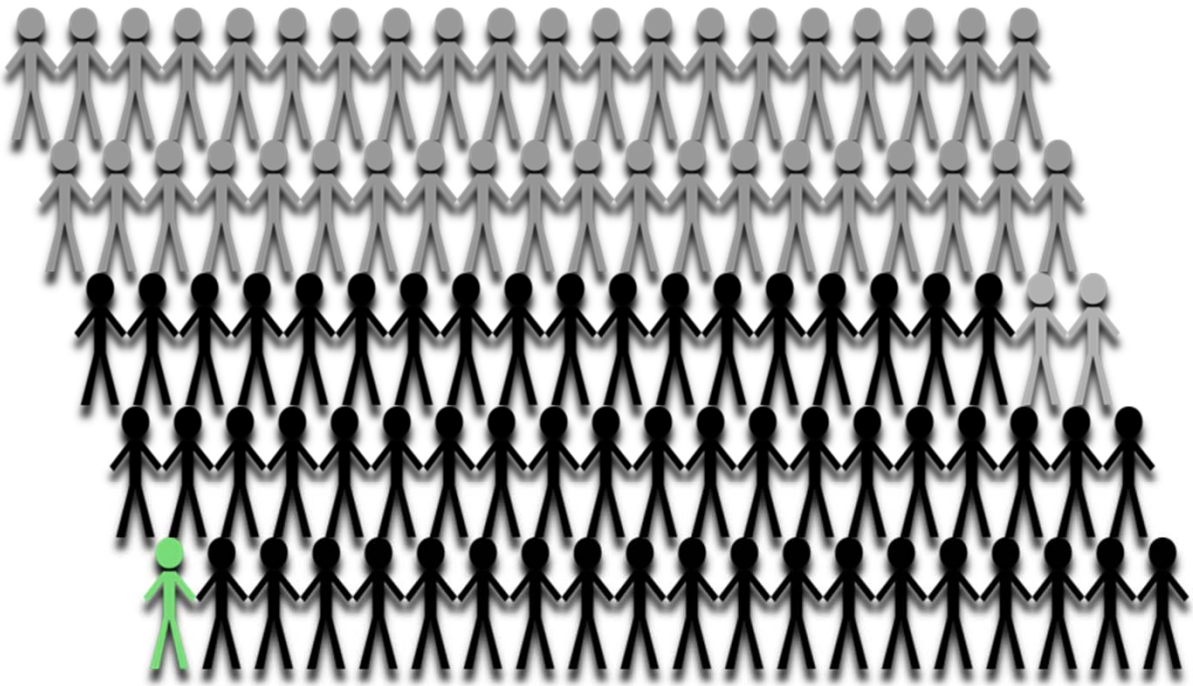
100 Alternative Lyme Tests



True Lyme Disease
1

True Negative
42

False Positive
57

Test performance as reported by Fallon in Clinical Infectious Diseases 2014

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BC Complex Chronic Disease Study

Lyme Disease Diagnosed by Alternative Methods: A Phenotype Similar to That of Chronic Fatigue Syndrome

Conclusions:

In British Columbia, a setting with low Lyme disease incidence, ADCLS (Alternatively Diagnosed Chronic Lyme Disease) patients have a similar phenotype to that of CFS chronic fatigue syndrome patients). Disagreement between alternative and reference laboratory Lyme testing results in this setting is most likely explained by false-positive results from the alternative laboratory.

Patrick et al, CID. 2015

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Challenges in laboratory based diagnosis of Lyme Disease

Pretest issue

- Type of specimens
- Collection time with respect to disease state
- If patient had taken antibiotic prior to give sample for testing
- Biodiversity
- New Borrelia species
- Lack of gold-standard samples

Post test issue

- Poor sensitivity early in the infection
- Difficult to diagnose reinfection
- Unable to monitor treatment outcome
- Unvalidated tests by private laboratories

Conclusions

- Patient suffering over 2-3 years with a negative serology results should be investigated further to find out for real causative agents.
- FP should be aware of the test reliability of private laboratories
- In a low endemic areas, physicians should be very careful about false positive results

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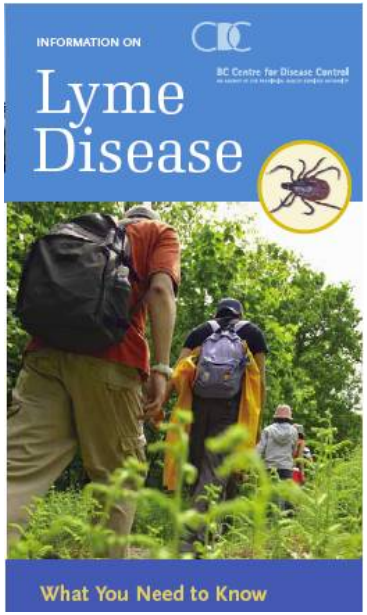
Important-Communication

- Pamphlets for parents at parks etc.
- Mailings and articles for physicians
- Messages in media
  - Twitter feed
  - Summer advisory



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Suggested Treatments for Adult Patients With the Most Common Clinical Manifestation sf Lyme Disease in NA

Manifestation	Antibiotic	Duration
Erythema migrans		
Erythema migrans	Doxycycline, 100 mg orally twice daily	10 d
	Amoxicillin, 500 mg orally 3 times daily	14 d
	Cefuroxime axetil, 500 mg orally twice daily	14 d
Erythema migrans in a patient unable to take beta-lactams or tetracyclines	Azithromycin, 500 mg orally once daily	7-10 d
Lyme meningitis		
Ambulatory	Doxycycline, 100 mg orally twice daily or 200 mg once daily	14 d
Hospitalized	Ceftriaxone, 2 g intravenously once daily	14 d
Lyme cranial neuropathy or radiculopathy	Doxycycline, 100 mg orally twice daily or 200 mg once daily	14d
Lyme cranial neuropathy or radiculopathy in a patient unable to take tetracyclines	Amoxicillin, 500 mg orally 3 times daily	14d
	Cefuroxime axetil, 500 mg orally twice daily	14d
Cardiac Lyme disease		
Ambulatory	Same as for erythema migrans	14 d (range,14-21 d)
Hospitalized	Ceftriaxone, 2 g intravenously once daily until stabilized or discharged Complete course with oral antibiotic recommended for erythema migrans	14 d (range,14-21 d)
Lyme arthritis		
Initial	Doxycycline, 100 mg orally twice daily	28 d
	Amoxicillin, 500 mg orally 3 times daily	28 d
	Cefuroxime axetil, 500 mg orally twice daily	28 d
Persistent Lyme arthritis after first course of oral therapy	Re-treat using 1 of the above oral regimens	28 d
	Ceftriaxone, 2 g intravenously once daily	14-28 d

Conclusions

- Health care professionals and residents need to be reminded about different aspects of Lyme disease including preventative measures
- “Prevention is better than Cure”
- Borrelia spp is sensitive to penicillin and shown to be effective and never been reported resistance to Borrelia spp.

Borrelia burgdoreferi Complex

↓

Borrelia burgdoreferi sensu Lato

↓

Borrelia burgdoreferi sensu stricto

↓

Lyme disease

↓

Western Pacific Coast Situation

Questions?

Questions?

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Next Up!

Dr. Vance Kawakami

CDC Epidemic Intelligence Service Officer, LT, U.S. Public Health Service, Public Health Seattle & King County, Communicable Disease Epidemiology & Immunization