Summer's Coming!
What Do You Need to Know about Ticks & Lyme Disease

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Pediatric Telehealth Rounds – 08 May 2015

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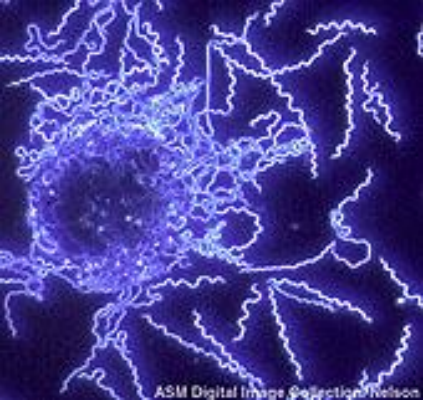
Objectives

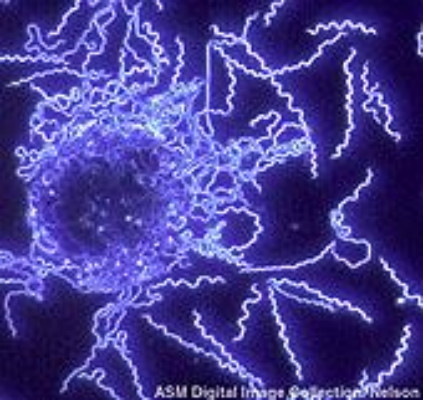
- To describe the recent changes in epidemiology of Lyme disease in Ontario & Canada
- To enable clinicians to recognize manifestations of Lyme disease in pediatric patients
- Describe diagnostic and treatment approach for Lyme disease in children



Lyme Disease
(Borreliosis)

Arthropod-borne disease caused by infection with spirochetes of the *Borrelia* species

- 3 main species are responsible for most human LD:
  - *B. burgdorferi sensu stricto* (North America, Europe)
  - *B. garinii* (Europe & Asia)
  - *B. afzeli* (Europe)
- Transmitted by ticks of the *Ixodes ricinus* complex:
  - *Ixodes scapularis* (NE/MW North America)
  - *I. pacificus* (Western North America)
  - *I. ricinus* (Europe)
  - *I. persulcatus* (Asia)



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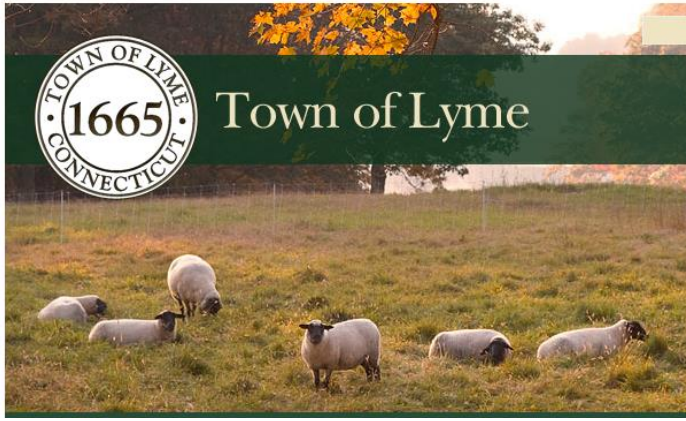
Lyme Disease



- Named after Lyme, Connecticut where in mid-1970s an epidemic form of arthritis was described, affecting 51 people in 3 communities

LYME ARTHRITIS

AN EPIDEMIC OF OLIGOARTICULAR ARTHRITIS IN CHILDREN AND ADULTS IN THREE CONNECTICUT COMMUNITIES

ALLEN C. STEERE, STEPHEN E. MALAWISTA, DAVID R. SNYDMAN, ROBERT E. SHOPE, WARREN A. ANDIMAN, MARTIN R. ROSS, and FRANCIS M. STEELE

Steere et al, *Arthritis & Rheumatism*, 1977

Lyme Disease Epidemiology:
North America

- Dramatic increases in reported cases of LD in US were seen over past 2 decades – usually associated with northeastern US states (Maine to Virginia) and north central states of Wisconsin and Minnesota
- >20,000 cases/yr

Fast Facts

Lyme disease is the most commonly reported vectorborne illness in the U.S. In 2009, it was the 5th most common Nationally Notifiable disease.

In 2010, 94% of Lyme disease cases were reported from 12 states:

Connecticut	New Jersey
Delaware	New Hampshire
Maine	New York
Maryland	Pennsylvania
Massachusetts	Virginia
Minnesota	Wisconsin

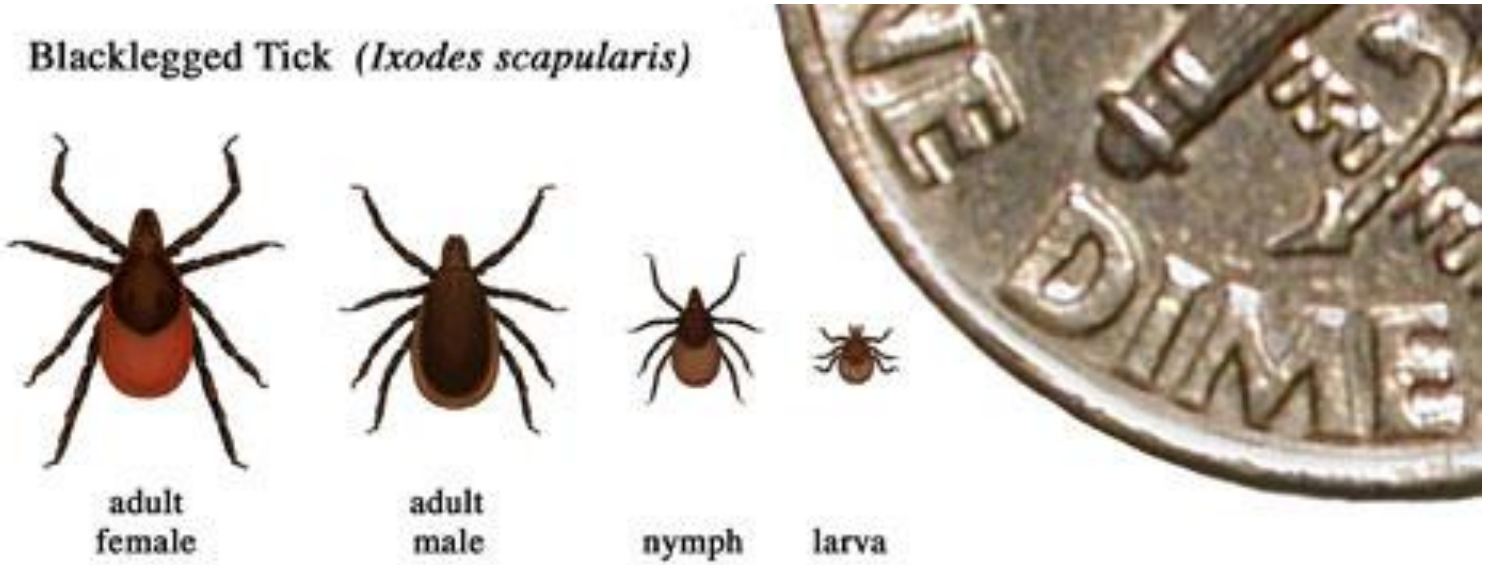
burgdorferi)

Lyme Disease Epidemiology:
Factors favouring LD spread in North America

- Woodland deforestation and white-tailed deer decimation during colonization has slowly reversed during 20th century – farmland reverted to forest, deer population recovered with few predators
- Thriving populations of the vector (ticks) and reservoir (white-footed mouse)
- Human populations encroached on woodlands via suburbanization and recreation

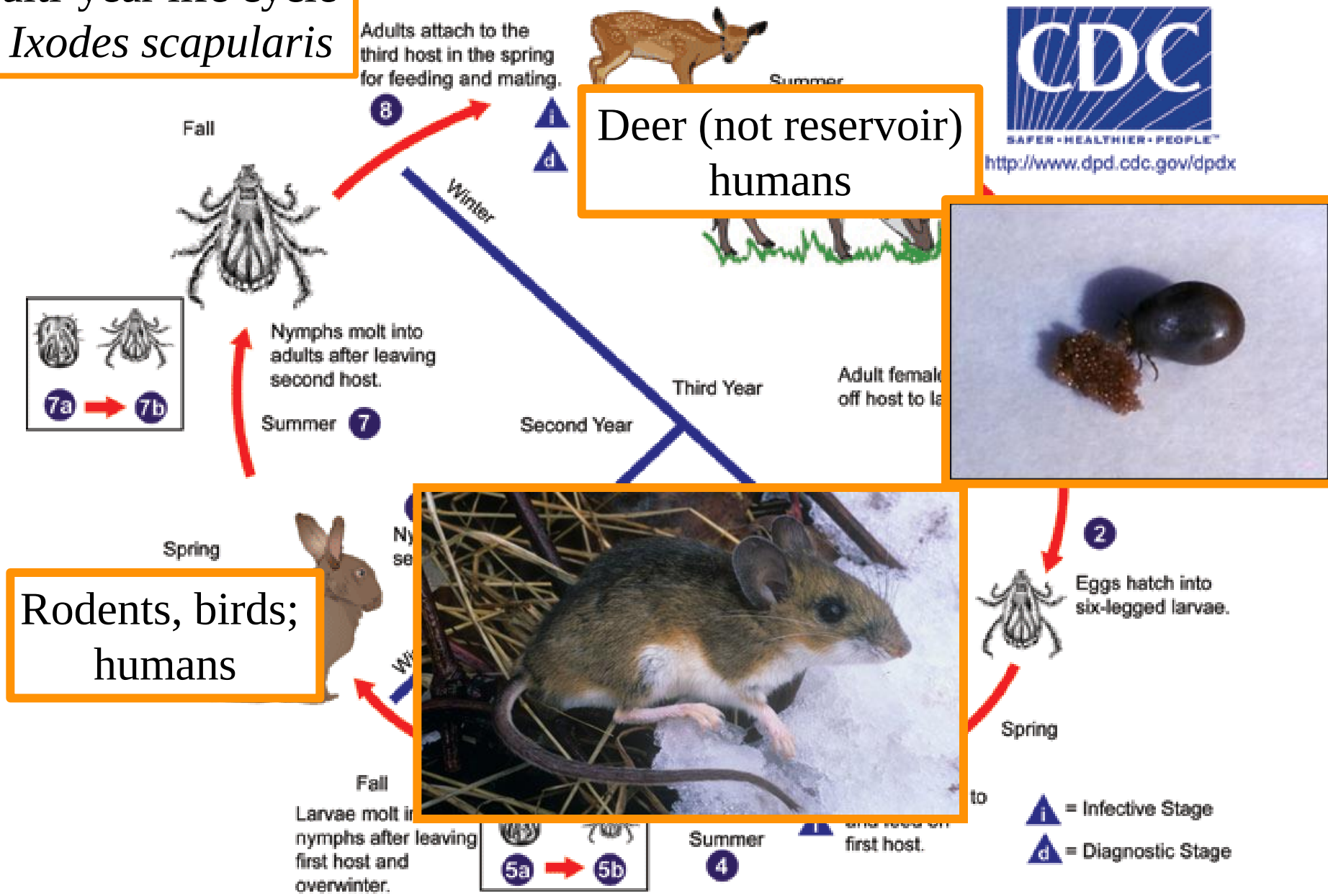
Lyme Disease
– Transmission

- Life cycle of *Ixodes scapularis*



www.cdc.gov

Multi-year life cycle of *Ixodes scapularis*



Deer (not reservoir) humans

Rodents, birds; humans

www.dpd.cdc.gov/dpdx

Lyme Disease
– Spread into New Locales

- While ticks are not big travelers, they can get carried into new geographic locales while attached to hosts
- Passerine birds are the most effective transportation – billions of birds migrate north from US to Canada each spring/summer, carrying ticks with them

Surveillance has revealed presence of *I. scapularis* ticks and establishment of populations in Canada:

- southern Ontario & Quebec
- southeastern Manitoba
- Maritime provinces (NB, NS)

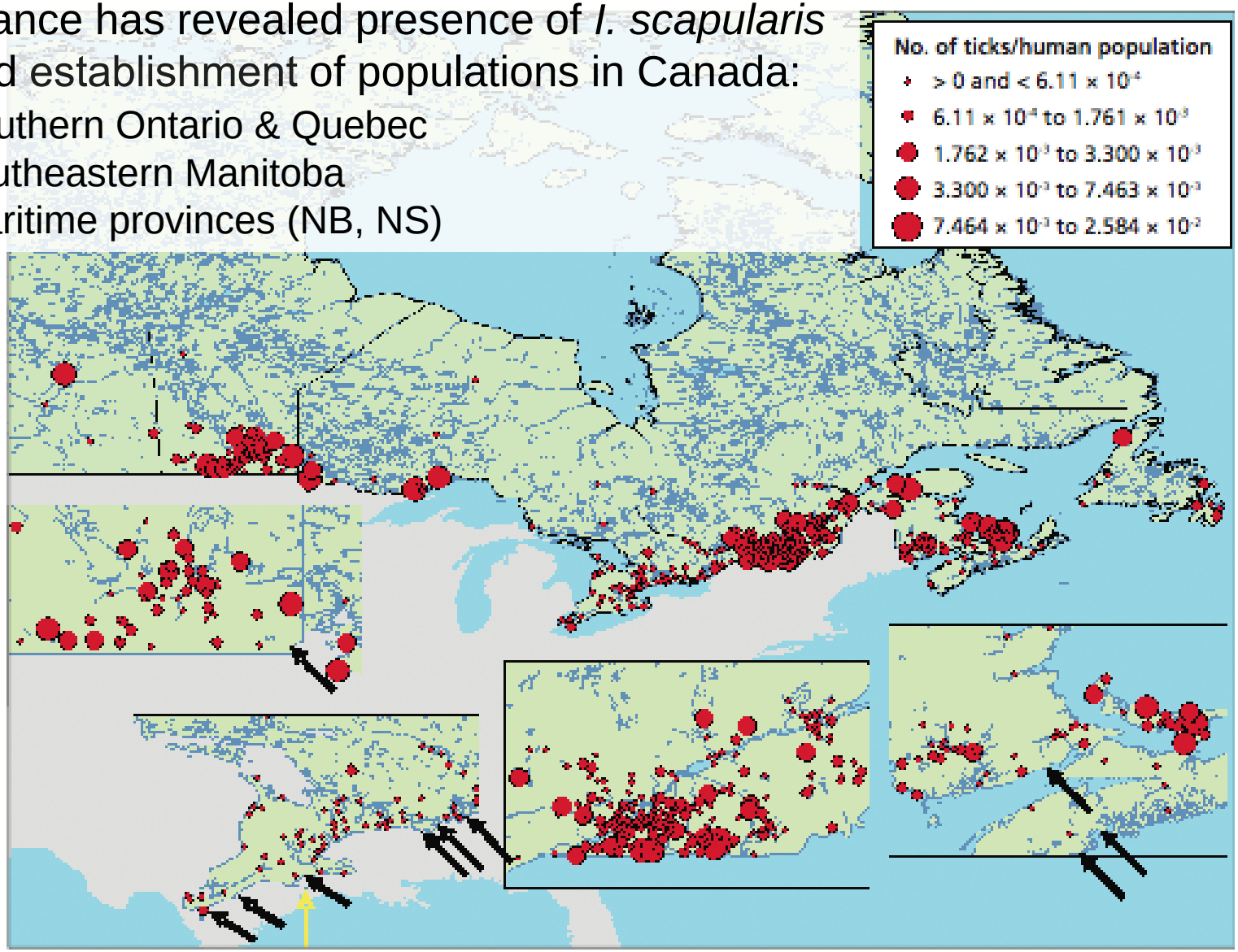
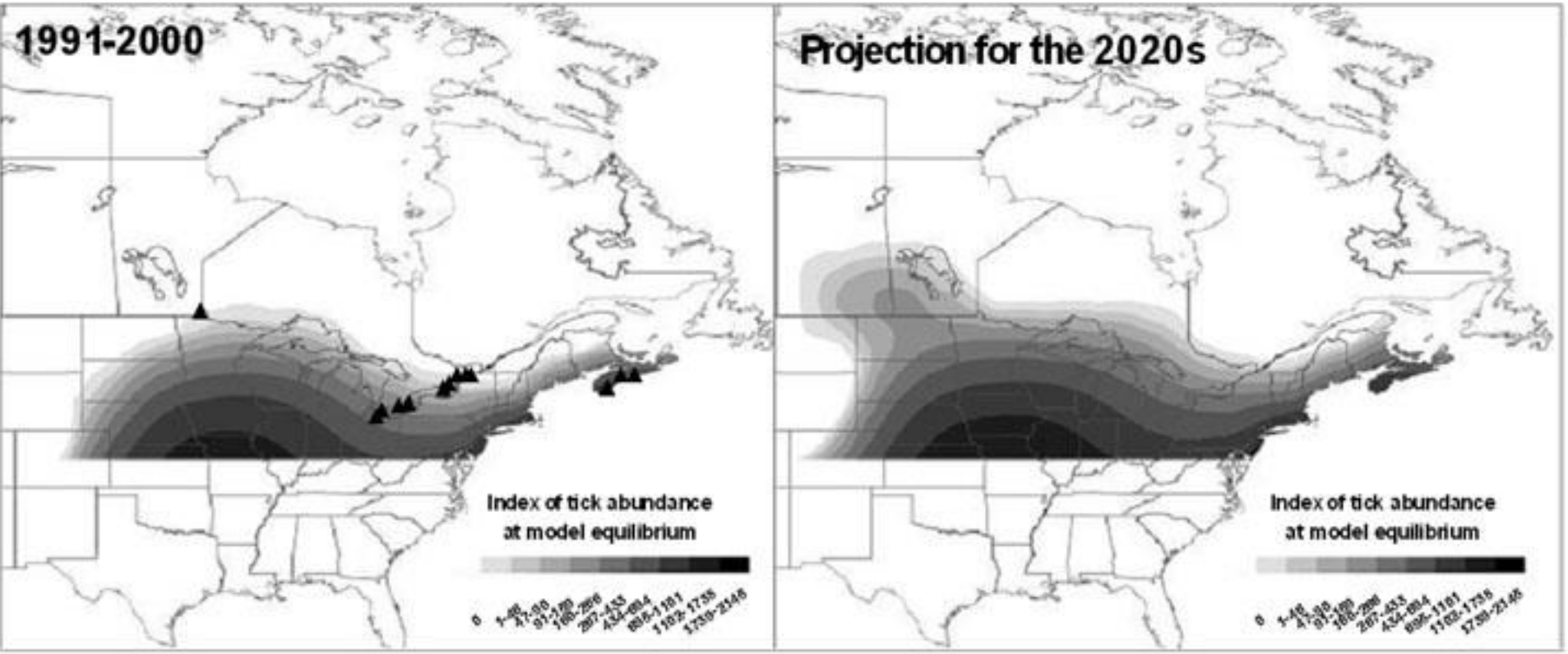


Figure 2: The distribution of *Ixodes scapularis*, reflecting information submitted to provincial and federal public health agencies from January 1990 to December 2003 and to the Lyme Disease Association of Ontario for 1993 to 1999 (red circles are centred on the centroid of the census subdivision from which the reports were submitted). Census subdivisions where resident populations of *I. scapularis* are currently known to occur are indicated by arrows, and the census subdivision containing the only *I. scapularis* population that was known in 1991 is indicated by the yellow arrow. Reproduced, with permission, from the Entomological Society of America.[12]

Emergence of Lyme Disease in Canada - Ogden, CMAJ 2009

Global warming trends are projected to lead to geographic spread of Lyme disease in Canada in future



The Rising Challenge of Lyme Borreliosis in Canada – Ogden, CCDR 2008

Endemic sites in Ontario for *I. scapularis*

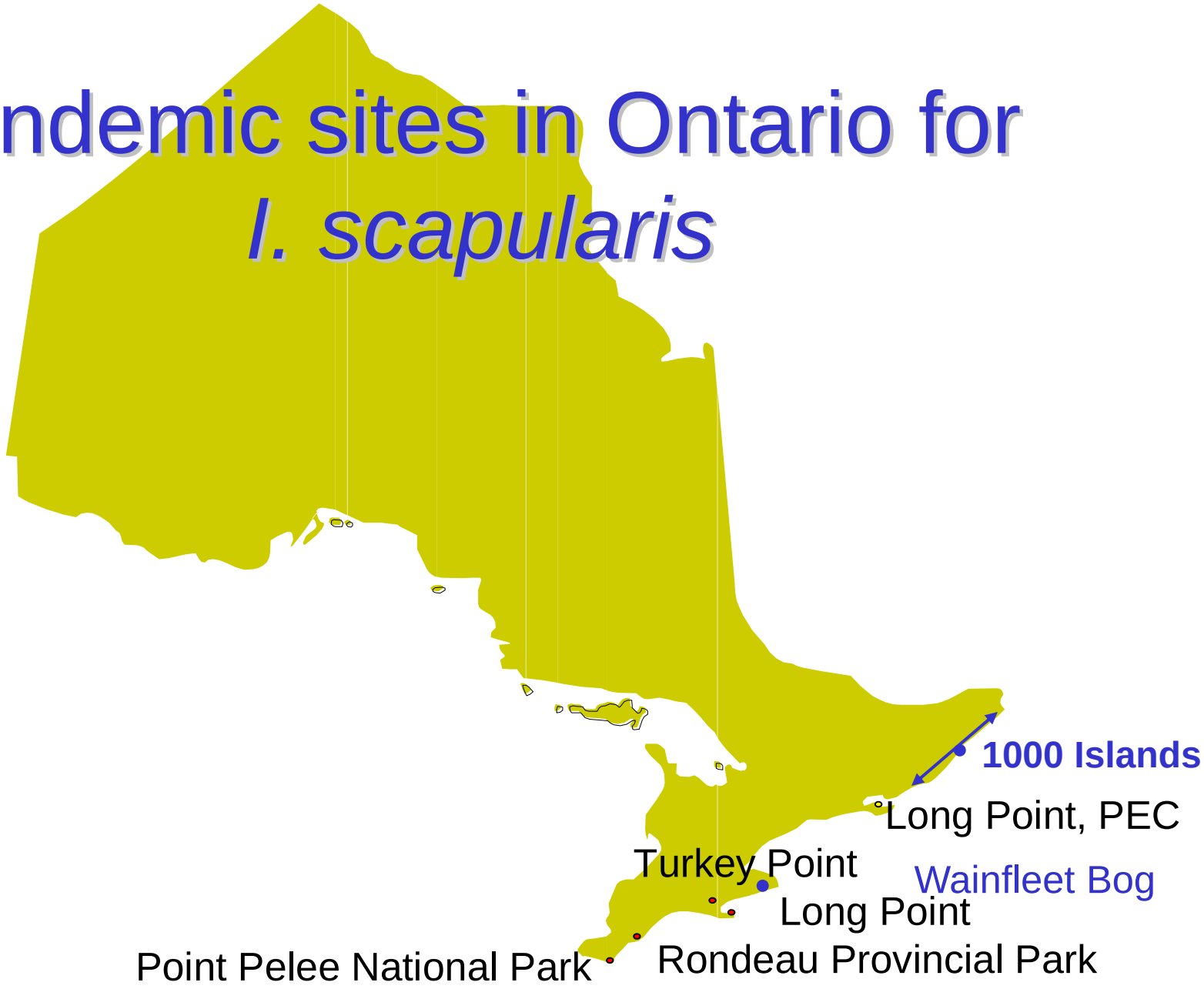
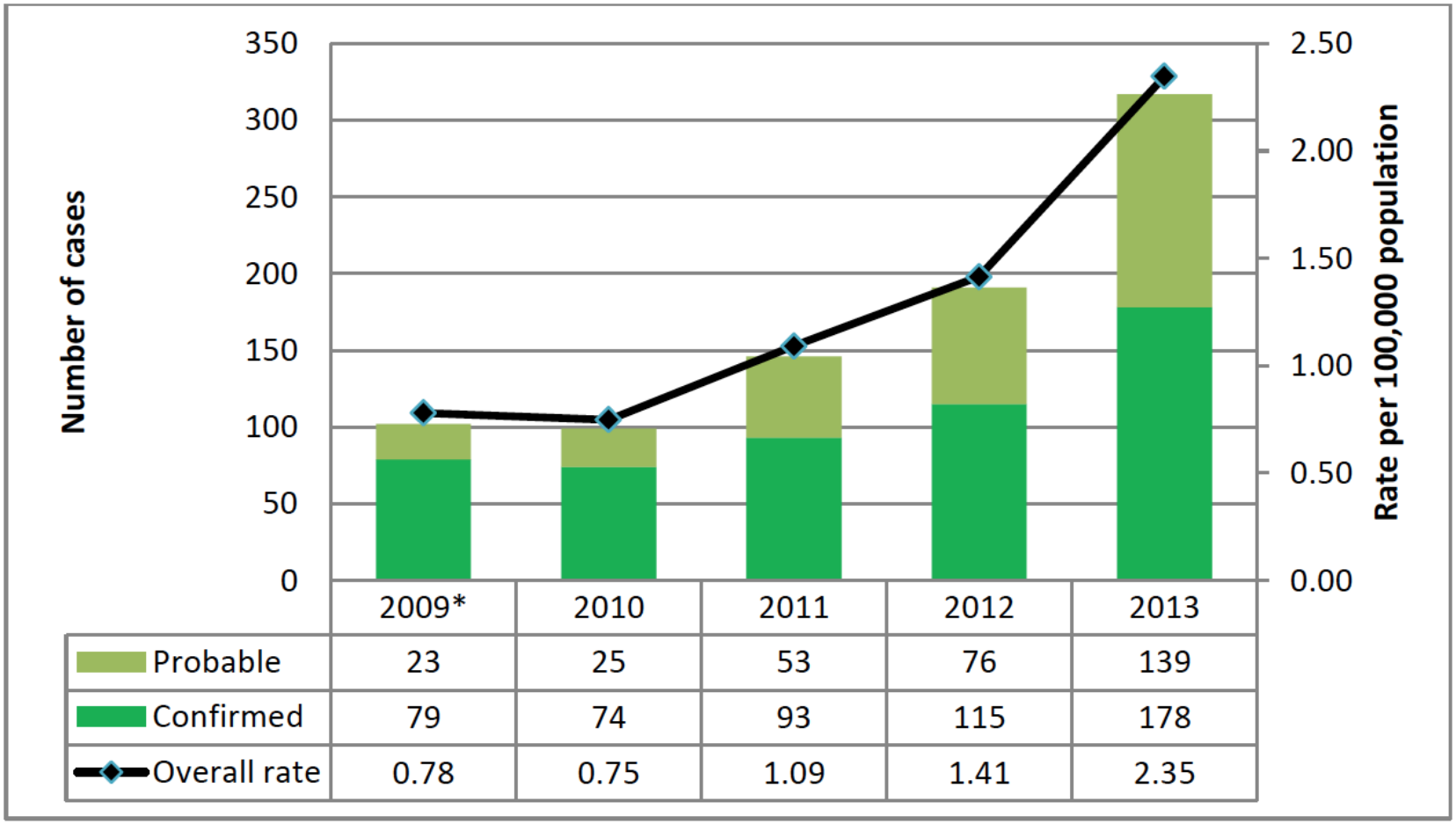


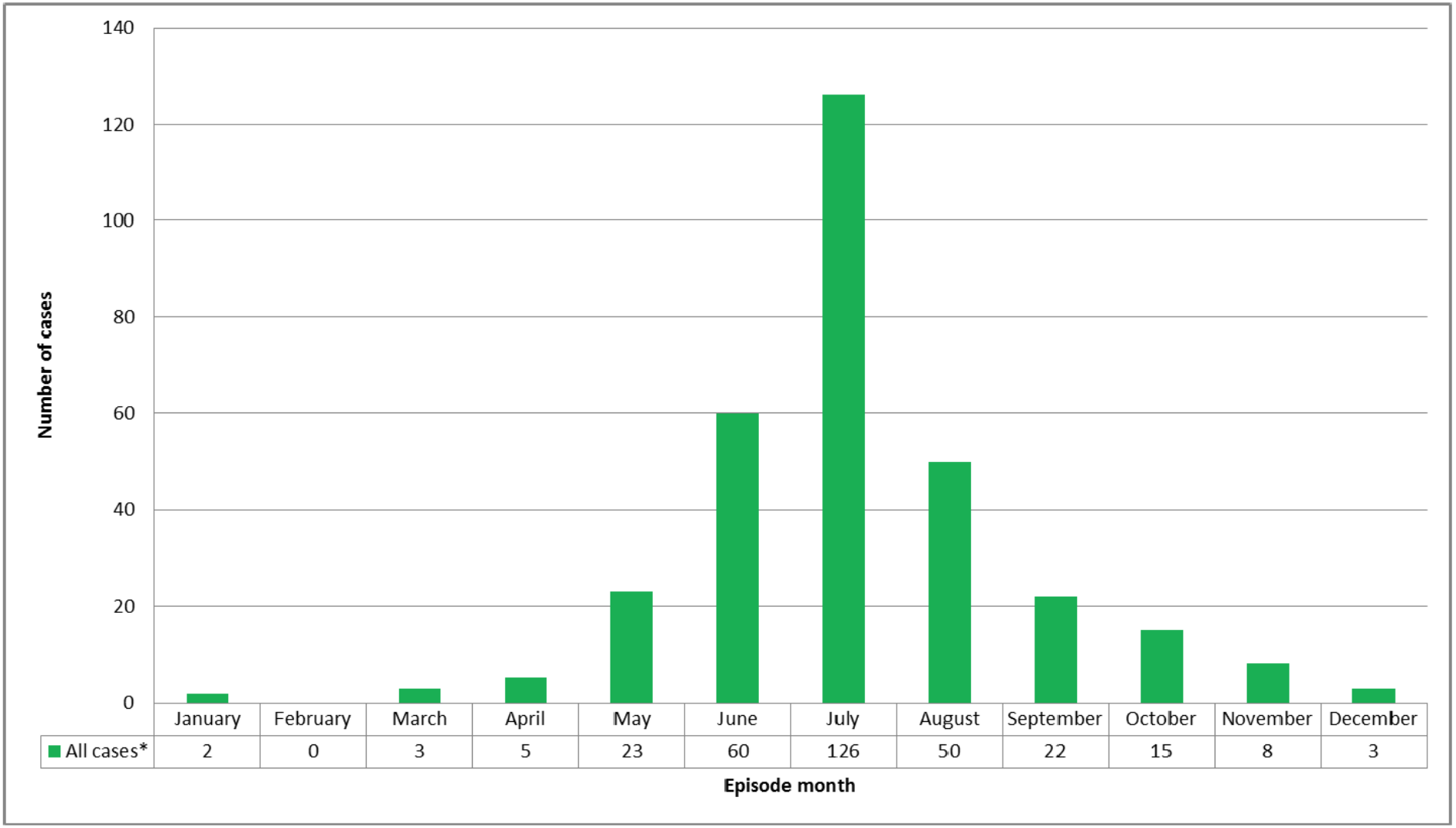
Figure 8: Number of cases of Lyme disease and incidence rate per 100,000 population: Ontario, 2009–2013



	2009*	2010	2011	2012	2013
Probable	23	25	53	76	139
Confirmed	79	74	93	115	178
Overall rate	0.78	0.75	1.09	1.41	2.35

Source: OAHPP – Vector Borne Diseases 2013 Summary Report

Figure 9: Distribution of Lyme disease cases* by month: Ontario, 2013



	January	February	March	April	May	June	July	August	September	October	November	December
All cases*	2	0	3	5	23	60	126	50	22	15	8	3

Source: OAHPP – Vector Borne Diseases 2013 Summary Report

Table 3. Lyme disease cases by exposure setting, and total number of I. scapularis submissions to PHO: Ontario, 2008–13

Exposure Location	Year											
	2008		2009		2010		2011		2012		2013	
	n	%	n	%	n	%	n	%	n	%	n	%
Ontario	55	56.1	47	46.1	41	41.4	98	67.1	119	62.3	186	58.7
Within Canada, outside Ontario	2	2.0	3	2.9	2	2.0	5	3.4	5	2.6	8	2.5
Outside Canada	35	35.7	34	33.3	32	32.3	34	23.3	39	20.4	51	16.1
Unknown	3	3.1	4	3.9	3	3.0	0	0.0	1	0.5	2	0.6
Missing	4	4.1	16	15.7	22	22.2	11	7.5	32	16.8	78	24.6
Total number of cases	98		102		99		146		191		317	
Total number of *I. scapularis* submissions	**1480**		**580**		**956**		**2291**		**2535**		**3039**	

Source: OAHPP – Vector Borne Diseases 2013 Summary Report

Figure 11: The location and number of blacklegged ticks submitted to Public Health Ontario, based on the submitter's community of residence: Ontario, 2013

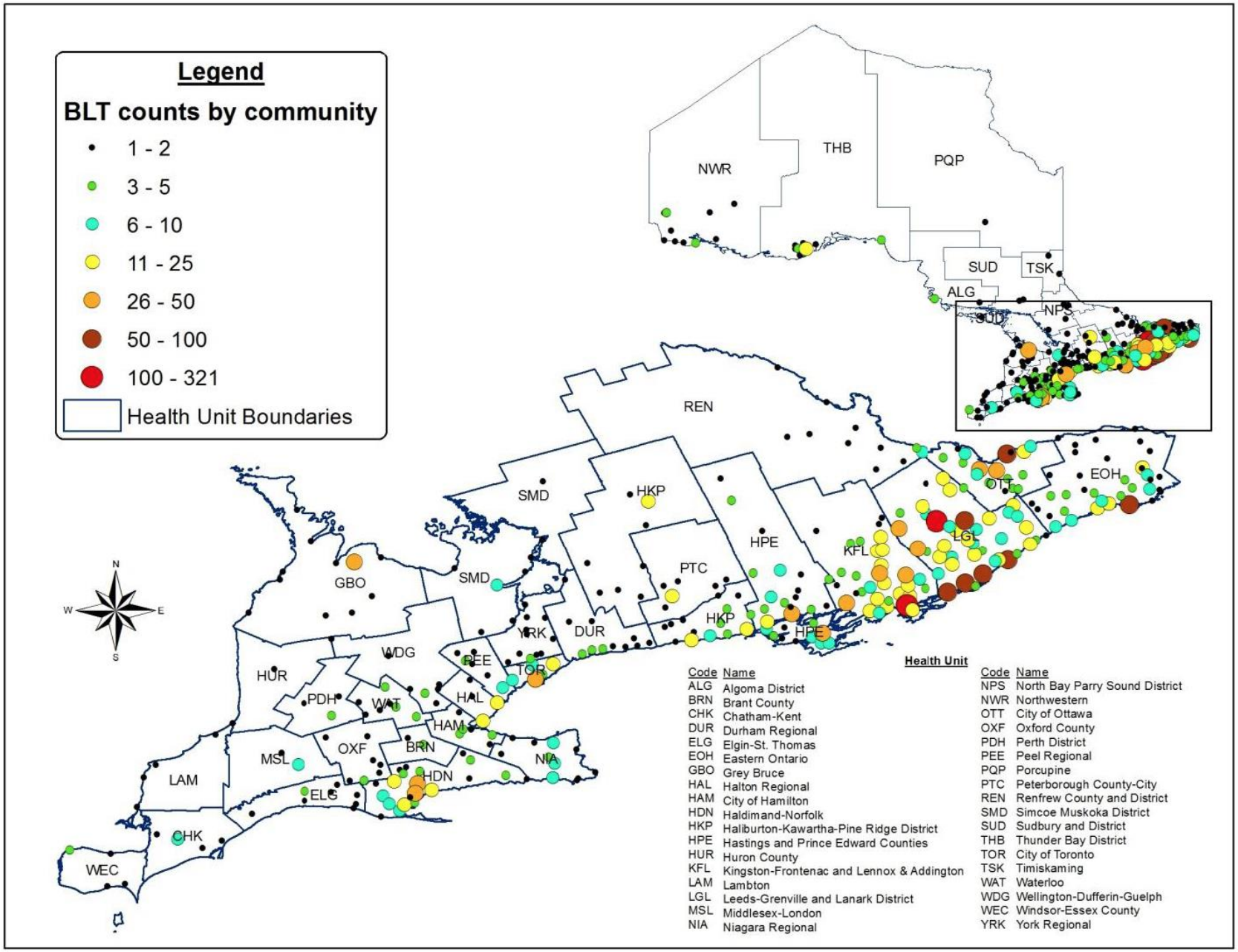


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Figure 10: Municipalities identified as the most likely exposure location for locally acquired Lyme disease cases: Ontario, 2013

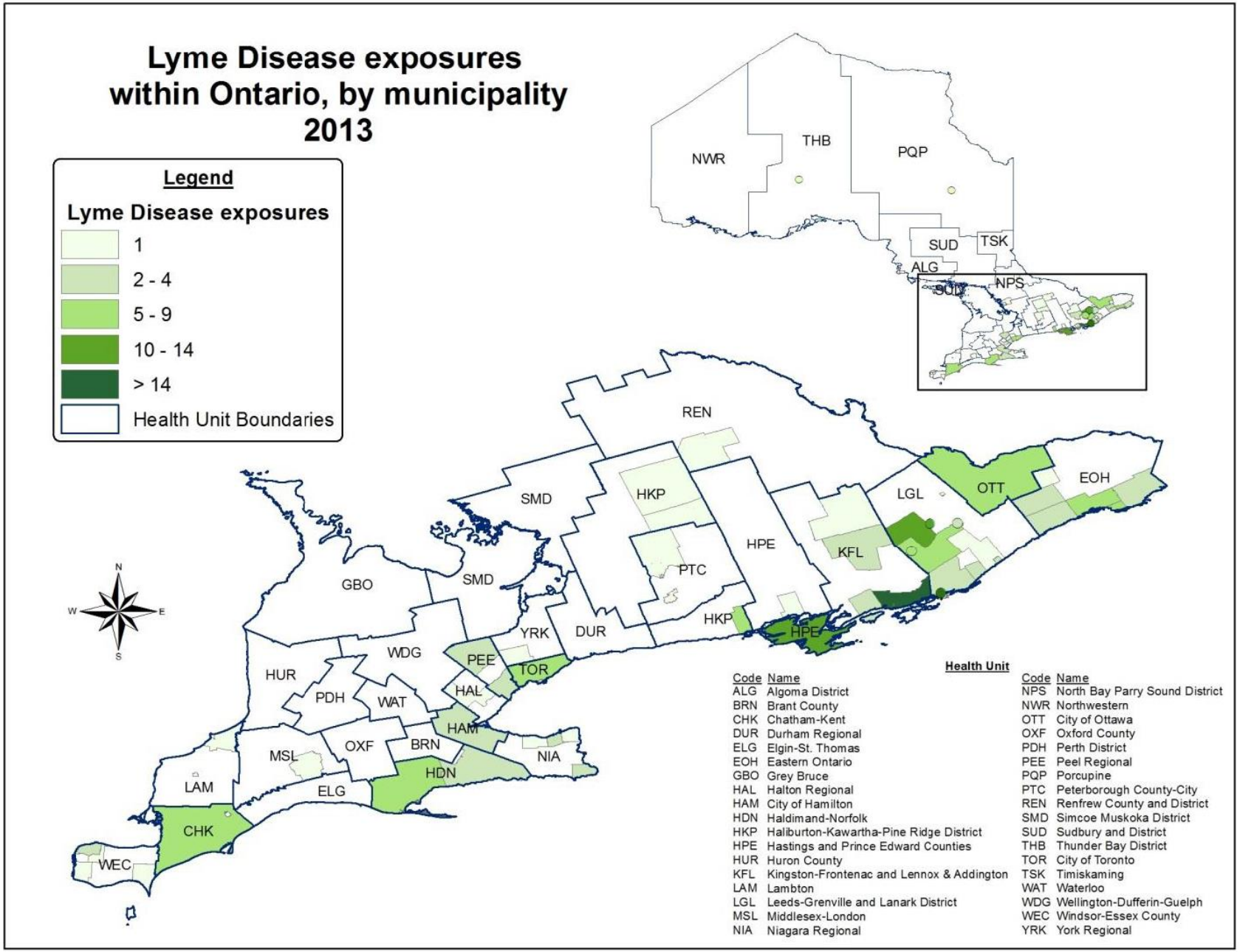

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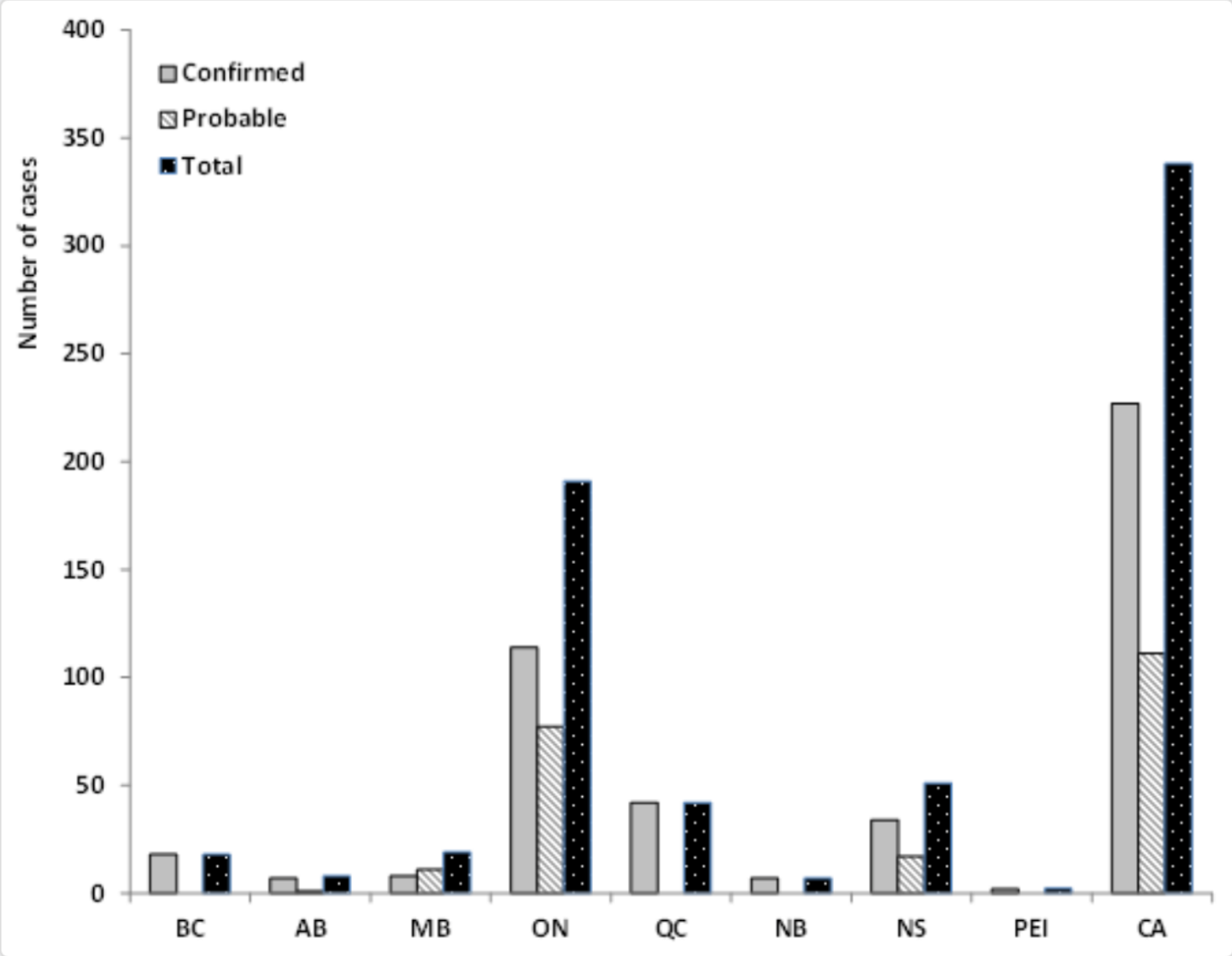
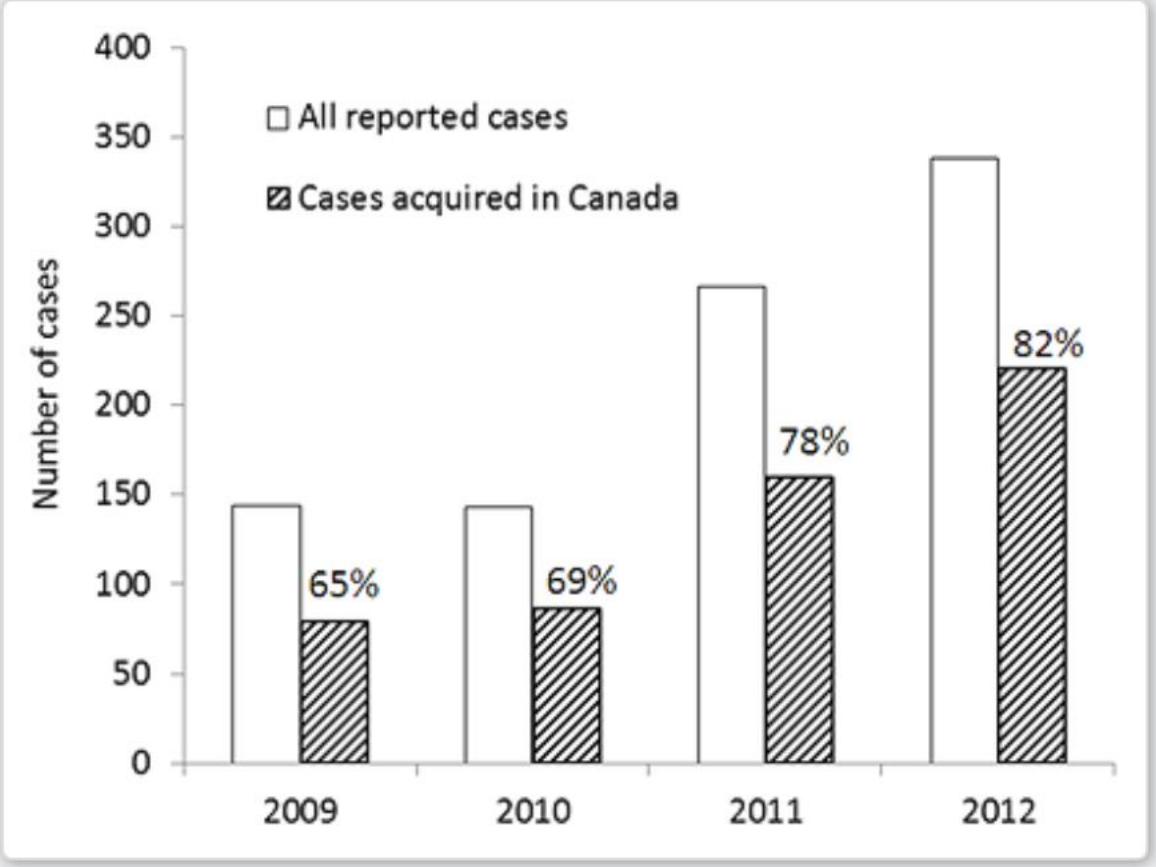
Figure 1. The numbers of reported Lyme disease cases by province in Canada in 2012.



▶ **Figure 1 description**

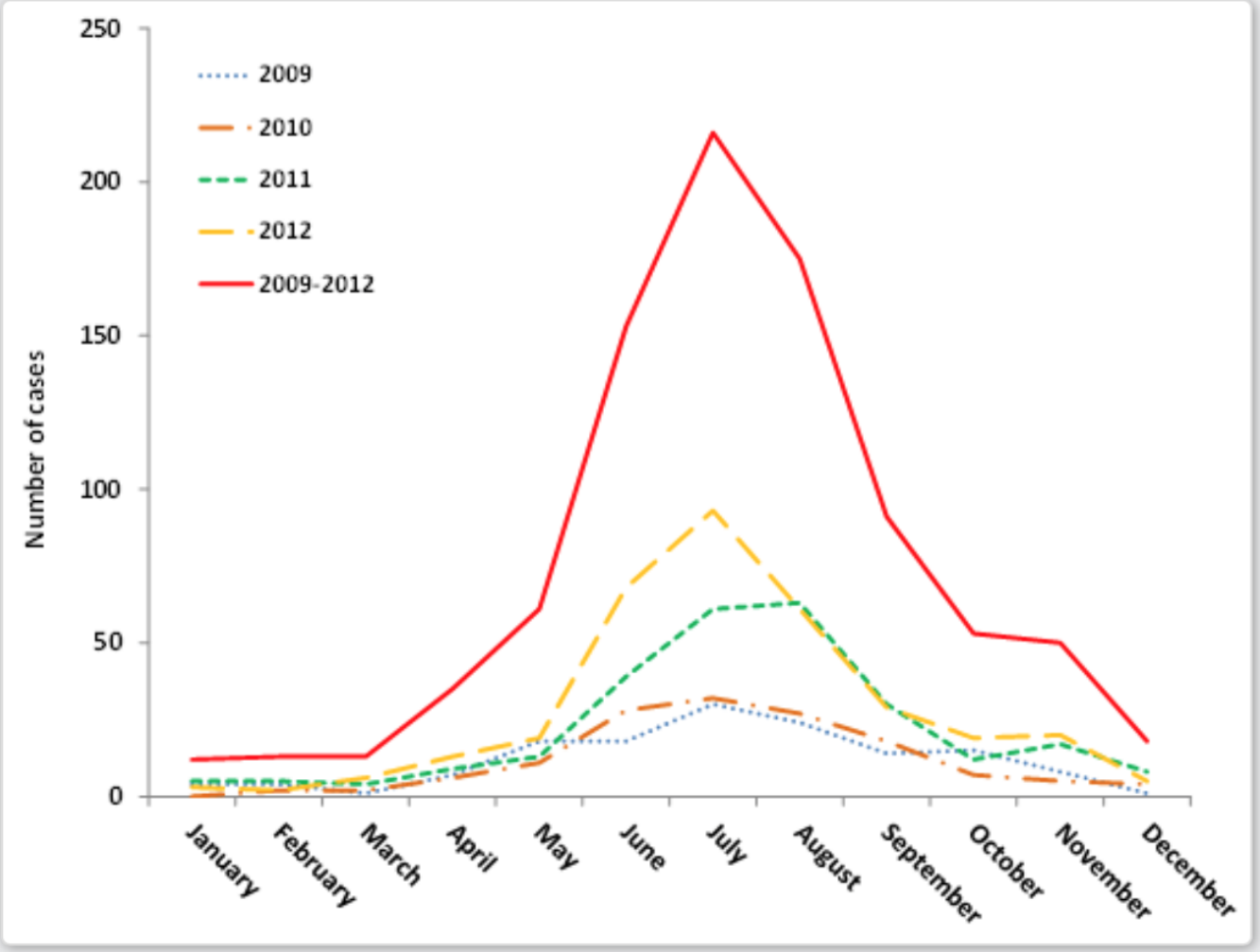
National Lyme Disease Surveillance in Canada 2009-2012, Health Canada

Figure 2. The numbers of reported Lyme disease cases in Canada 2009-2012.



National Lyme Disease Surveillance in Canada 2009-2012, Health Canada

Figure 4. The numbers of Lyme disease cases reported in the LDES, by month of illness onset and by year, 2009-2012.



National Lyme Disease Surveillance in Canada 2009-2012, Health Canada

Outcomes of passive surveillance in 2010

Province	# ticks	Bb +ve (%)
AB	42	13 (31.0)
SK	1	0
MB	253	36 (13.8)
ON	962	**112 (11.6)**
QC	1002	158 (15.8)
NB	271	39 (14.4)
NS	676	74 (10.9)
PEI	122	19 (15.6)
NF	27	4 (14.8)
Total	**1179**	**455 (13.5)**

- Bb +ve = *Borrelia burgdorferi*-positive ticks

(R. Lindsay, Public Health Agency of Canada)

Lyme Disease
– Ontario & Canada

- In summary:
  - More ticks submitted to Ministry of Health
  - ~10% of *I. scapularis* tested + for *B. burgdorferi*
  - #s of cases of Lyme and proportion of cases acquired locally are increasing
  - Global warming & other factors suggest it will only increase further

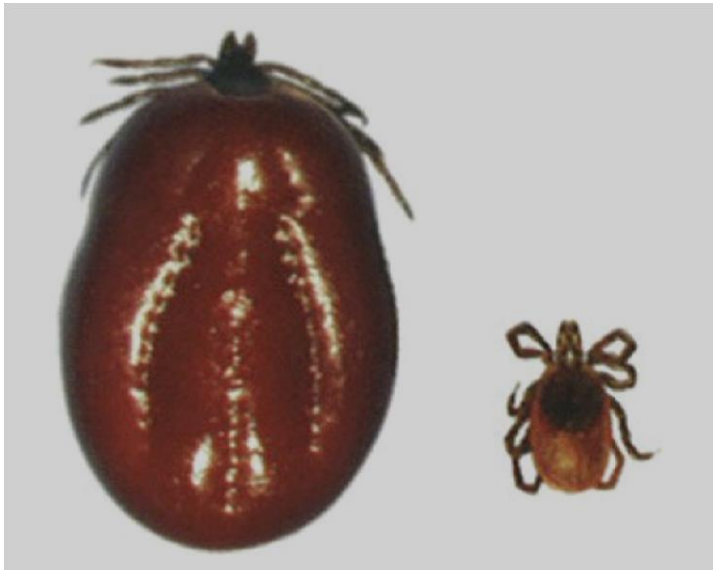
Lyme Disease
– Transmission

- Ticks are usually acquired through outdoor activity in long grass – where ticks wait to attach to potential hosts
- Probability of disease transmission depends on **duration of attachment** (>24-36 hrs necessary) and **rate of tick positivity** in region (>20% infected ticks represents higher risk)

Lyme Disease
– Transmission

- Duration of tick attachment sometimes not clear
- Degree of engorgement is suggestive of duration (fatter = longer)

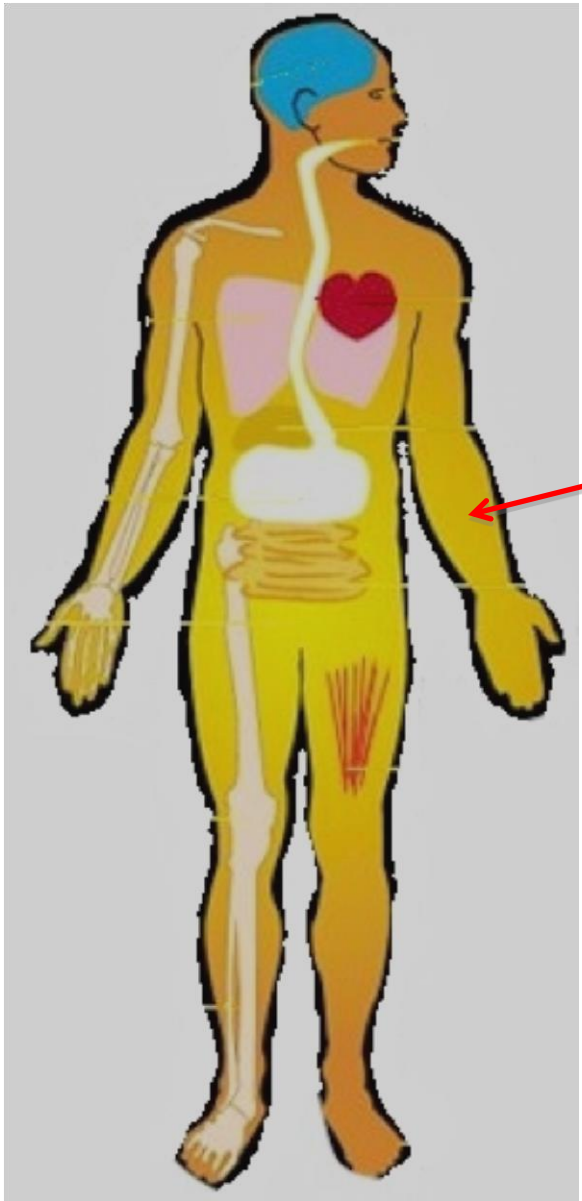
Figure 1. From left to right, an *Ixodes scapularis* larva, nymph, adult male tick, and adult female tick. The picture is a generous gift from Dr. Richard Falco (Fordham University).



Lyme Disease
– Clinical Presentation

- Presentation divided into:
  - Early localized disease
  - Early disseminated disease
  - Late disease

Lyme Disease
– Clinical Presentation



Early Localized Disease

- *Erythema migrans* rash

Which of these rashes is Erythema migrans – the rash of Lyme Disease?

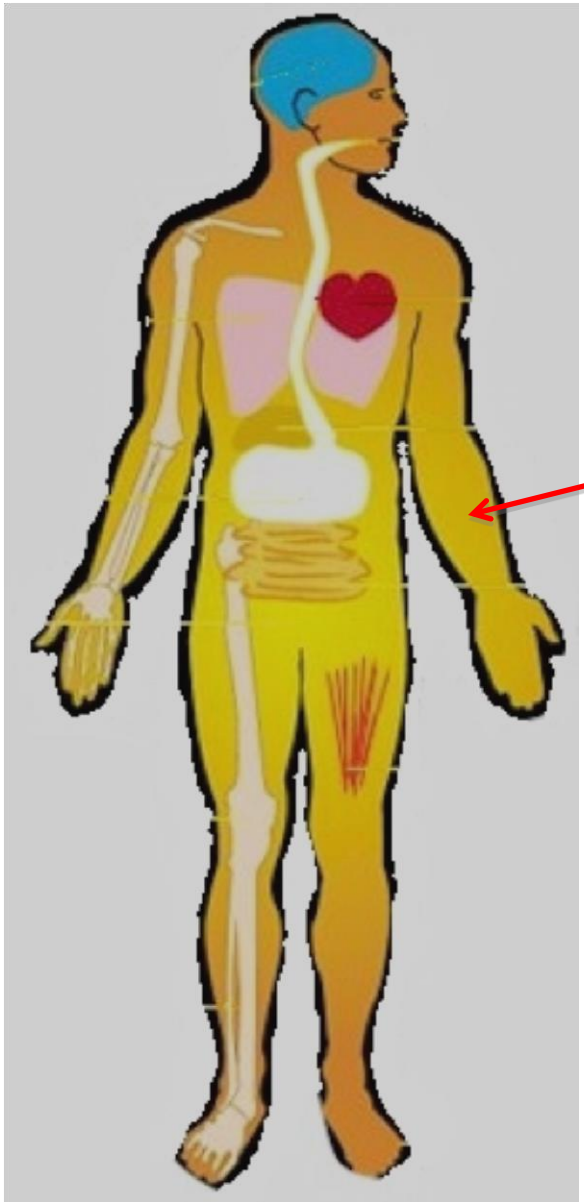
1

3

2

4

Lyme Disease
– Clinical Presentation

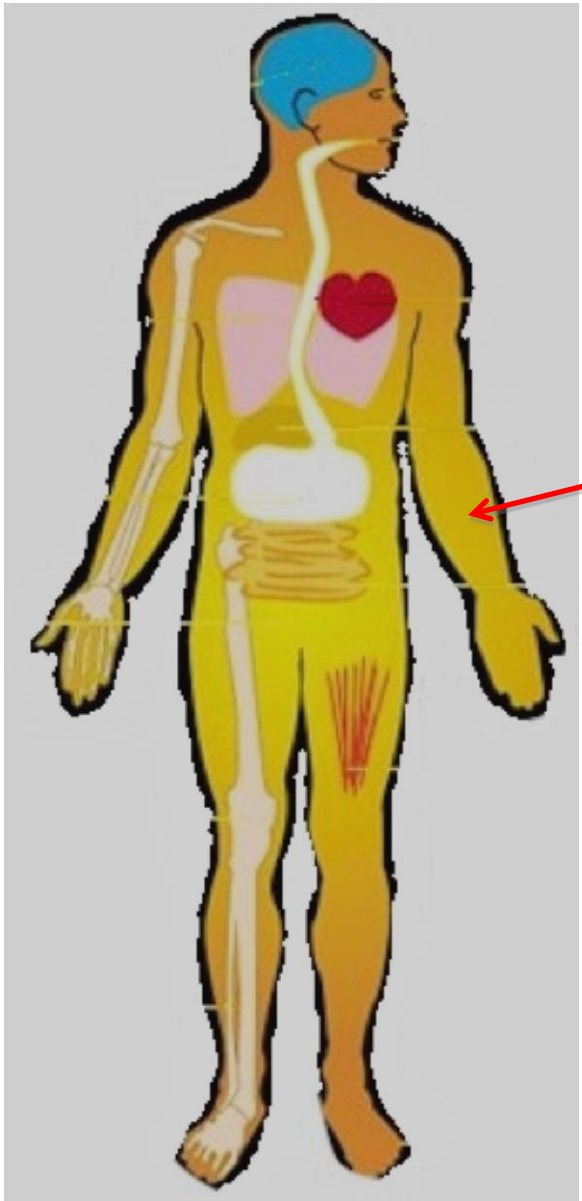


Early Localized Disease

- *Erythema migrans* rash

- Onset ~7-14 days after tick bite (range 3-32days)
- Often uniformly erythematous, but can appear as a target lesion with central clearing
- Occasionally can have a vesicular or necrotic centre

Lyme Disease
– Clinical Presentation



Early Localized Disease

- *Erythema migrans* rash
- Rash can be pruritic, painful, or asymptomatic
- Associated fever, myalgia, headache, malaise are variably present
- Gradually expands to ~15cm diameter (can be up to 30cm)
- Lasts 1-2 weeks then resolves

Erythema migrans vs tick bite hypersensitivity

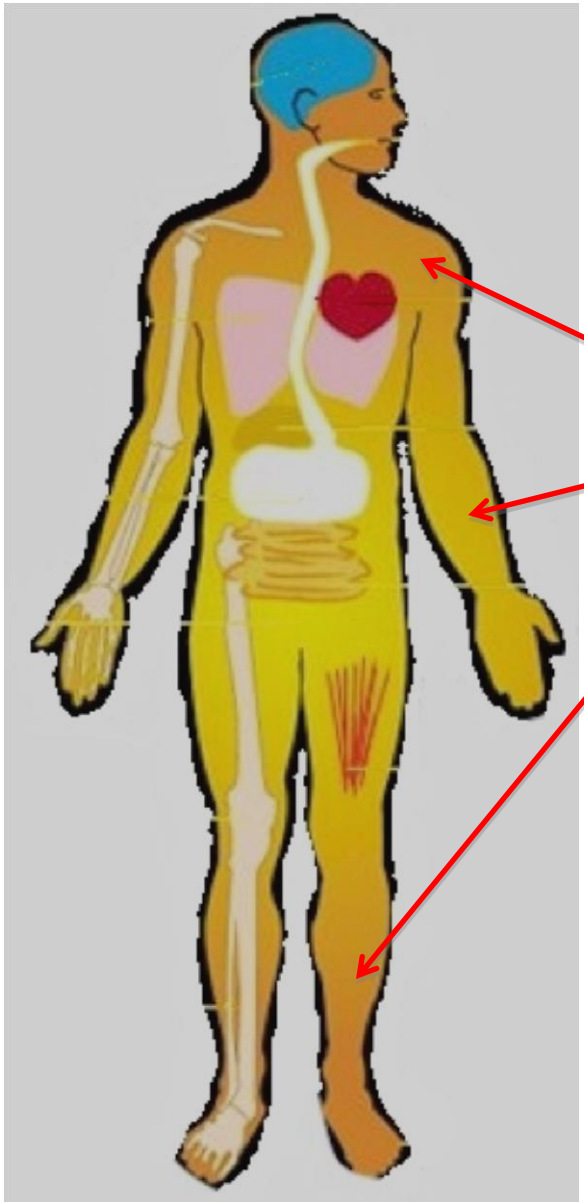
Tick bite hypersensitivity

- Develops while tick still attached or within 48 hrs
- Usually <5cm in largest diameter
- Sometimes urticarial appearance
- Begin to disappear within 24-48 hrs

Erythema migrans

- Usually becomes apparent 7-14 days after tick bite
- At least 5cm in diameter
- Typically increases in size over the first 24-48 hrs (mark with a pen and observe without ABx)

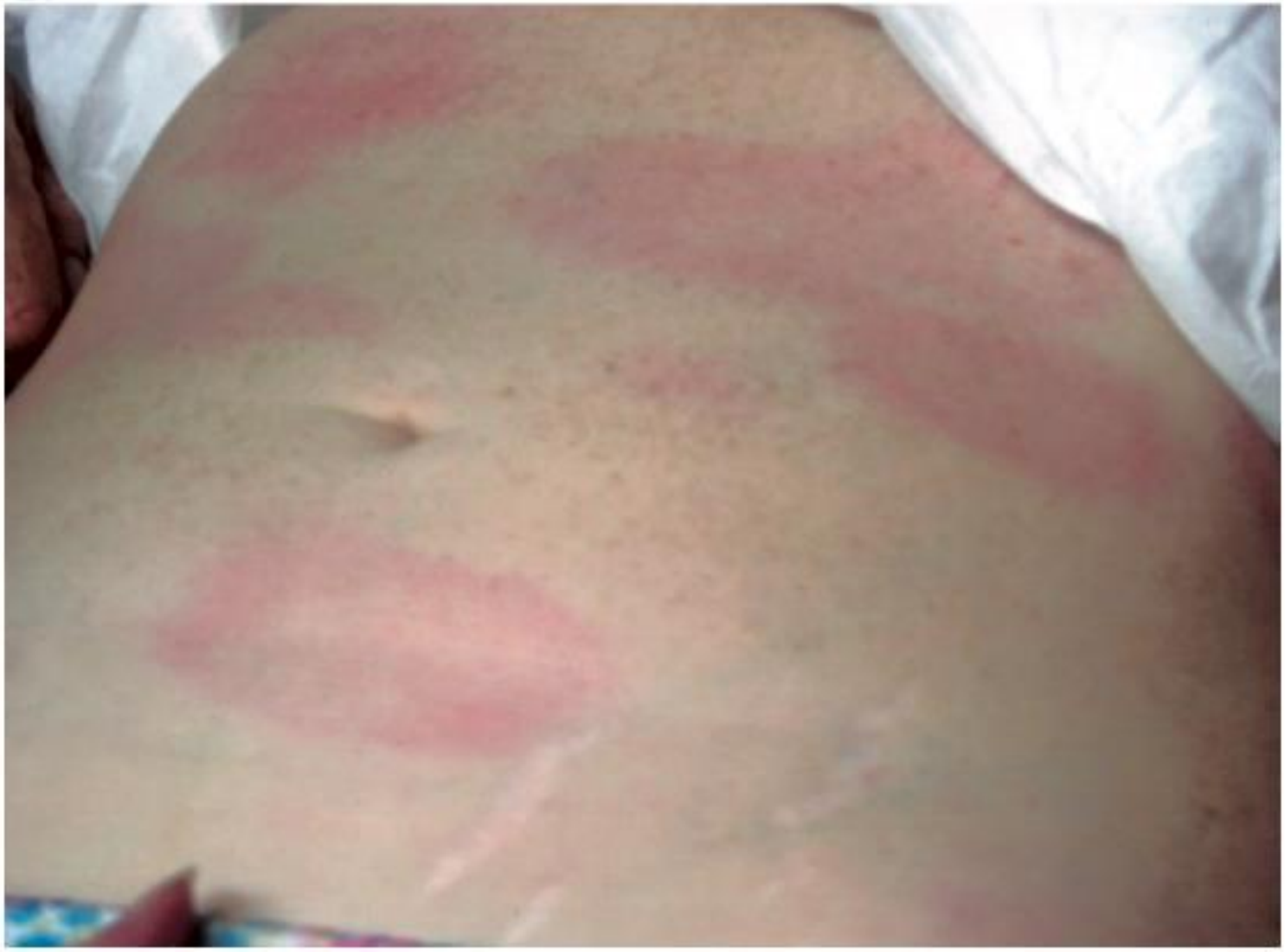
Lyme Disease
– Clinical Presentation



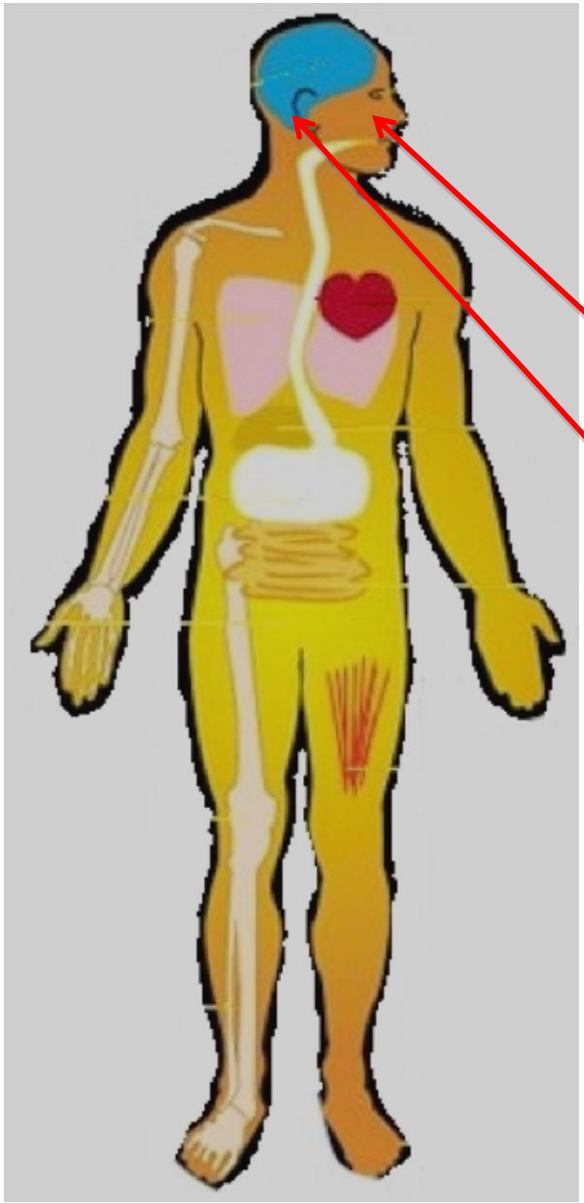
Early Disseminated Disease

- Spread of erythema migrans rash – via hematogenous spread
- Multiple lesions appear, days to weeks after 1st lesions, usually smaller than 1^0 lesion
- Can be accompanied by systemic symptoms – fever, myalgia, headache, malaise, regional LAD, conjunctivitis

Early Disseminated –



Lyme Disease
– Clinical Presentation



Early Disseminated Disease

- Neurologic –
  - Cranial neuritis (**facial palsy***, diplopia, hearing loss, facial numbness, vertigo)
  - **Aseptic meningitis***
  - Radiculoneuritis
  - Peripheral neuropathy (sensory +/or motor)
  - Plexopathy
  - Myopathy
  - Encephalopathy/encephalomyelitis
  - Pseudotumour cerebri
  - GBS

* = usual pediatric presentations

Lyme Aseptic Meningitis

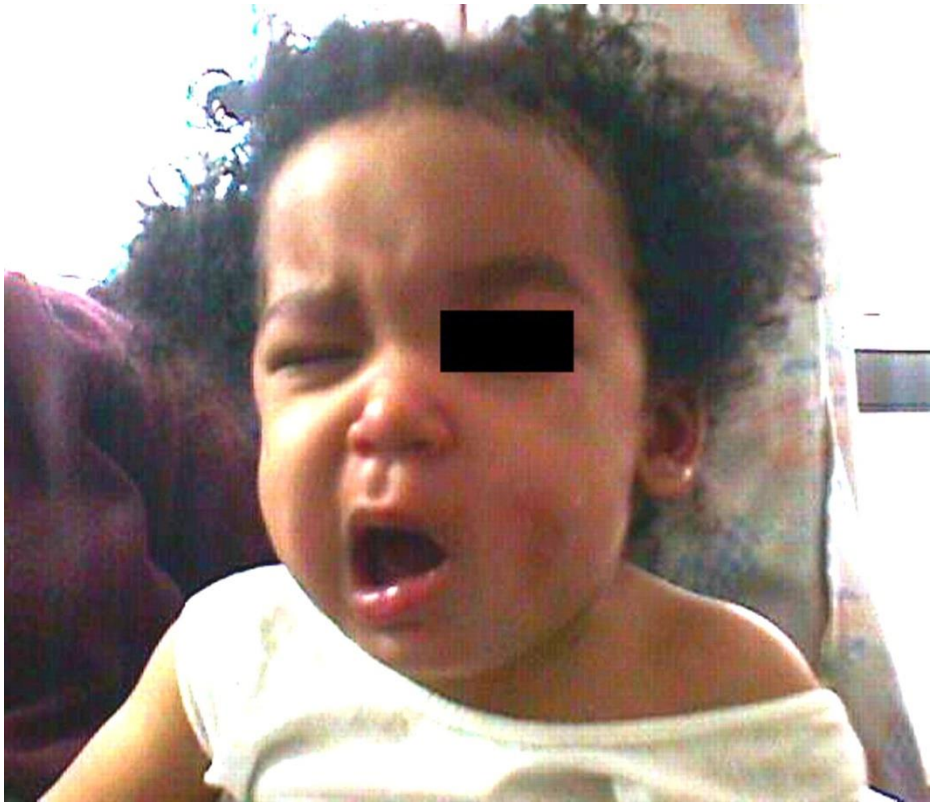
- Hx of erythema migrans recalled in ~40% of LAM; if EM present, meningitis onset follows by ~2-10 weeks
- Headache is most common feature (30-90%; frontal/occipital, mild to severe)
- Neck stiffness less common (10-20%)
- Compared with viral AM, LAM pts less likely to be febrile, sx longer in duration (>7days compared to 2days in viral AM)
- >/= 1 of EM, cranial nerve palsy, or papilledema present in ~90% of LAM

Lyme Aseptic Meningitis

- Lymphocytic/monocytic pleocytosis, 100-200 WBC; normal to low gluc; elevated protein
- Lyme serology will be + in most patients with early Lyme CNS dz (LAM); if negative at time of presentation, convalescent serology 2-4 wks later may convert
- Other tests:
  - CSF Lyme Ab (assessing intrathecal Ab production)
  - PCR (usually only + early in disease course)

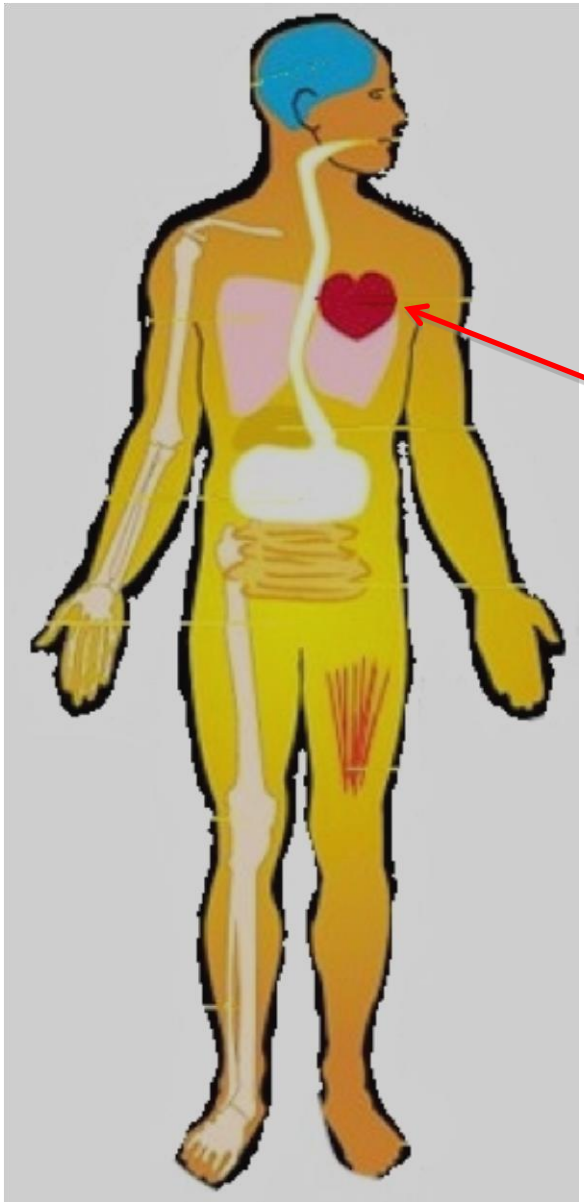
Lyme Facial Palsy

- Presents in similar time frame as LAM – weeks to months after infection
- Usually lasts 2-8 weeks, resolves completely
- When LP done – can see similar pleocytosis as LAM



AAP Red Book Online

Lyme Disease
– Clinical Presentation



Early Disseminated Disease

- Carditis
  - Conduction system disease (AV block)*
  - Pericarditis
  - Myocarditis
  - Pericardial effusion
  - LV dysfunction

* = most common cardiac presentation

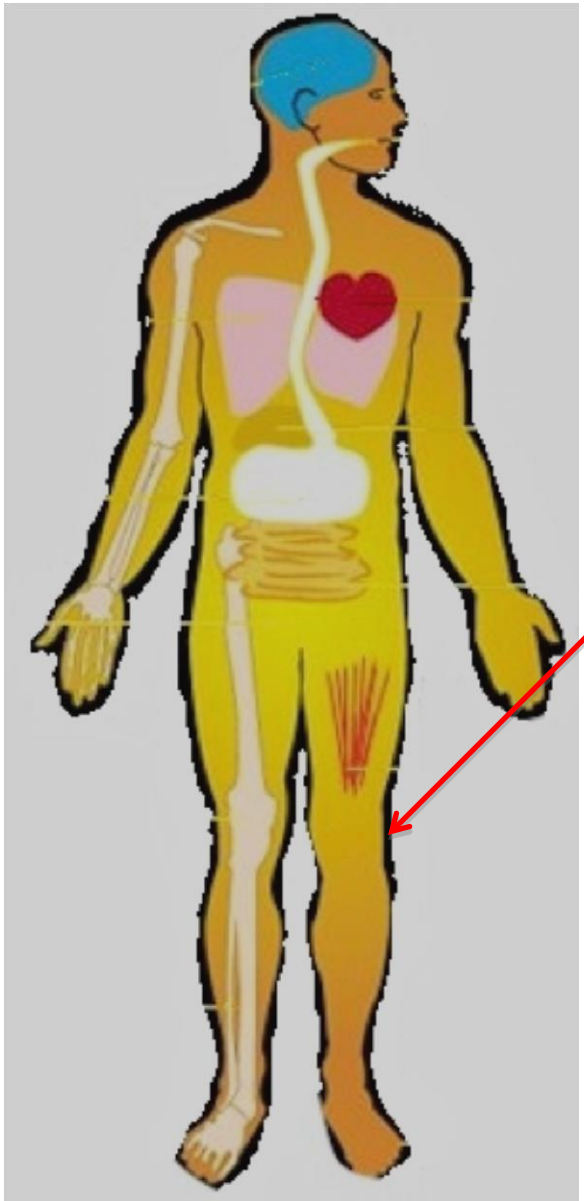
Lyme Carditis

- Presents in early disseminated disease phase, a median of 3 weeks after onset of EM
- Cardiac involvement in 4-15%, lower in pediatric population
- Investigate for carditis if age > 10 years, symptomatic, or presence of arthralgia

Lyme Carditis

- Conduction system disease
  - 1st, 2nd, or 3rd degree AV block with variability
  - Ventricular conduction system disease also possible (wide QRS beats, BBB)
  - Prolonged QTc interval
  - Sinus node dysfunction, asystole (rare)
  - Case report of atrial fibrillation
  - Conduction system disease may be more diffuse in setting of myocarditis

Lyme Disease
– Clinical Presentation

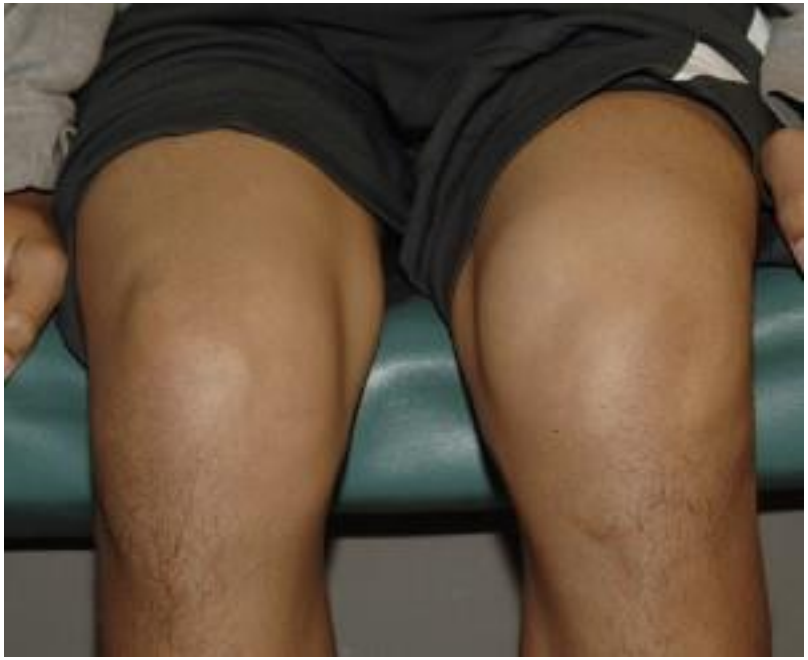


Late Disease

- Arthritis

Lyme Arthritis

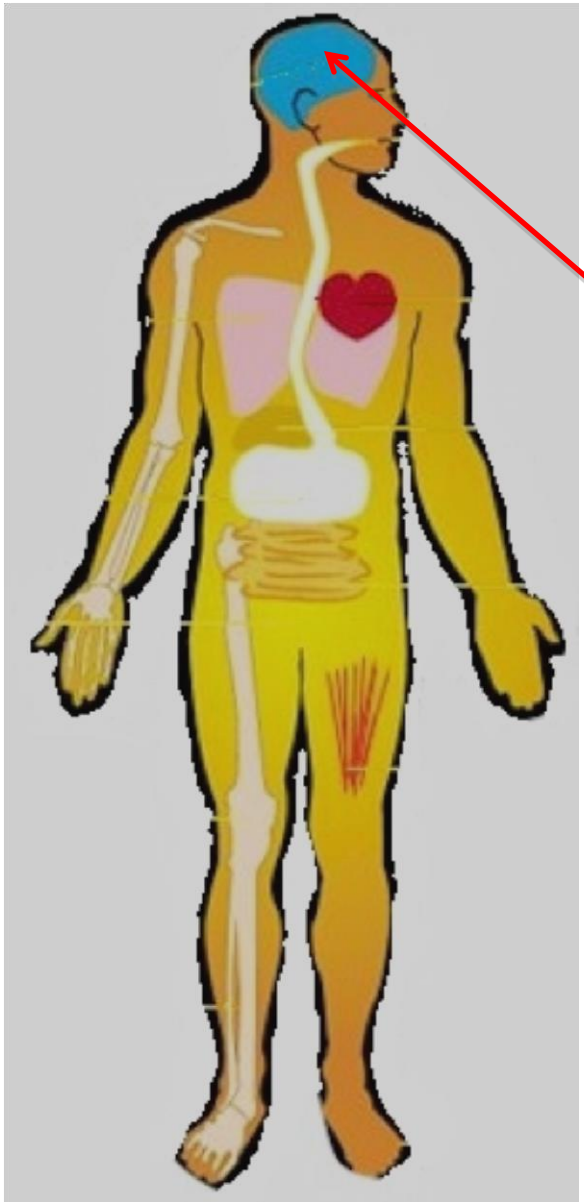
- Presenting complaint in 7% of children
- Large joints primarily (knee >90%)
- Swollen, tender, large volume effusion, but modest pain & limitation of motion



Lyme Arthritis

- Attacks last wks to months, separated by periods of complete remission
- Recurrent arthritis occurs in all untreated patients, often in other joints
- Joint fluid WBC 500-110,000 cells/mm^3 (PMNs)
- Can send Lyme PCR from joint fluid
- With treatment, sx abate within 4-7 d, complete resolution with 2-6 wks

Lyme Disease
– Clinical Presentation

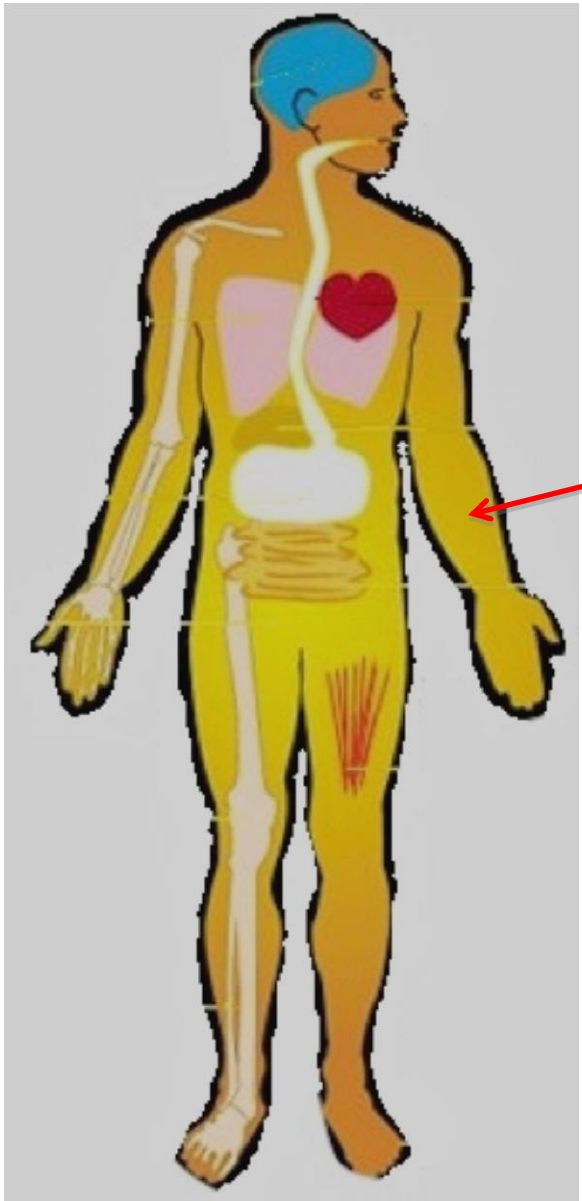


Late Disease

- CNS
  - Late neurologic syndrome (“Lyme encephalopathy” – subtle cognitive disturbances)
  - Chronic encephalomyelitis
  - Chronic axonal polyneuropathy

Rarely seen in adults, extremely rare in pediatrics

Lyme Disease
– Clinical Presentation



Late Disease

- *Acrodermatitis chronica atrophicans* rash

Acrodermatitis chronica atrophicans

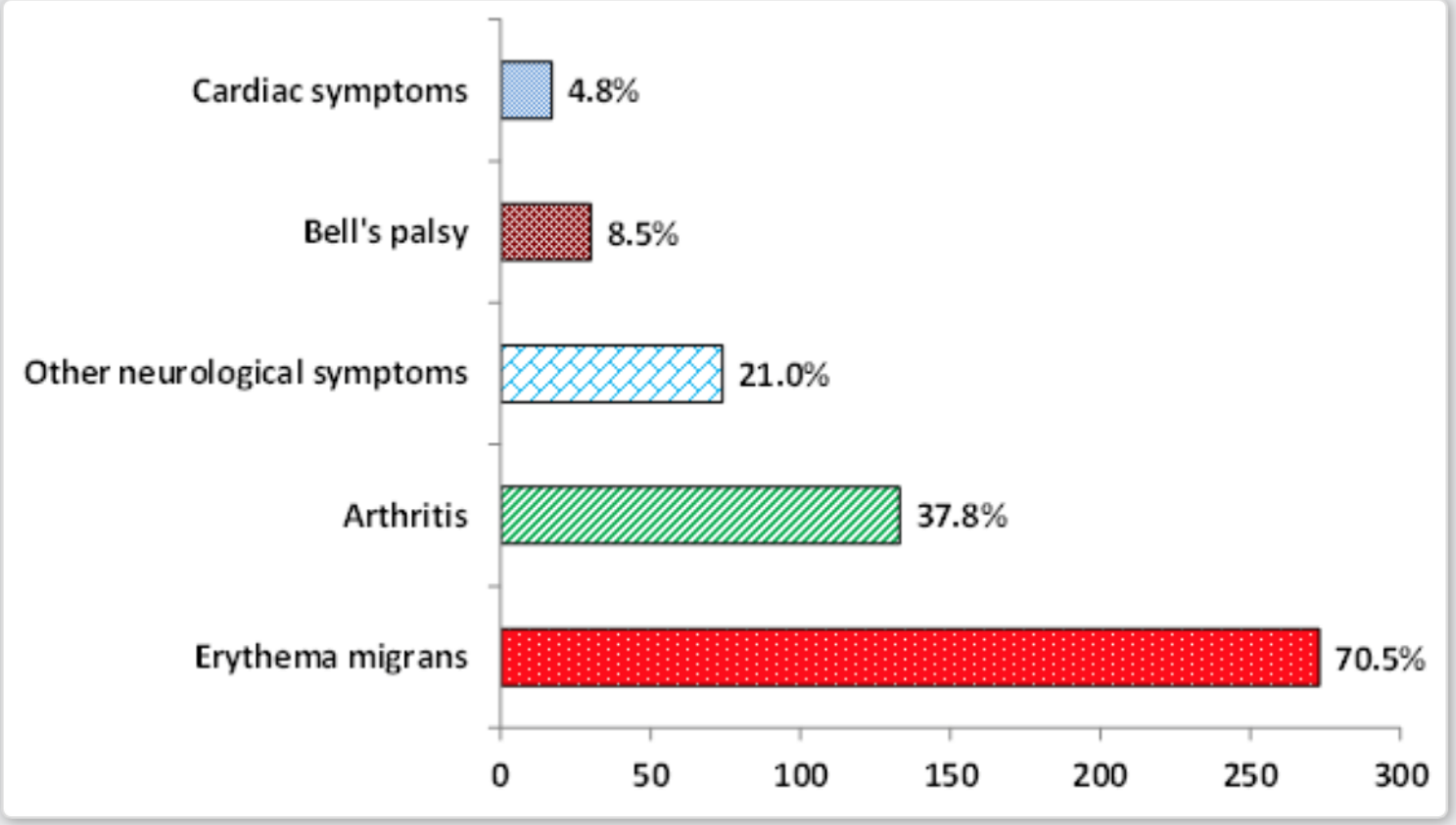
- Long-standing red or blue-red lesions, usually on extensor surfaces
- Initial “doughy” swelling, then lesions become atrophic
- Possible induration or nodules over bony prominences

Figure 5: **Examples of acrodermatitis chronic atrophicans**
Acrodermatitis chronic atrophicans (ACA) is typically located on the extensor sites of extremities: (A) ulnar and hand lesions, (B) bluish-red lesion on the back of a patient’s hand and waxy appearance of the skin of fingers, (C) lesions on a patient’s left foot and lower leg.

Post-Lyme Disease Syndrome

- Ongoing pain, neurocognitive symptoms, or fatigue despited adequate antimicrobial therapy
- If sx last >6 months, sometimes called post-Lyme disease syndrome or "*chronic Lyme disease*" (misnomer)
- Usually no evidence of persistent inflammation or usual objective Lyme findings
- No evidence for role of prolonged/repeated courses of ABx

Figure 6. The clinical manifestations of Lyme disease cases for which these data were reported, 2009-2012.



National Lyme Disease Surveillance in Canada 2009-2012, Health Canada

Lyme Diagnosis

- For early localized LD (ie. EM rash), *clinical diagnosis* is recommended as serology will often be negative at this point, and early antibiotic therapy can abrogate the seroconversion
- For other, later stages of LD, serologic testing is suggested

Lyme Diagnosis

- Two-step serologic testing approach is recommended in North America
  - First – screening EIA – usually very sensitive but less specific (false positives)
  - If EIA positive or equivocal – then separate IgM and IgG immunoblots (Western blot) are done on same sample.
  - Sx for 4 wks or more should lead to positive IgG WB. If negative after 6 weeks of Sx without Rx, then unlikely to be LD

Lyme Diagnosis

- Criteria for WB positivity based on CDC/NYS criteria, requiring IgM or IgG bands of specific molecular weights
- Many people will have IgG-reactivity with certain bands from exposure to other non-*B.burgdorferi* spirochetes, so meeting stringent criteria for dx is essential

Lyme Diagnosis – Non-recommended testing

- There is a strong community movement that believes in the role of “Chronic Lyme Disease” as an explanation for various ill-defined maladies (eg. fibromyalgia, CFS, neurologic symptom)
- Private laboratories in US (such as IGeneX) offer their own Western Blot testing, but with “more liberal reporting criteria”
- Treatment recommendations suggested by some “Lyme experts” are often not in line with mainstream medical practice

LYME IgM WESTERN BLOT .....

REVISED 9/23/10--

IGeneX interpretation is based on internal validation studies. By IGeneX criteria, IgM WB is considered positive if two or more of the double starred bands below are present. The IgM WB is considered negative if less than 2 starred bands are present. A positive result suggests exposure to B burgdorferi. By CDC/NYS criteria, IgM WB is reported positive if 2 of the following bands are present:23-25,39,41kDa. The IgM WB is negative if less than 2 bands are present.

LIMITATION: Positive result for 31 and/or 34kDa may be present after Lyme vaccination in uninfected persons. Infection with HSV,EBV,HCV and/or syphillis (RPR+) may give false (+) results.

****PRESENCE OF ONLY ONE DOUBLE STARRED BAND OR INDETERMINATE DOUBLE STARRED BANDS IN A NEGATIVE REPORT MAY INDICATE CLINICAL SIGNIFICANCE.****
THEREFORE, WE RECOMMEND TESTING WITH ANOTHER METHOD AND/OR RETEST IN 4-6 WEEKS.

BAND INTENSITY: Negative (-): No band detected. Indeterminate (IND): Band present with intensity < calibration standard. Positive (1+ to 4+): Band present at an intensity > or = to calibration standard.

IGENEX IGM RESULT	POSITIVE
CDC/NYS RESULT	NEGATIVE
18 kDa.	-
22 kDa.	-
**23-25 kDa.	IND
28 kDa.	-
30 kDa.	-
**31 kDa.	+
**34 kDa.	IND
**39 kDa.	IND
**41 kDa.	++
45 kDa.	-
58 kDa.	-
66 kDa.	-
73 kDa.	-
**83-93 kDa.	+

Diagnosis should not be based on laboratory tests alone. Results should be interpreted in conjunction with clinical symptoms and patient history.

Continued on next page

Lyme Treatment

- Evidence-based treatment recommendations have been written by the Infectious Diseases Society of America (2006)
- In general early localized & disseminated disease can be treated with oral doxycycline or amoxicillin
- Neurologic disease (early or late) should receive IV therapy

IDSA Lyme Guidelines

Table 2. Recommended antimicrobial regimens for treatment of patients with Lyme disease.

Drug	Dosage for adults	Dosage for children
Preferred oral regimens		
Amoxicillin	500 mg 3 times per day[a]	50 mg/kg per day in 3 divided doses (maximum, 500 mg per dose)[a]
Doxycycline	100 mg twice per day[b]	Not recommended for children aged <8 years For children aged ≥8 years, 4 mg/kg per day in 2 divided doses (maximum, 100 mg per dose)
Cefuroxime axetil	500 mg twice per day	30 mg/kg per day in 2 divided doses (maximum, 500 mg per dose)
Alternative oral regimens		
Selected macrolides[c]	For recommended dosing regimens, see footnote *d* in table 3	For recommended dosing regimens, see footnote in table 3
Preferred parenteral regimen		
Ceftriaxone	2 g intravenously once per day	50–75 mg/kg intravenously per day in a single dose (maximum, 2 g)
Alternative parenteral regimens		
Cefotaxime	2 g intravenously every 8 h[d]	150–200 mg/kg per day intravenously in 3–4 divided doses (maximum, 6 g per day)[d]
Penicillin G	18–24 million U per day intravenously, divided every 4 h[d]	200,000–400,000 U/kg per day divided every 4 h[d] (not to exceed 18–24 million U per day)

[a] Although a higher dosage given twice per day might be equally as effective, in view of the absence of data on efficacy, twice-daily administration is not recommended.
[b] Tetracyclines are relatively contraindicated in pregnant or lactating women and in children <8 years of age.
[c] Because of their lower efficacy, macrolides are reserved for patients who are unable to take or who are intolerant of tetracyclines, penicillins, and cephalosporins.
[d] Dosage should be reduced for patients with impaired renal function.

IDSA Lyme Guidelines

Table 3. Recommended therapy for patients with Lyme disease.

Indication	Treatment	Duration, days (range)
Tick bite in the United States	Doxycycline, 200 mg in a single dose[a,b]; (4 mg/kg in children ≥8 years of age) and/or observation	…
Erythema migrans	Oral regimen[c,d]	14 (14–21)[e]
Early neurologic disease		
Meningitis or radiculopathy	Parenteral regimen[c,f]	14 (10–28)
Cranial nerve palsy[a,g]	Oral regimen[c]	14 (14–21)
Cardiac disease	Oral regimen[a,c,h] or parenteral regimen[a,c,h]	14 (14–21)
Borrelial lymphocytoma	Oral regimen[c,d]	14 (14–21)
Late disease		
Arthritis without neurologic disease	Oral regimen[c]	28
Recurrent arthritis after oral regimen	Oral regimen[a,c]	28
	or parenteral regimen[a,c]	14 (14–28)
Antibiotic-refractory arthritis[i]	Symptomatic therapy[j]	…
Central or peripheral nervous system disease	Parenteral regimen[c]	14 (14–28)
Acrodermatitis chronica atrophicans	Oral regimen[c]	21 (14–28)
Post–Lyme disease syndrome	Consider and evaluate other potential causes of symptoms; if none is found, then administer symptomatic therapy[a]	…

IDSA Lyme Guidelines

- Role for ABx prophylaxis after tick bites?
- Good evidence showing efficacy in preventing clinical Lyme disease with single-dose doxycycline in those >8yrs
- No similar studies in younger children using amoxicillin as prophylaxis
- IDSA recommends watchful waiting with close monitoring for development of EM rash
- Threshold for population rates of carriage for *B.burgdorferi* in ticks not clear for when to recommend single-dose doxy (?>20%)

Summary & Take-Home Points

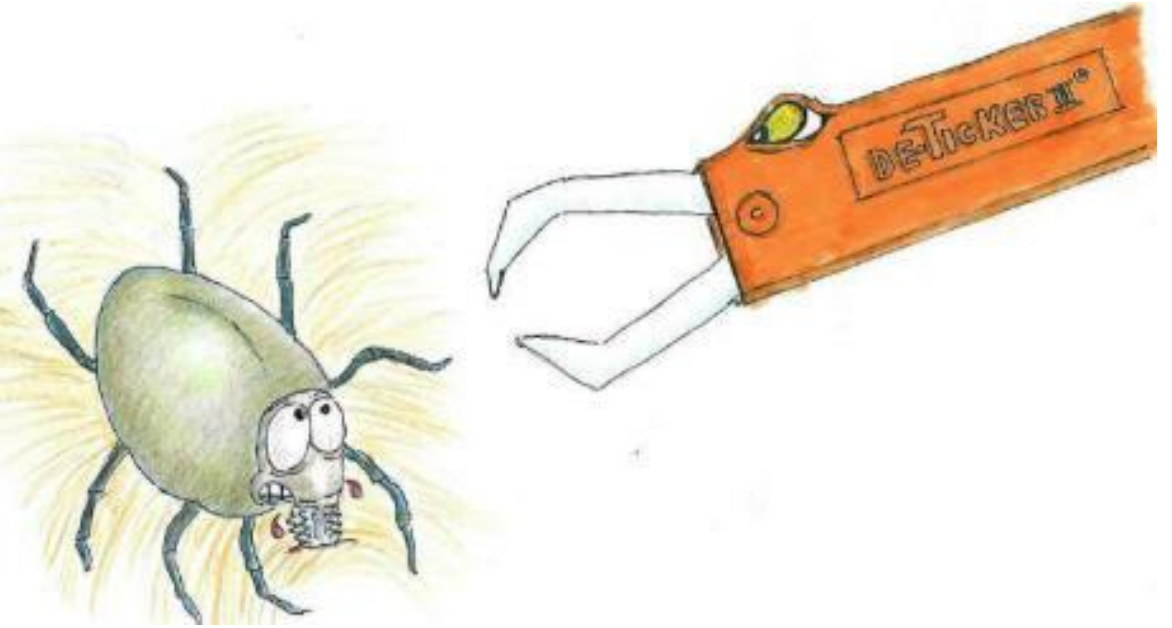
- The vector (*Ixodes* scapularis) and causative agent (*Borrelia burgdorferi*) of Lyme Disease are on the rise in ON
- Health care providers need to familiarize themselves with clinical manifestations of LD, and consider it amongst their differential diagnoses for patients with compatible illnesses

Visual Lyme Disease Review

Summary & Take-Home Points

- Multiple resources on ***epidemiology, clinical disease, treatment*** and ***prevention*** are available through:
  - IDSA
    - www.idsociety.org
  - PHAC
    - http://www.phac-aspc.gc.ca/id-mi/lyme-eng.php
  - Ottawa Public Health
    - http://ottawa.ca/en/health_safety/conditions/lyme/index.html
  - CDC
    - http://www.cdc.gov/lyme/

www.mdavid.com.au
I'm here about my facial tick.
MDavid


DETICKER II

Questions?

Thank you!

for participating in today's

Pediatric Telehealth Rounds

Join us next time:

with Dr. Julie Quet for

Tics & Tourettes

June 26th, 2015

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