



# SPECIAL PANEL PRESENTATION

---

## Lyme Disease: Big, Bad *Borrelia burgdorferi* & the Tiny Tick

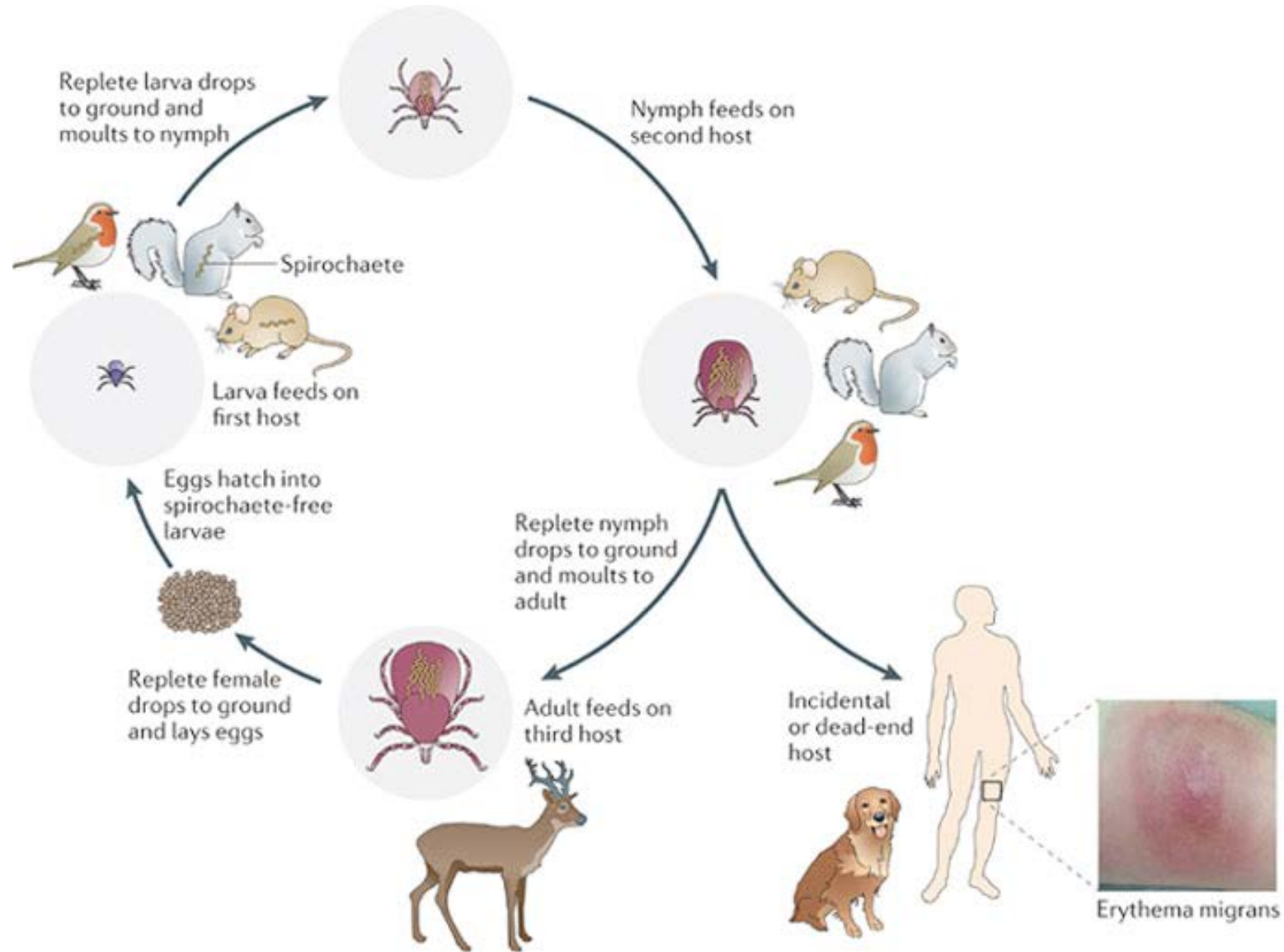
Ralph C. Budd, M.D., University Distinguished Professor of Medicine, and  
Director, Vermont Center for Immunology & Infectious Diseases;

Bradley Tompkins, M.P.H., Infectious Disease Epidemiologist and Program  
Chief, Vermont Department of Health;

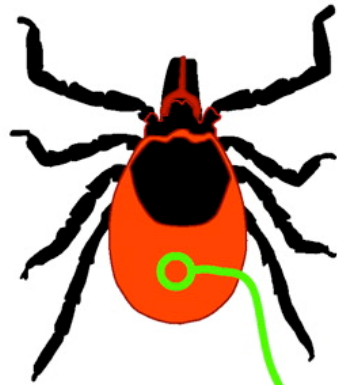
Molly Markowitz, Student, Larner College of Medicine Class of 2018



# Tick Life Cycle

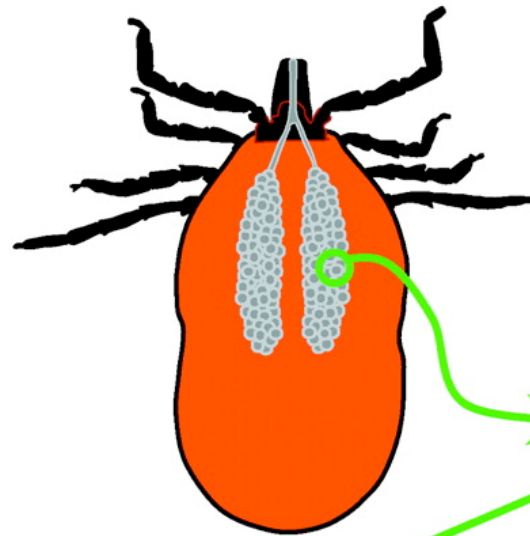


**Infected unfed nymph**  
**23 °C, elevated pH**



**Midgut lumen  
spirochetes**  
OspA +  
OspB +  
OspC -

**72 hr feeding nymph**  
**37 °C, lower pH**



**Transition  
stage?**  
OspA +  
OspB +  
OspC +

**Salivary gland  
spirochetes**  
OspA -  
OspB -  
OspC +  
Other group I  
lipoproteins

Blistering Lesions



Uniformly Red Lesions



**Erythema migrans  
can present itself in  
many different forms**

Disseminated Lesions



Blue-Red Lesions

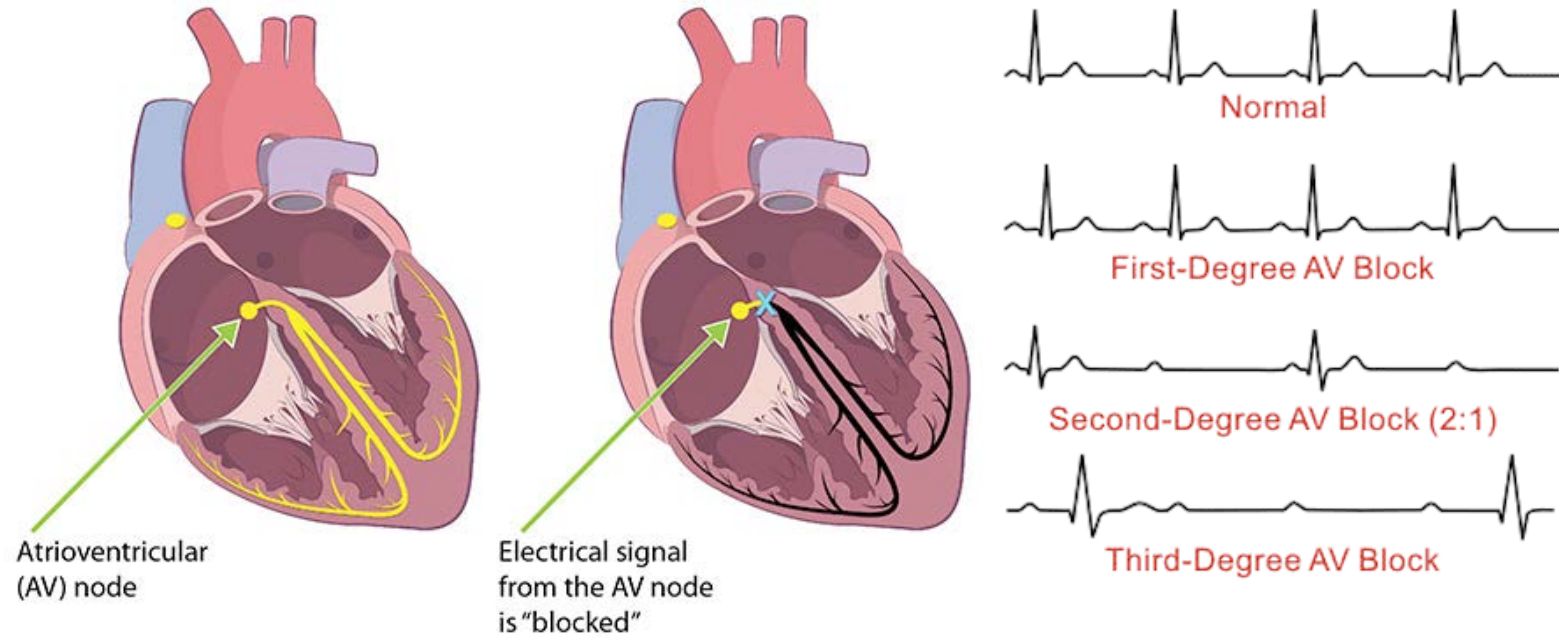


Bullseye (Target)/ Central Clearing Lesions



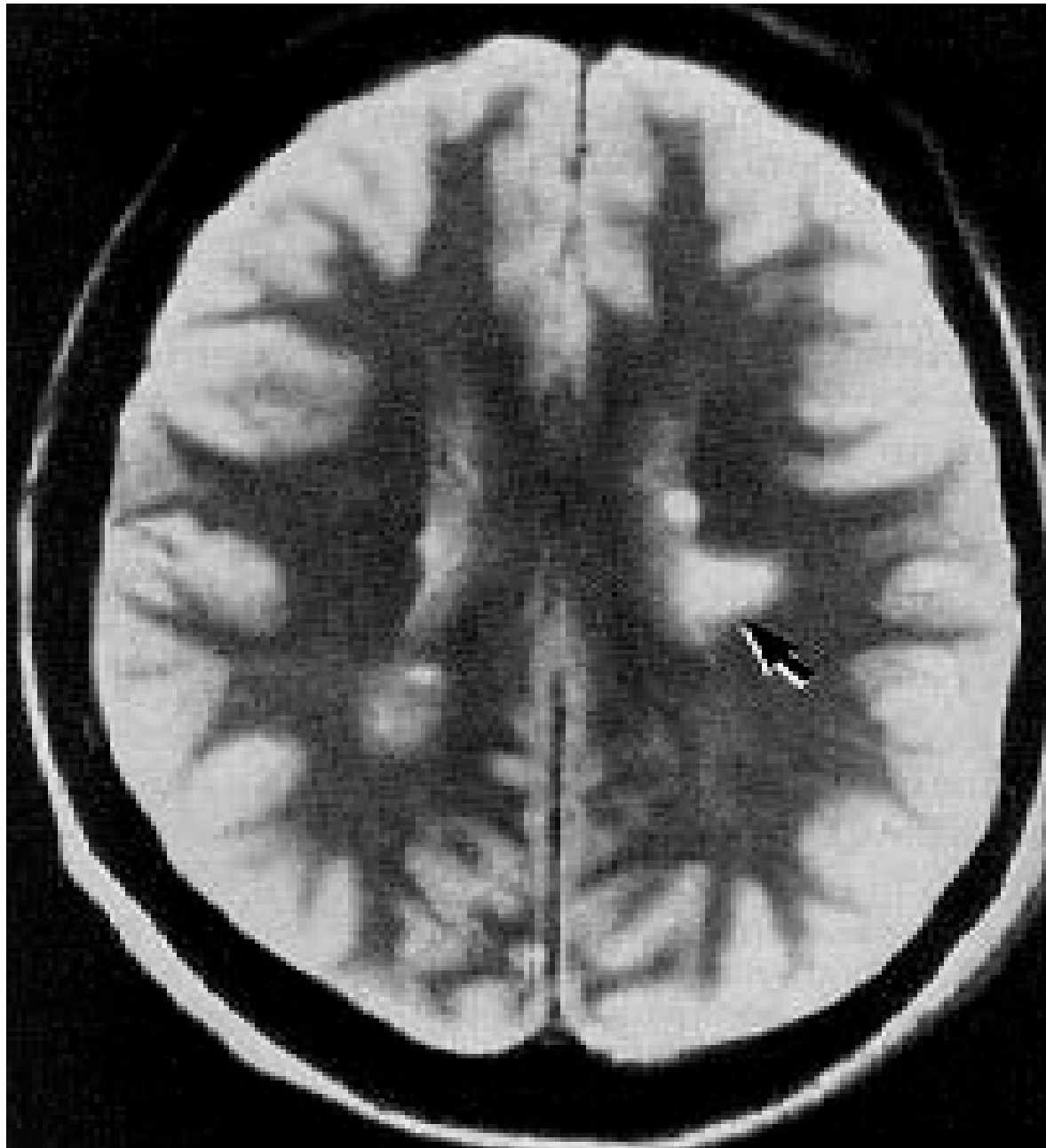


## Heart block in Lyme disease

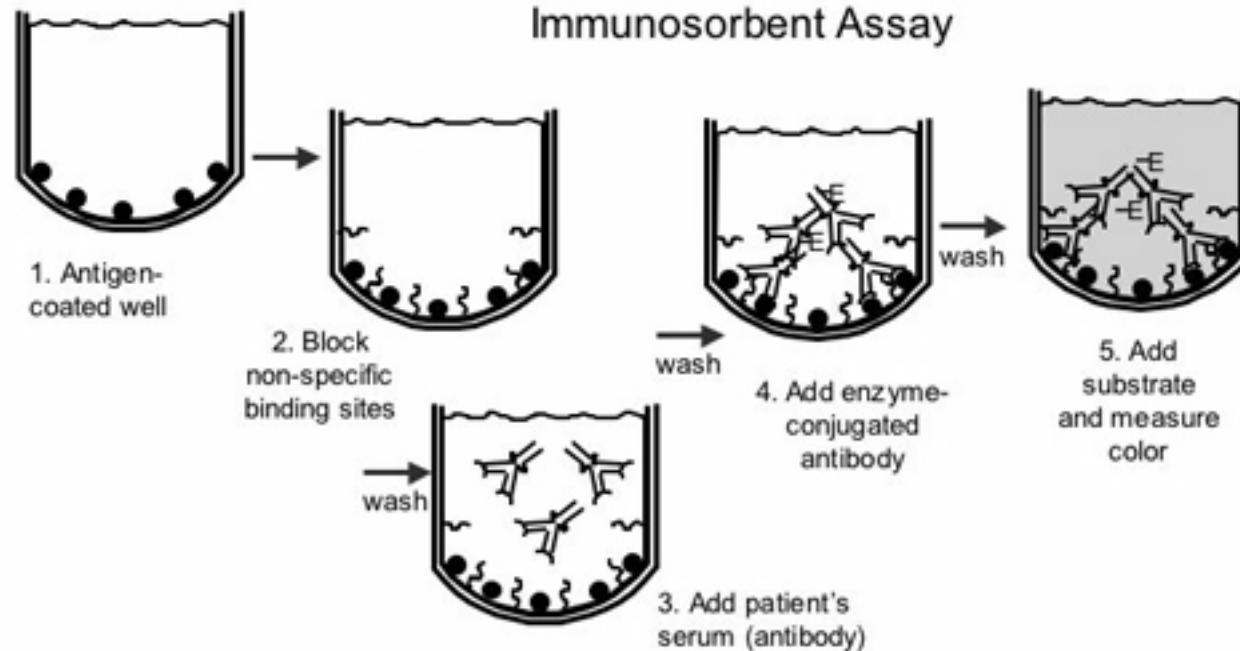






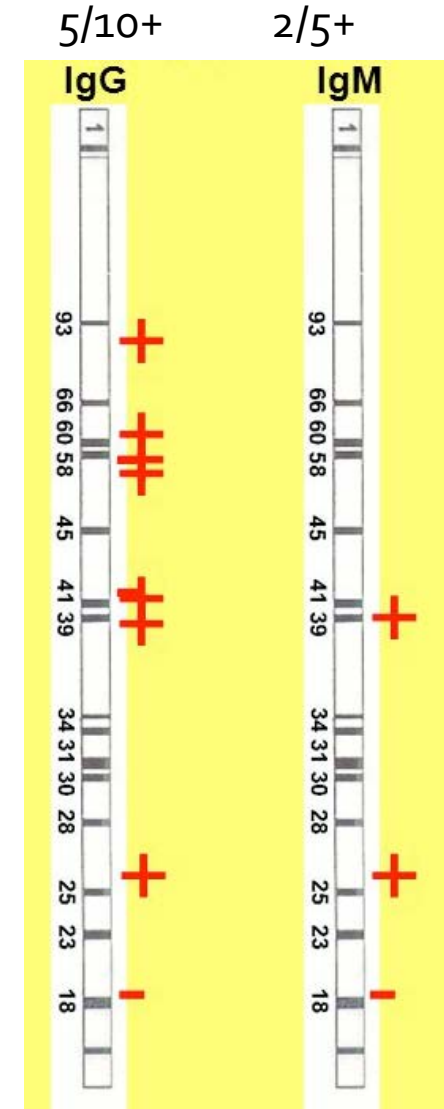
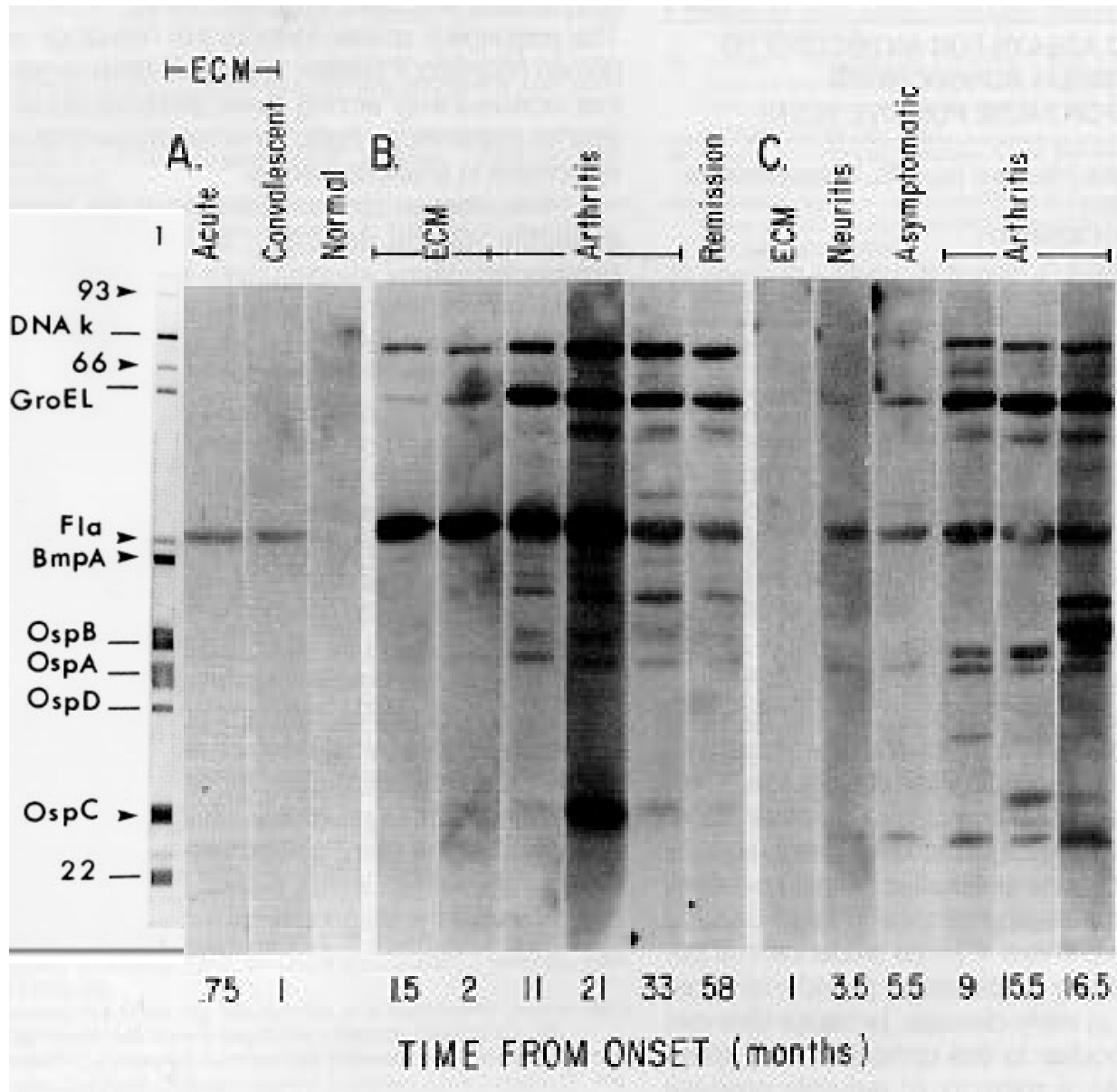


## ELISA: Enzyme-Linked Immunosorbent Assay



The most common and useful lab tests measure a patient's serologic response to *Borrelia burgdorferi*. IgM responses are first detected within two weeks of infection, peak at three to six weeks, then falls to normal by six months. IgG can usually be detected by four to six weeks; and peak many months after onset of disease. The IgG response lasts for many years.

## Anti-*Borrelia* antibody production during infection



## TREATMENT OF LYME DISEASE<sup>1</sup>

	Drug	Adult Dosage	Pediatric Dosage <sup>2</sup>
ERYTHEMA MIGRANS	Doxycycline <sup>3</sup> ( <i>Vibra-</i> <i>mycin</i> , and others)	100 mg PO b.i.d. x 21 d	≥8 yrs: 1-2 mg/kg b.i.d.
	OR Amoxicillin ( <i>Amoxil</i> , and others)	500 mg PO t.i.d. x 21 d	50 mg/kg/day divided t.i.d.
	OR Cefuroxime axetil ( <i>Ceftin</i> )	500 mg PO b.i.d. x 21 d	30 mg/kg/day divided b.i.d.
NEUROLOGIC DISEASE			
Facial nerve palsy	Doxycycline <sup>3</sup>	100 mg PO b.i.d. x 21-28 d	
	OR Amoxicillin	500 mg PO t.i.d. x 21-28 d	25-50 mg/kg/day divided t.i.d.
More serious CNS disease	Ceftriaxone ( <i>Rocephin</i> )	2 g/day IV x 14-28 d	75-100 mg/kg/day IV
	OR Cefotaxime ( <i>Claforan</i> )	2g IV q8h x 14-28 d	150-200 mg/kg/day in 3-4 doses
	OR Penicillin G	20-24 million units/day IV x 14-28 d	300,000 units/kg/day IV
CARDIAC DISEASE			
Mild (first degree AV block)	Doxycycline <sup>3</sup>	100 mg PO b.i.d. x 21-28 d	
	OR Amoxicillin	500 mg PO t.i.d. x 21-28 d	25-50 mg/kg/day divided t.i.d.
More serious <sup>4</sup>	Ceftriaxone	2 g/day IV x 14-21 d	50-75 mg/kg/day IV
	OR Penicillin G	18-24 million units/day IV x 14-21 d	300,000 units/kg/day IV
ARTHRITIS <sup>5</sup>			
Oral	Doxycycline <sup>3</sup>	100 mg PO b.i.d. x 28 d	
	OR Amoxicillin	500 mg PO t.i.d. x 28 d	50 mg/kg/day divided t.i.d.
Parenteral	Ceftriaxone	2 g/day IV x 14-28 d	50-75 mg/kg/day IV
	OR Penicillin G	18-24 million units/day IV x 14-28 d	300,000 units/kg/day IV

1. The duration of treatment is not well established. Relapse has occurred with all of these regimens; patients who relapse may need a second course of treatment. There is no evidence that either repeated or prolonged treatment benefits subjective symptoms attributed to Lyme disease.

2. Should not exceed adult dosage.

3. Neither doxycycline nor any other tetracycline should be used for children less than eight years old or for pregnant or lactating women.

4. A temporary pacemaker may be necessary.

5. In late disease, the response to treatment may be delayed for several weeks or months.

## Lyme Vaccine

**LYMErix:** In 1998, the FDA approved LYMErix, a Lyme disease vaccine utilizing a recombinant OspA antigen. The approval was based on large clinical studies that demonstrated its safety and effectiveness. Subsequently, some clinicians raised concerns that the vaccine itself might be causing a "reactive" arthritis in some genetically pre-disposed people. The manufacturer SmithKline withdrew the product.

**VLA15:** FDA just announced plans to expedite approval of a vaccine for Lyme disease. Valneva, the maker of the vaccine candidate, known as VLA15, recently completed an initial evaluation in a small, early stage clinical trial. Now the company has been given a green light by the regulatory agency through a program known as Fast Track to move onto a larger trial at the beginning of 2018. Additionally it will announce findings from the first trial around the same time.



# Tickborne Diseases Present in Vermont

1. Lyme disease
2. Anaplasmosis
3. Babesiosis
4. *Borrelia miyamotoi*
5. Ehrlichiosis
6. Spotted fever group rickettsiosis
7. Tularemia
8. Powassan virus disease
9. Heartland virus disease (?)

MOST COMMON



LEAST COMMON

## Causative Agent in Vermont: *Borrelia burgdorferi*

- Upper Midwest: *Borrelia burgdorferi* & *Borrelia mayonni*
- Europe & Asia: *Borrelia afzelii* & *Borrelia garinii*

## Brief History of Lyme Disease

- Lyme disease was first recognized in late 1970's<sup>(1)</sup>
- Museum specimens from 1890's contain the bacterium<sup>(2)</sup>
- Pathogen was in North America prior to last ice age<sup>(3)</sup>
  - ~20,000 years ago



# Lyme Disease Vector: Blacklegged Tick

- *Borrelia burgdorferi* is transmitted through tick bite
  - ▣ Blacklegged tick (*Ixodes scapularis*)
- Ticks feed on small, warm-blooded animals (host)
  - ▣ Ticks pick up *Borrelia burgdorferi* during a feeding
  - ▣ Ticks do not hatch with *Borrelia burgdorferi*
- Ticks get onto a host through questing
  - ▣ Do not jump (like fleas)
  - ▣ Do not fall down from trees above



# Blacklegged Tick: Evolved Pathogen Spreader

- Ticks must feed on a host for multiple days
- Components of tick saliva help evade defenses<sup>(4)</sup>
  1. Pain and itch pathway inhibitors
  2. Anticoagulants
  3. Vasodilators
  4. Platelet aggregation inhibitors
  5. Wound healing modulators



# Pathogen Prevalence in Vermont Ticks

Pathogens Detected	Percentage of Ticks (n = 2,209)*
<i>Anaplasma phagocytophilum</i>	7.0%
<i>Borrelia burgdorferi</i>	52.9%
<i>Babesia microti</i>	0.8%
Single Pathogen Carriage Rate	60.7%

- Majority of blacklegged ticks carry one pathogen
- 4.7% of ticks infected with >1 pathogen

\* Data contributed by VAAFM  
& Lyndon State College

# Lyme Disease is a Zoonotic Disease

- ~~□ White-tailed deer are responsible for Lyme disease~~



COMMUNITY NATURE & SCIENCE

## Deer Culling Discussed Amid Worry Over Tick Diseases

Alex Elvin Thursday, July 7, 2016 - 6:11pm

“Deer tick”

## Deer overpopulation helps spread Lyme

News-Times, The (Danbury, CT) Published 1:00 am, Monday, November 24, 2008

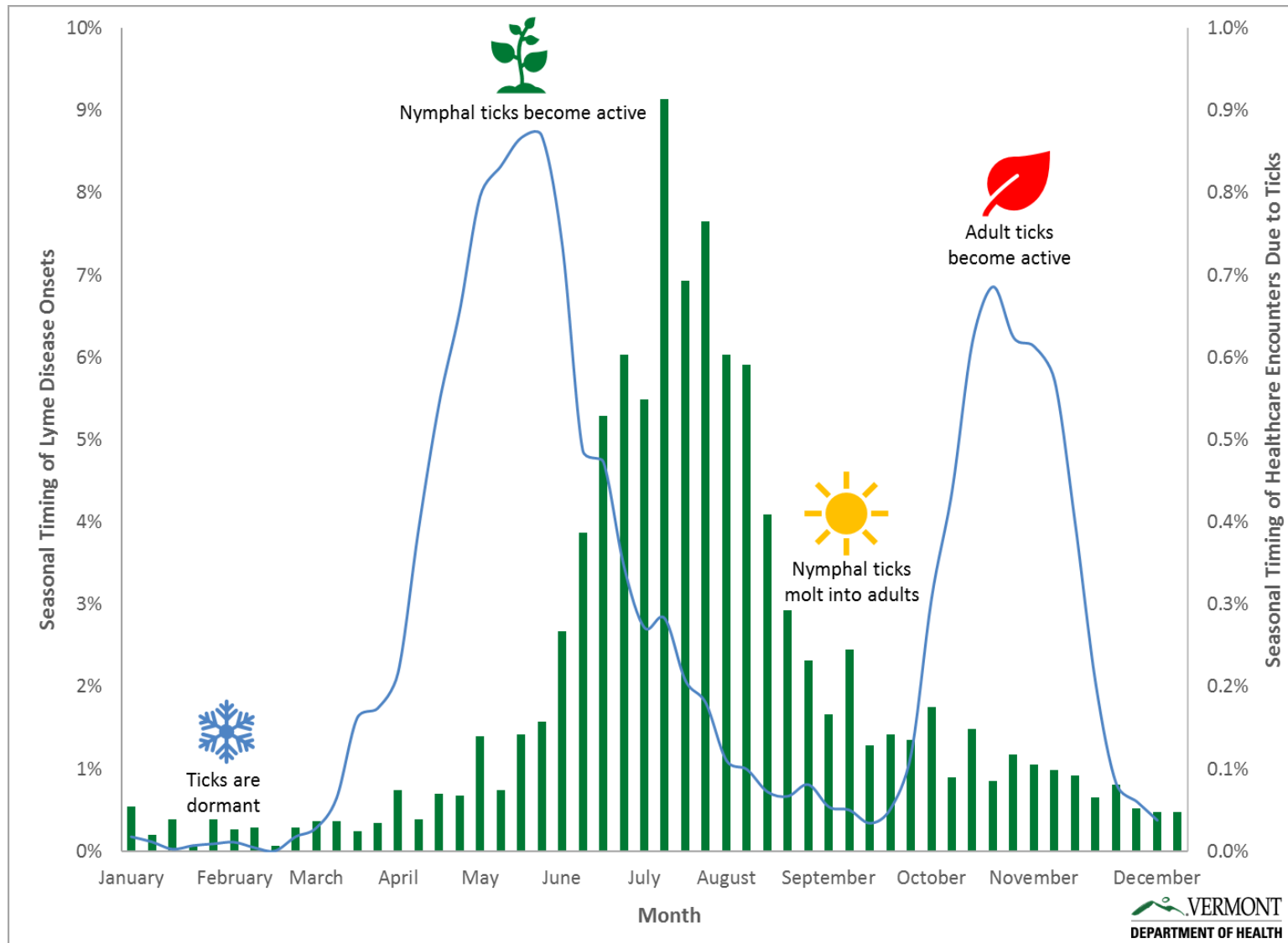


# Lyme Disease is a Zoonotic Disease

- Competent reservoirs for Lyme disease (*Borrelia burgdorferi*)<sup>(6)</sup>

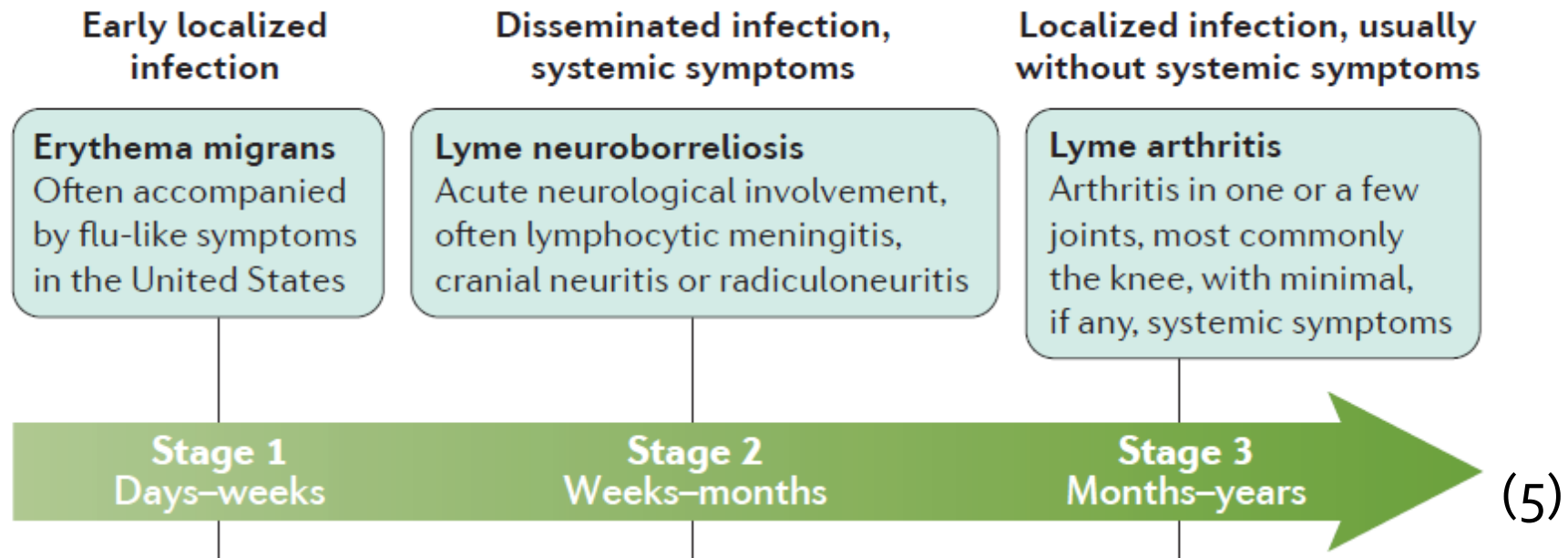


# Seasonal Risk for Lyme Disease in Vermont

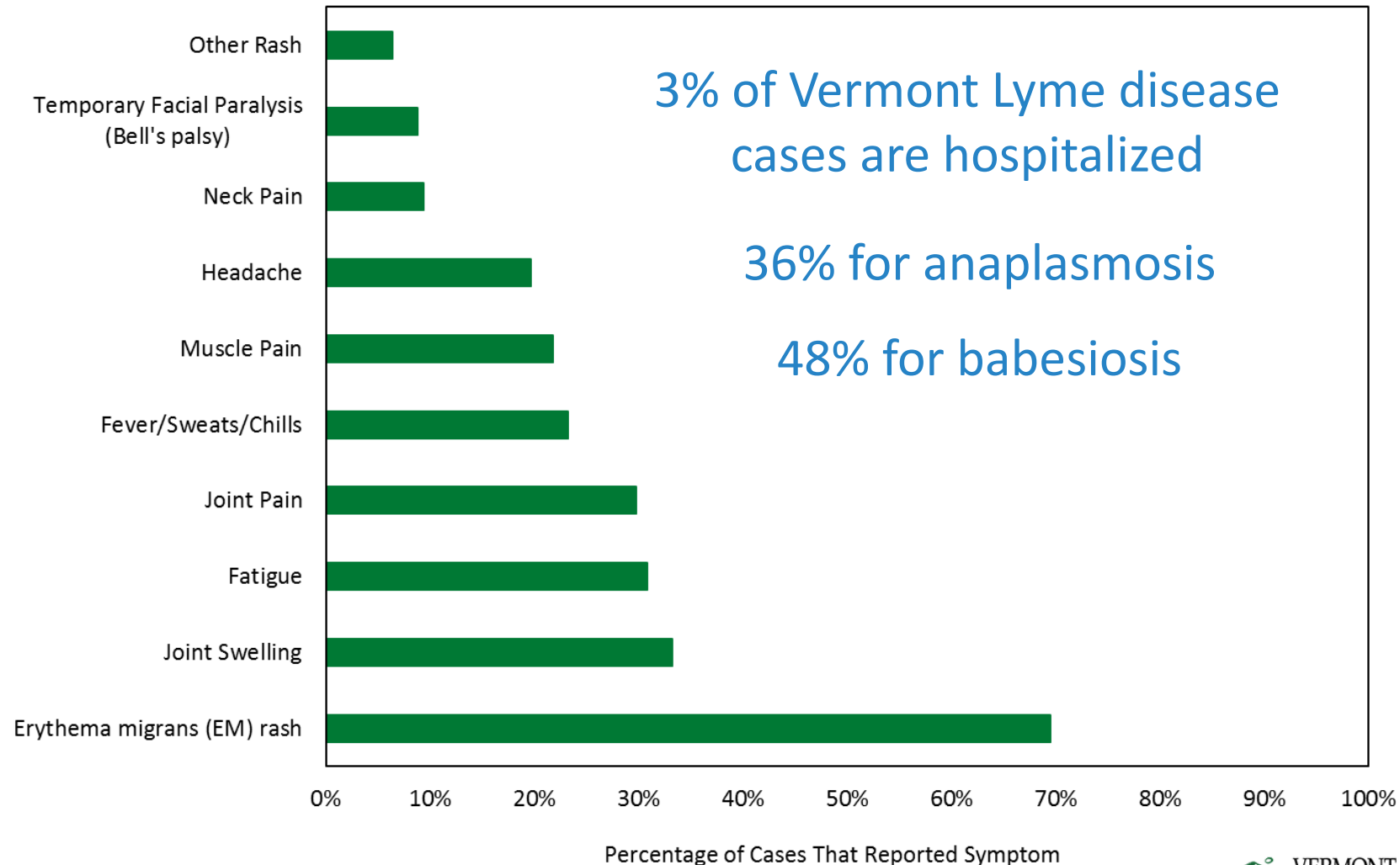


# Lyme Disease Illness

- Symptoms do not begin right away
  - ▣ Incubation period: 3 – 30 days

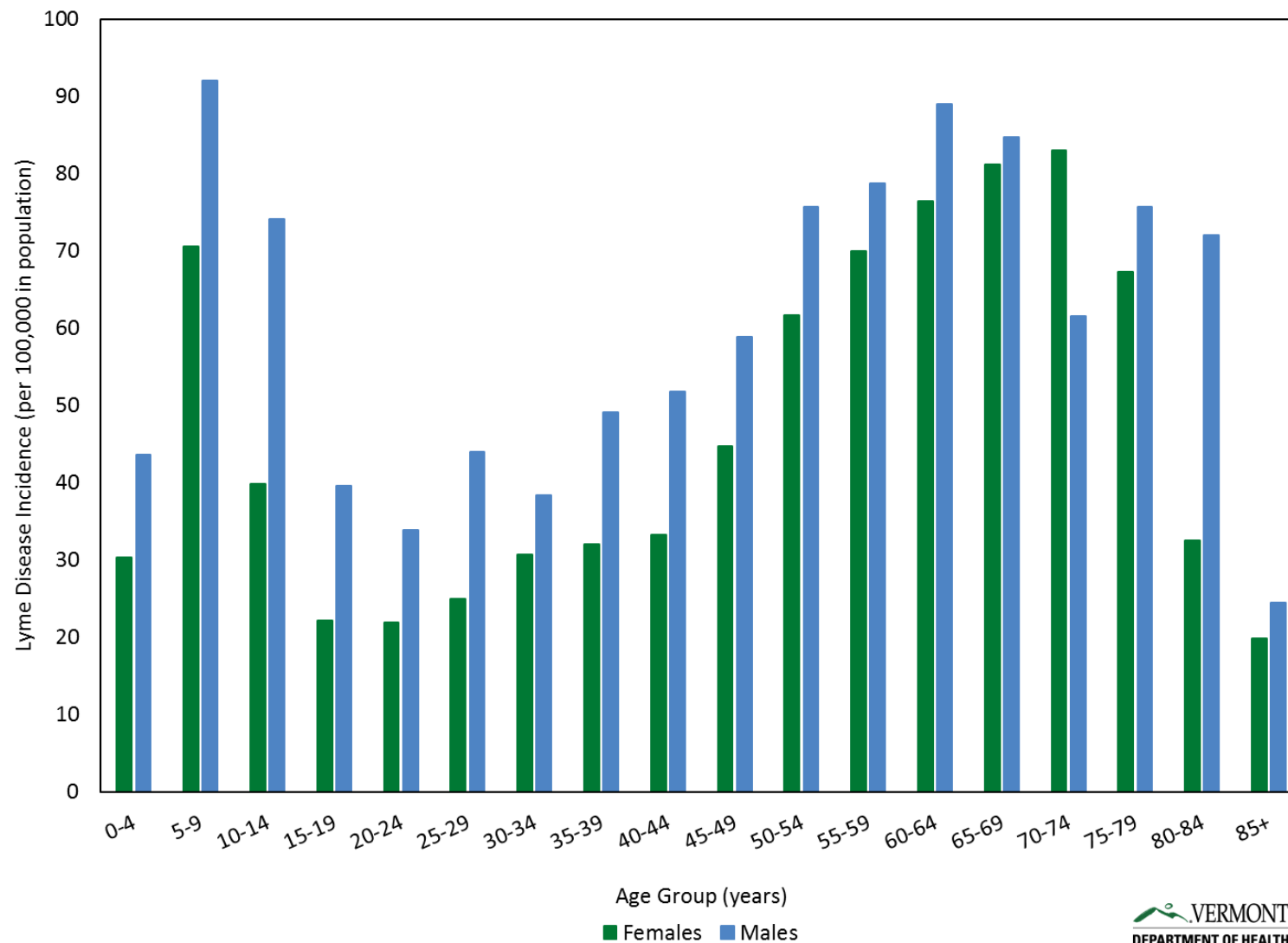


# Most Commonly Reported Symptoms of Lyme Disease

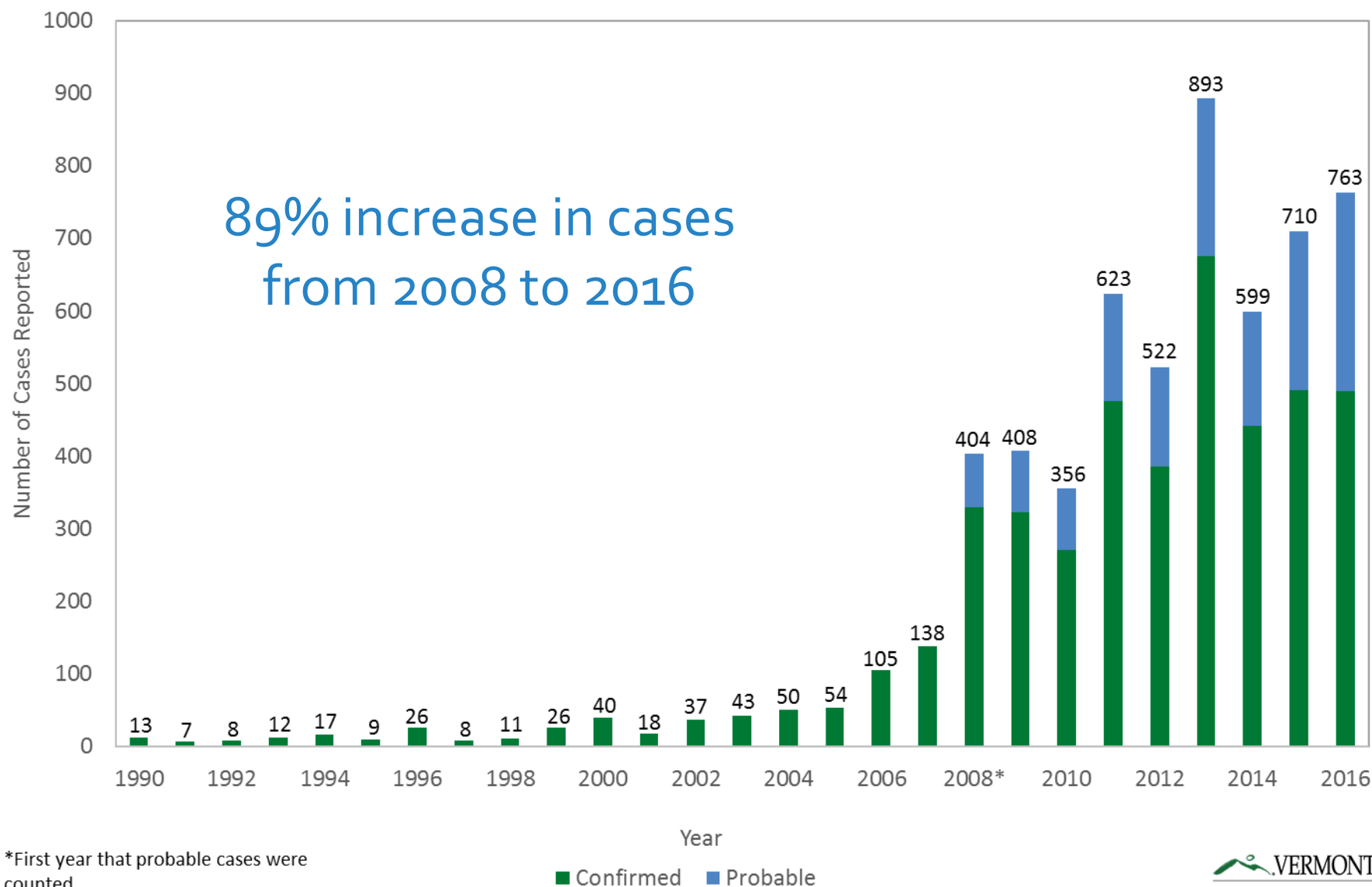




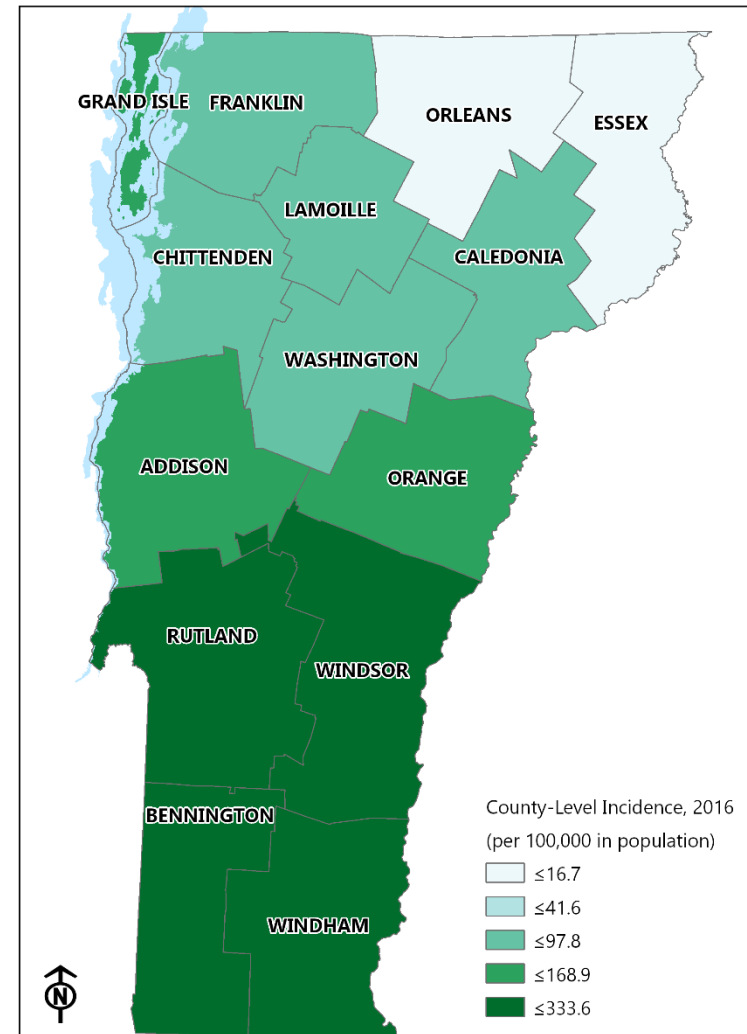
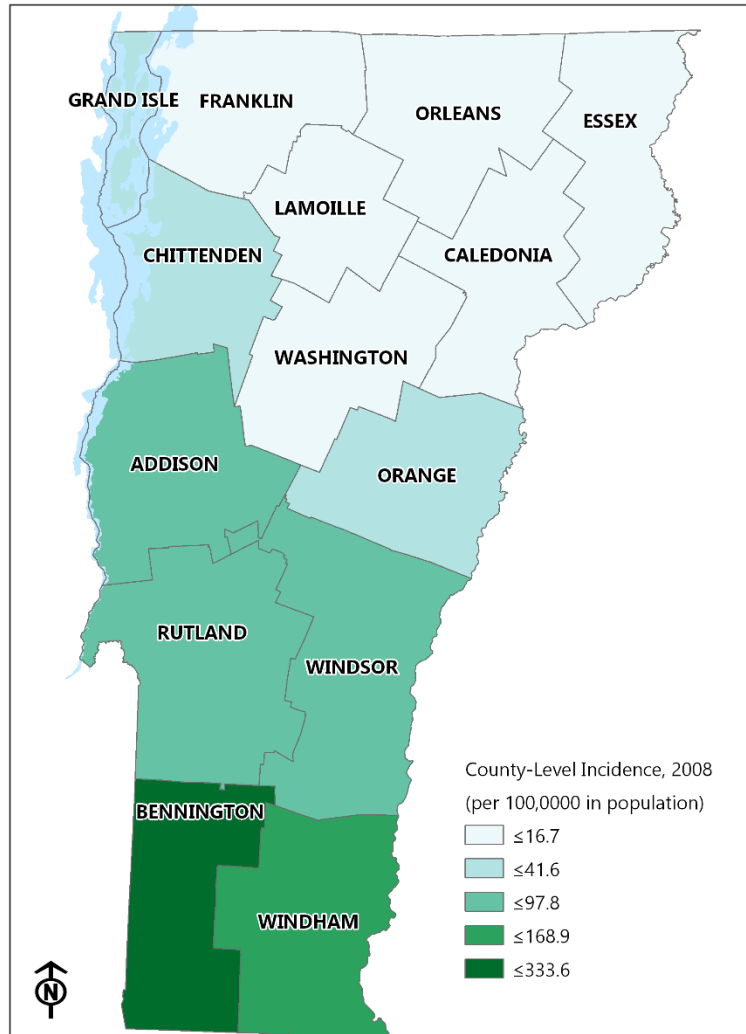
# Who Is At Risk for Lyme Disease in Vermont?



# Increasing Cases of Lyme Disease in Vermont



# Geographic Expansion of Lyme Disease



# Human Habitat is Tick Habitat







# Lyme Corps

## CDC

**PLEASE POST**

### Lyme Disease In Vermont

**What is Lyme Disease?**

- A bacterial infection transmitted to people through the bite of an infected blacklegged tick (aka deer tick) (Figure 1).
- The tick must be attached to a person for at least 24 hours to transmit the infection.

**Where is Lyme Disease in Vermont?**

- Lyme Disease has been reported from every county, though the risk is highest in southern Vermont.
- According to the Vermont Department of Health, over the last decade the number of cases reported has steadily increased (Figure 2).

**What are the early signs and symptoms of Lyme Disease?**

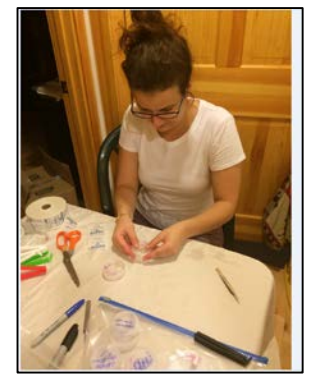
- In 70% of cases people will develop a gradually expanding, circular rash (often with a bull's-eye appearance) in the tick bite site (Figure 3).
- Flu-like symptoms: headache, fever, and muscle pain.

**How can Lyme Disease be prevented?**

- Avoid Ticks:** When outdoors, walk in the center of trails and avoid wooded areas.
- Repel Ticks:** Use 20-30% DEET on skin/don't forget clothing and gear with permethrin.
- Remove Ticks:** Bathe or shower within 2 hours after spending time outside in tick-prone areas. Conduct a full body tick check using a mirror. Inspect pets and gear for ticks.

**Information & ticks can be found on the Vermont website: [www.vermont.gov/health/vermont-disease-control](http://www.vermont.gov/health/vermont-disease-control)**



**The University of Vermont**

### The Tick & Gun: Allowing Blacklegged Ticks to Penetrate, Wounds and Drains to Prevent Tickborne Diseases

by Dr. Christina Nelson, Dr. Priyanka Sahni, Dr. Amy Yu, Dr. Priyanka Sahni, Dr. Amy Yu

**PREVENT LYME DISEASE!**

- WEAR REPELLENT
- CHECK FOR TICKS DAILY
- SHOWER SOON AFTER BEING OUTDOORS
- CALL YOUR DOCTOR IF YOU GET A FEVER OR RASH

For more information: [www.cdc.gov](http://www.cdc.gov)



**Primarily Vermont**

### The Ticks Are Out! Get the Facts About Lyme Disease

By Molly Markowitz

Lyme disease is on the rise in Vermont. According to the Vermont Department of Health, over the last decade the number of cases reported has steadily increased.

**Diagnosis and Testing**

There is a two-tiered testing approach for Lyme disease diagnosis and testing. According to the Centers for Disease Control (CDC) recommendations, Lyme disease should be diagnosed based on a combination of signs and symptoms and a history of possible exposure to an infected tick. Testing a NECT required for patients who present with a definite exposure to an infected tick. In these cases, the patient can be presumptively diagnosed with early stage Lyme disease and provided antibiotic treatment.

In all other cases, laboratory testing should be used because other signs of Lyme disease such as arthralgia, facial palsy, arthritis, and meningitis are nonspecific and could be caused by other conditions.

When testing is indicated, the CDC recommends serologic using a two-tiered (two-step) approach. The first step is an ELISA (enzyme-linked immunosorbent assay) test. If the first test is negative or equivocal then the second step is a Western blot, which should be performed. The overall results are only considered positive for Lyme disease if the Western blot is positive. [www.cdc.gov/ncidod/dzdx/lyme-disease/two-tier-testing](http://www.cdc.gov/ncidod/dzdx/lyme-disease/two-tier-testing)

The Western blot test for two types of antibodies, IgM and IgG. IgM antibodies are produced by the first immune response during early stage Lyme disease. Therefore, it is only appropriate to order testing for IgM antibodies during the first 30 days of symptoms. After 30 days, testing for only the IgG antibody is sufficient since the host's full immune response should be detectable by then. At this point IgM testing is unnecessary and may be counterproductive, leading to false positives. [www.cdc.gov/ncidod/dzdx/lyme-disease/two-tier-testing](http://www.cdc.gov/ncidod/dzdx/lyme-disease/two-tier-testing)

**Two-Tiered Testing for Lyme Disease**

**PLEASE POST**

**AHEC**

Connecting students to careers, professionals to communities, and communities to better health

**The University of Vermont Medical Center**

Published by Alexandra Tursi 171 May 29 - 171

**Tick season is here. Here's everything you need to know to stay safe.**

**The Ticks Are Out! Get the Facts About Lyme Disease In Vermont**

According to the Centers for Disease Control (CDC) more than 300,000 Americans contract Lyme disease each year.

[MEDCENTERBLOG.UVMHEALTH.ORG](http://MEDCENTERBLOG.UVMHEALTH.ORG)

41,520 people reached

Boost Post

**THE University of Vermont MEDICAL CENTER**

41,520 People Reached

755 Likes, Comments & Shares

309 Likes	197 On Post	112 On Shares
112 Comments	34 On Post	78 On Shares
334 Shares	334 On Post	0 On Shares

2,753 Post Clicks

2 Photo Views	1,920 Link Clicks	831 Other Clicks
---------------	-------------------	------------------

**NEGATIVE FEEDBACK**

14 Hide Post	4 Hide All Posts
0 Report as Spam	0 Unlike Page



**AAP Medical Student News**

Issue 28 Winter 2016

### Lyme Corps

**Joining Lyme Corps to Educate My Community**

By Molly Markowitz

Last fall, the University of Vermont College of Medicine hosted a talk given by Dr. Christina Nelson, a medical epidemiologist with the Division of Vector-Borne Diseases at the Centers for Disease Control and Prevention (CDC) in Fort Collins, Colorado. Dr. Nelson spoke about Lyme disease pathophysiology and prevention. According to the CDC, 300,000 Americans contract Lyme disease each year, and the incidence has steadily increased over the past two decades. At the end of her talk, Dr. Nelson described a program called Lyme Corps, a CDC-sponsored, interdisciplinary program for medical students, public health students, and residents from the University of Vermont.

I was motivated to join Lyme Corps because I grew up in a rural community in Maine where there is a high incidence of Lyme disease. I have personally known many individuals who have been affected by this disease. And, when I volunteered at my local (Continued)

**References:**

1. Mass shootings toll exceeds 900 in past seven years. USA TODAY. <http://www.usatoday.com/story/news/nation/2015/05/22/mass-shootings-toll-exceeds-900-in-past-seven-years/8597641/>. Accessed January 23, 2016.
2. Institute for Health Metrics and Evaluation. <http://www.healthdata.org/institute-health-metrics-and-evaluation>. Accessed January 23, 2016.
3. Moultonhouse MC, Lee L, Flegler E. Children injured by violence in the United States: emergency department visits, 2000-2008. *Acad Emerg Med Off J Soc Acad Emerg Med*. 2011; 18(5):545-549.
4. Flegler EW, Lee L, Moultonhouse MC, Moultonhouse D, Moultonhouse R. Firearms legislation and firearm-related fatalities in the United States, 2000-2008. *Acad Emerg Med Off J Soc Acad Emerg Med*. 2011; 18(5):545-549.
5. Senate Democrats to force debate on gun violence research funding. The Huffington Post. [http://www.huffpost.com/entry/senate-democrats-to-force-debate-on-gun-violence-research-funding\\_n\\_56a133ba-b6b6b6b6b6b6b6b6](http://www.huffpost.com/entry/senate-democrats-to-force-debate-on-gun-violence-research-funding_n_56a133ba-b6b6b6b6b6b6b6b6). Accessed January 23, 2016.
6. More Than 50 in 10 American Say Guns Make Homes Safer. Gallup.com. <http://www.gallup.com/poll/171233/more-american-say-guns-make-homes-safer.aspx>. Accessed January 23, 2016.
7. Farah MM, Simon ME, Ruffmann AL. Firearms in the home: general perceptions. *Psychiatry*. 1999; 62(4):311-319.
8. Jackson GA, Farah MM, Ruffmann AL, Simon ME. Seeing is believing: what do you do when they find a real gun? *Psychiatry*. 2001; 64(3):317-320.
9. Priyanka Sahni (left) and Amy Yu (right) are both second year medical students at Harvard Medical School.

# Lyme Disease Prevention



**Reducing exposure to ticks is the best available defense against tickborne diseases**

## **1. Avoid Ticks**

- When outdoors, walk in the center of trails and avoid wooded areas

## **2. Repel Ticks**

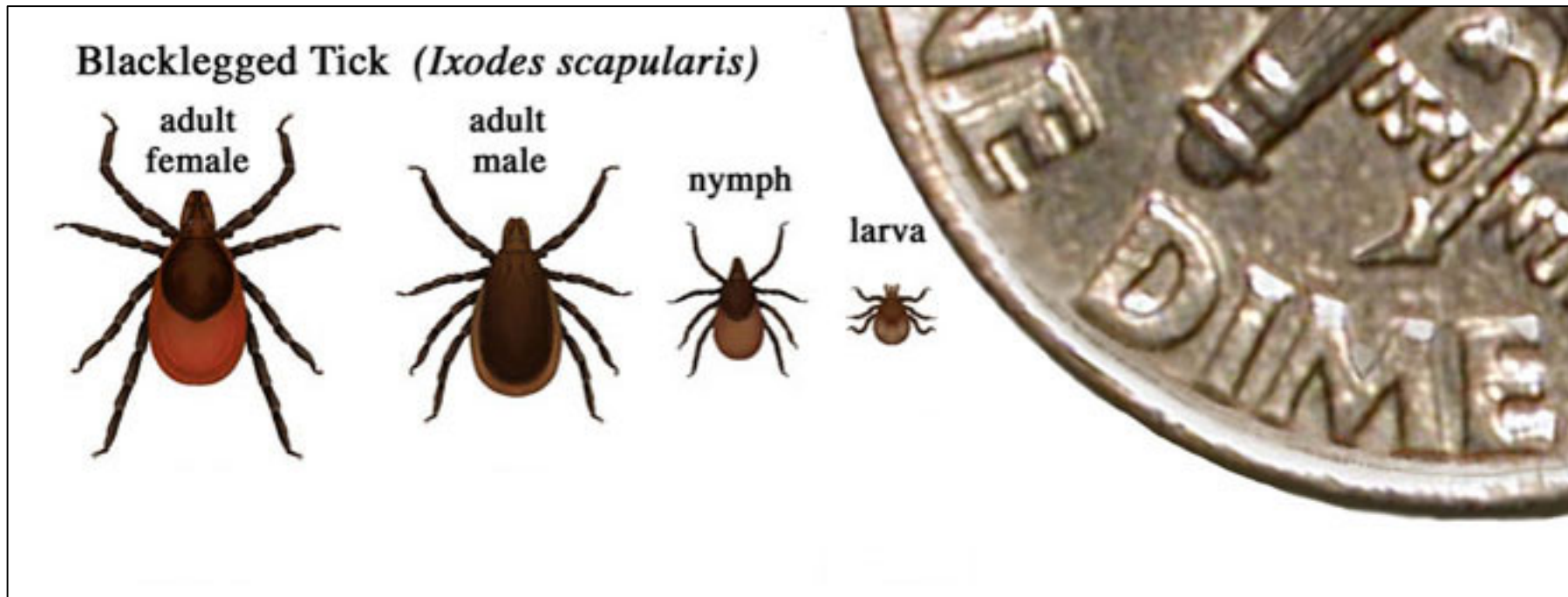
- Use 20-30% DEET on skin/clothing
- Treat clothing/gear with permethrin

## **3. Remove Ticks**

1. Bathe or shower within 2 hours after spending time outside in tick prone areas
2. Conduct a full body tick check using a mirror
3. Inspect pets and gear for ticks

## Take-home Message:

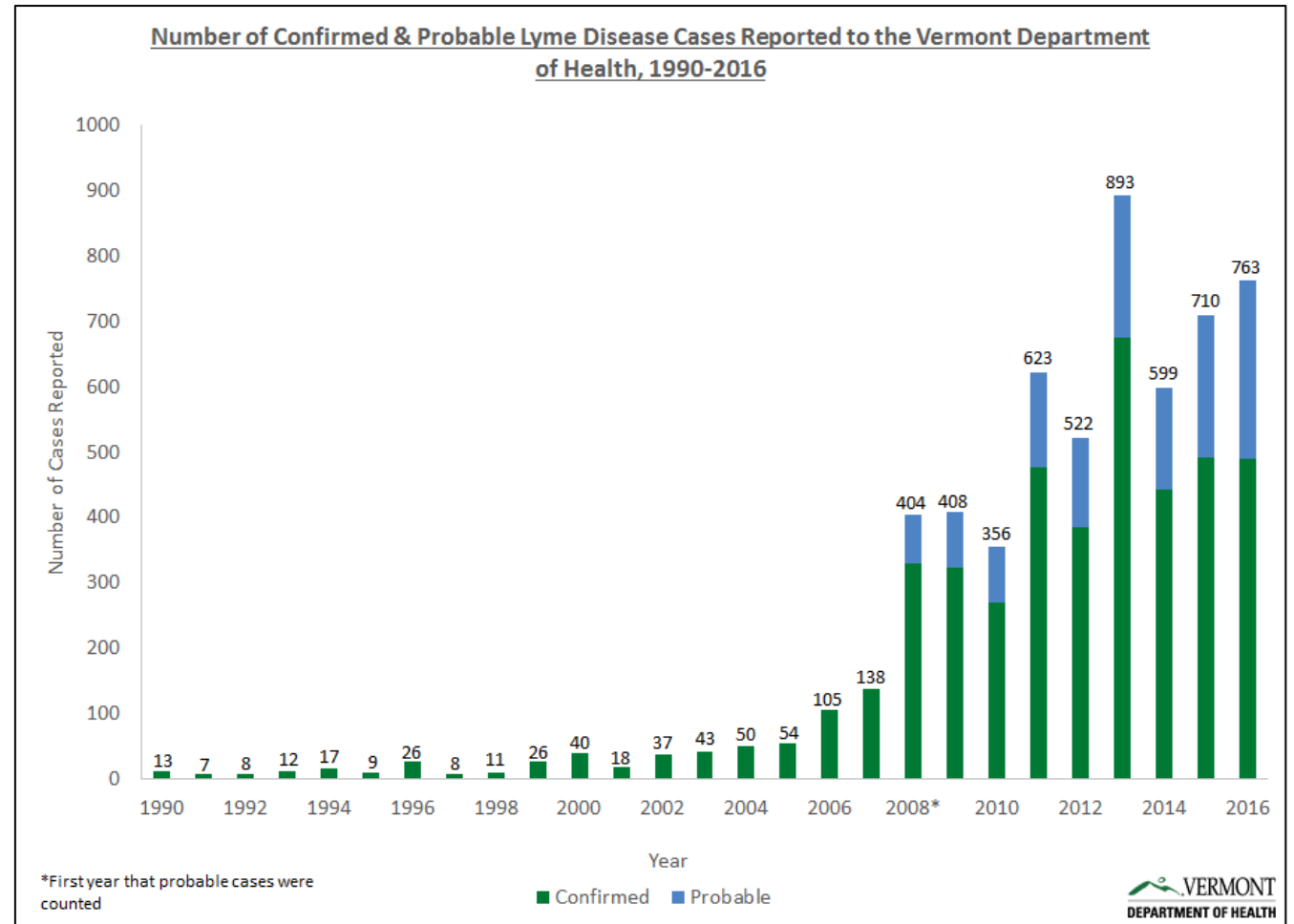
- Ticks are really small!
- You are looking for something the size of a poppy or sesame seed





# The Problem

- Reported cases of Lyme disease and other tickborne diseases are **INCREASING**
- Prevention recommendations can be difficult to implement
- We needed a new strategy!



# Past Recommendations for Washer/Dryer

**After spending time outdoors in potential tick habitat:**

- Tumble clothes in a dryer on **high heat** for **one hour** to kill remaining ticks





## Ticks and Tick-borne Diseases

Volume 7, Issue 5, July 2016, Pages 958–963



### The heat is on: Killing blacklegged ticks in residential washers and dryers to prevent tickborne diseases

Christina A. Nelson<sup>a</sup>,  , Catherine M. Hayes<sup>b</sup>, Molly A. Markowitz<sup>b</sup>, Jacqueline J. Flynn<sup>c</sup>, Alan C. Graham<sup>d</sup>, Mark J. Delorey<sup>a</sup>, Paul S. Mead<sup>a</sup>, Marc C. Dolan<sup>a</sup>



# Current Recommendations for Washer/Dryer

## After spending time outdoors in potential tick habitat:

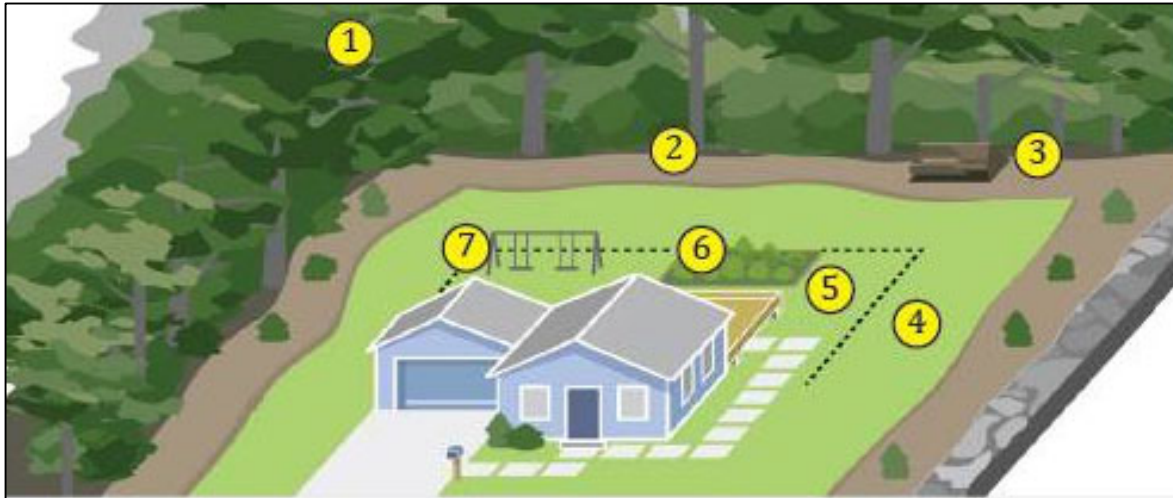
- Tumble **dry clothes** in a dryer on **high heat for 10 minutes** to kill ticks on dry clothing after you come indoors
  - If the clothes are damp, additional time may be needed
- If the clothes are soiled and **require washing first, hot water is recommended**
  - After washing, tumble dry on **low heat for 90 min or high heat for 60 min.** The clothes should be warm and completely dry



# How to Create a Tick Safe Yard

- Clear tall grasses and brush around homes and at the edge of lawns.
- Place a 3-ft wide barrier of wood chips or gravel between lawns and wooded areas
- Mow the lawn frequently and keep leaves raked.
- Stack wood neatly and in a dry area (discourages rodents that ticks feed on).
- Keep playground equipment, decks, and patios away from yard edges and trees and place them in a sunny location, if possible.
- Remove any old furniture, mattresses, or trash from the yard that may give ticks a place to hide.





- |          |                            |   |
|----------|----------------------------|---|
| <b>1</b> | <b>Tick zone</b>           | Avoid areas with forest and brush where deer, rodents, and ticks are common.                              |
| <b>2</b> | <b>Wood chip barrier</b>   | Use a 3 ft. barrier of wood chips or rock to separate the "tick zone" and rock walls from the lawn.       |
| <b>3</b> | <b>Wood pile</b>           | Keep wood piles on the wood chip barrier, away from the home.   |
| <b>4</b> | <b>Tick migration zone</b> | Maintain a 9 ft. barrier of lawn between the wood chips and areas such as patios, gardens, and play sets. |
| <b>5</b> | <b>Tick safe zone</b>      | Enjoy daily living activities such as gardening and outdoor play inside this perimeter.                   |
| <b>6</b> | <b>Gardens</b>             | Plant deer resistant crops. If desired, an 8-ft. fence can keep deer out of the yard.                     |
| <b>7</b> | <b>Play sets</b>           | Keep play sets in the "tick safe zone" in sunny areas where ticks have difficulty surviving.              |

*Based on a diagram by K. Stafford, Connecticut Agricultural Experiment Station*



### **Take-home Message:**


- Ticks like warm moist environments.
- Prevention means minimizing these environments

# Preventing Tick Bites for Pets

- Check your pets for ticks daily, especially after they spend time outdoors!
- If you find a tick on your pet, remove it right away
- Reduce tick habitat in your yard
- Consider using tick preventives on your pet, repellent and pesticides products

**Take-home Message:** Talk with your veterinarian about preventing tick bites on pets

## Pet ownership increases human risk of encountering ticks

E. H. Jones<sup>1</sup>  | A. F. Hinckley<sup>2</sup> | S. A. Hook<sup>2</sup> | J. I. Meek<sup>3</sup> | B. Backenson<sup>4</sup> | K. J. Kugeler<sup>2</sup> | K. A. Feldman<sup>1</sup>

<sup>1</sup>Maryland Department of Health and Mental Hygiene, Baltimore, MD, USA

<sup>2</sup>Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, CO, USA

<sup>3</sup>Connecticut Emerging Infections Program, Yale School of Public Health, New Haven, CT, USA

### Summary

We examined whether pet ownership increased the risk for tick encounters and tick-borne disease among residents of three Lyme disease-endemic states as a nested cohort within a randomized controlled trial. Information about pet ownership, use of tick control for pets, property characteristics, tick encounters and human tickborne disease were captured through surveys, and associations were assessed using univariate

# Lyme Disease Vaccine

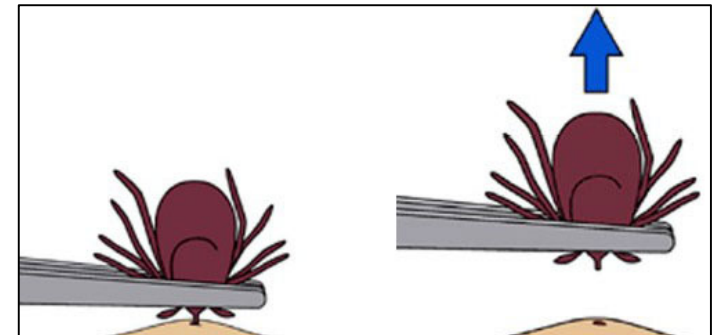
- It is no longer available.
- Protection provided by this vaccine diminishes over time. Therefore, if you received the Lyme disease vaccine before 2002, you are probably no longer protected against Lyme disease.



**Stay tuned!**

# I have been bitten by a tick....

1. Remove the tick with fine-tipped tweezers.
2. Clean the bite area with rubbing alcohol, an iodine scrub, or soap and water.
3. The chances of getting Lyme disease from a tick bite depend on:
  - The type of tick, **blacklegged ticks**
  - Where the bite happened, mostly Northeastern/Midwest US
  - How long it was attached, for at **least 24-36 hours**





# When to use Prophylactic Antibiotics

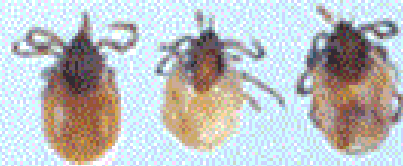
**All four criteria should be met:**

1. Tick is identified as a **blacklegged tick/deer tick**, that is estimated to have been **attached for  $\geq 36$  h** on the basis of the degree of engorgement of the tick with blood or of certainty about the time of exposure to the tick
2. **Prophylaxis can be started within 72 h** of the time that the tick was removed
3. Ecologic information indicates that the local rate of infection of ticks with ***B. burgdorferi*** is  **$\geq 20\%$**  (Vermont)
4. Doxycycline treatment is not contraindicated.

**Take-home Message:** Contact your doctor with questions or concerns



**0H**



**24H**



**48H**

**72H**



**>96H**



## References:

- <https://www.cdc.gov/lyme/index.html>
- <http://www.healthvermont.gov/disease-control/tickborne-diseases/lyme-disease>
- Some slide content courtesy of Dr. Christina Nelson from the CDC



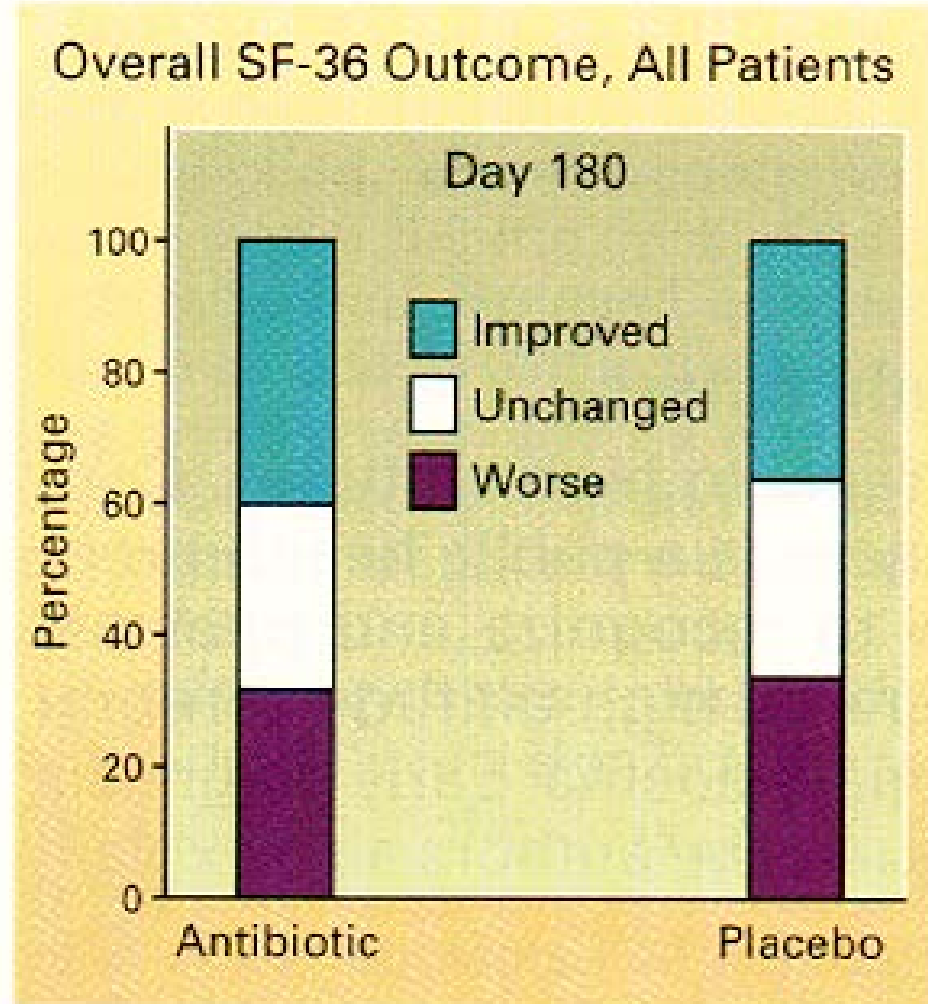
# Chronic Lyme Disease

- What do we know we know?
- What do we know that we don't know?
- What don't we know that we don't know?

## Antibiotic-Refractory Lyme Arthritis

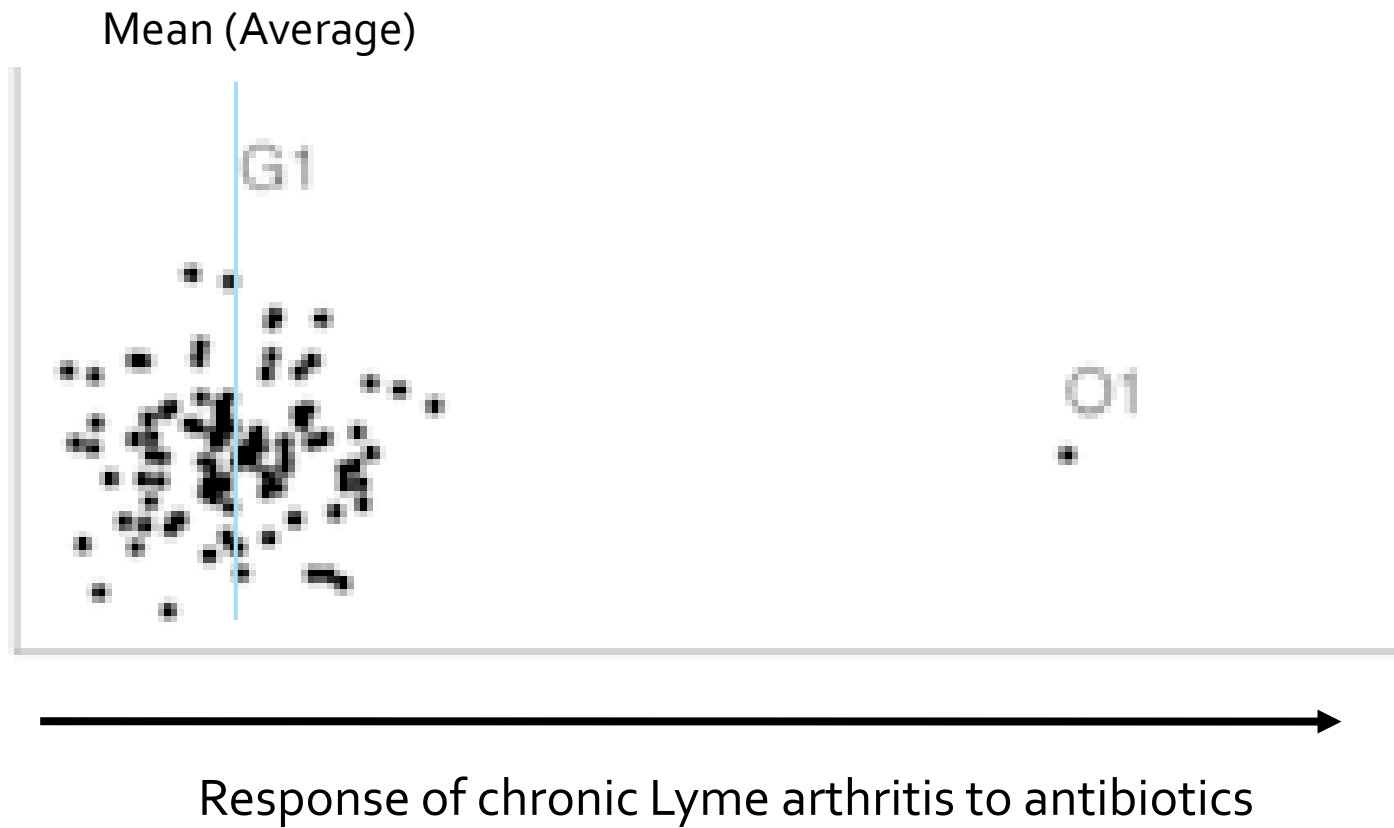
- Persistent intact *Borrelia*
- Persistent debris of *Borrelia*
- Infection-induced autoimmunity (OspA and LFA-1)
- Genetic predisposition is similar to rheumatoid arthritis (HLA-DR<sub>4</sub>, GusB deficiency)
- Tissue damage may promote chronic inflammation without *Borrelia*
- Residual effects of previous inflammation

## Long-term antibiotics in chronic Lyme arthritis



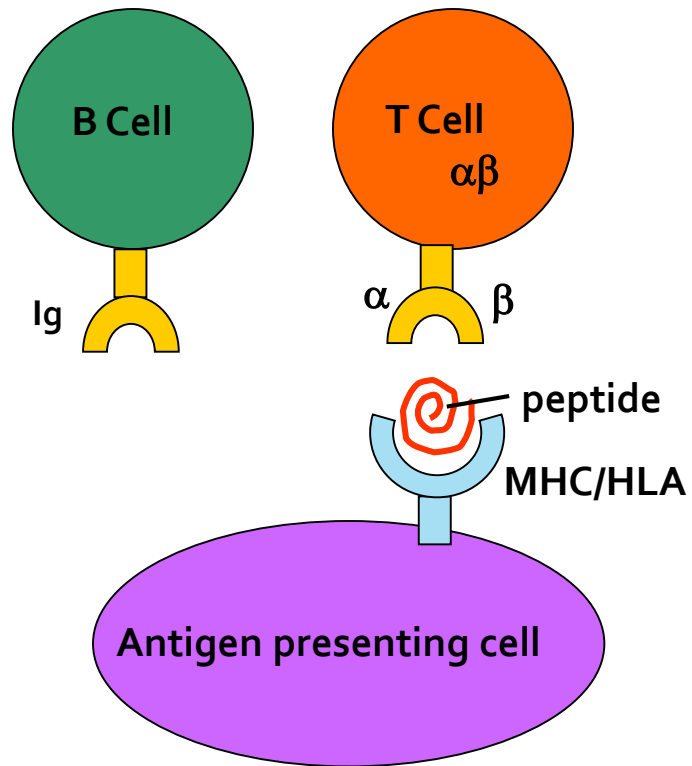
115 patients randomized to placebo or i.v. ceftriaxone 2 g for 1 mth, then oral doxycycline 200 mg for 2 mth

## Value of the Outlier



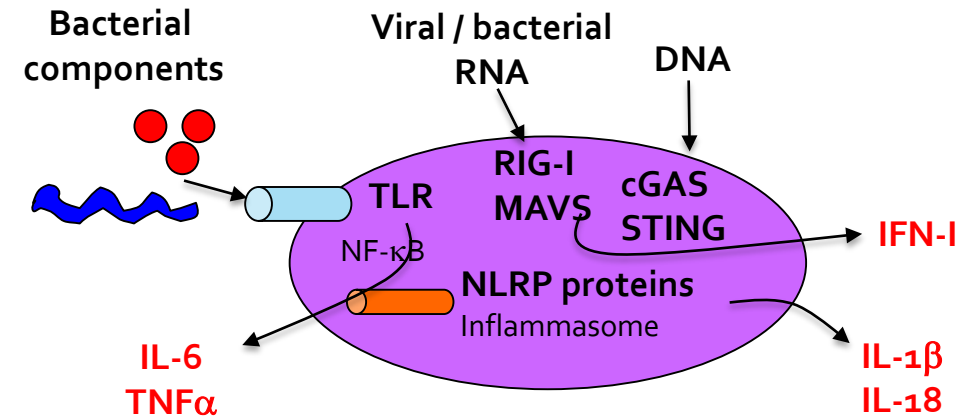


## Adaptive Immune Response

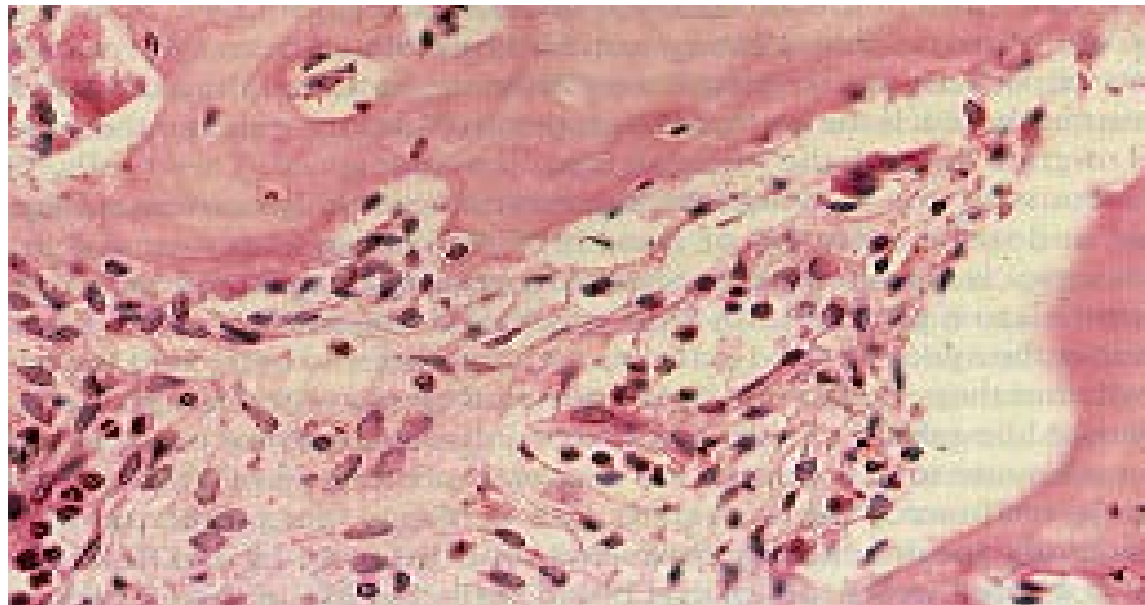
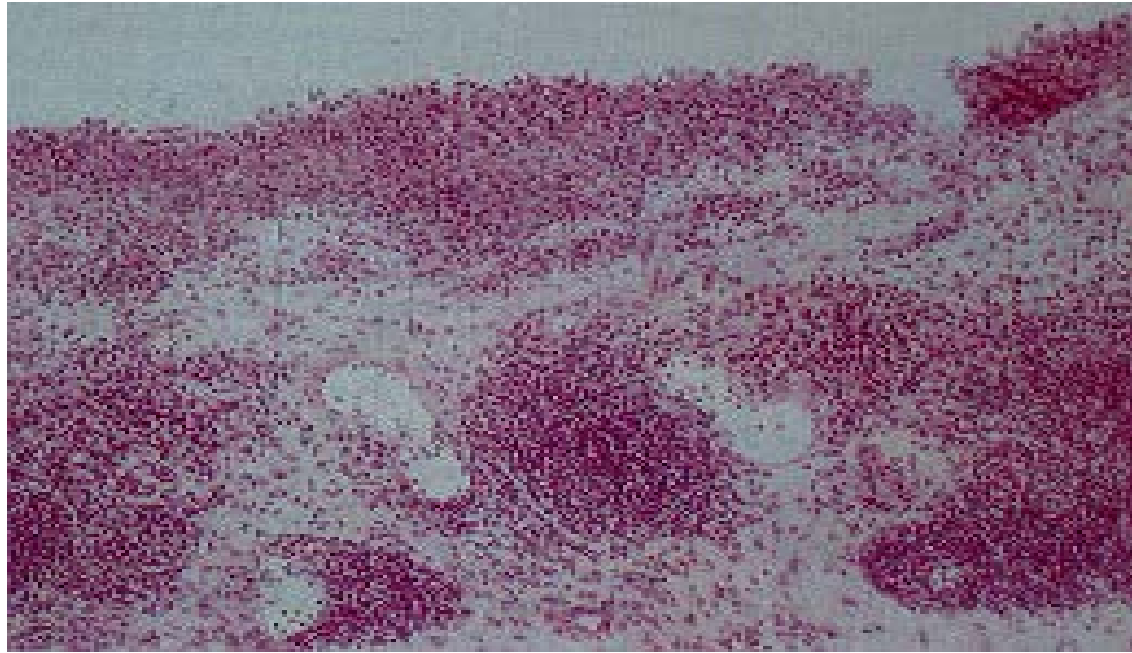


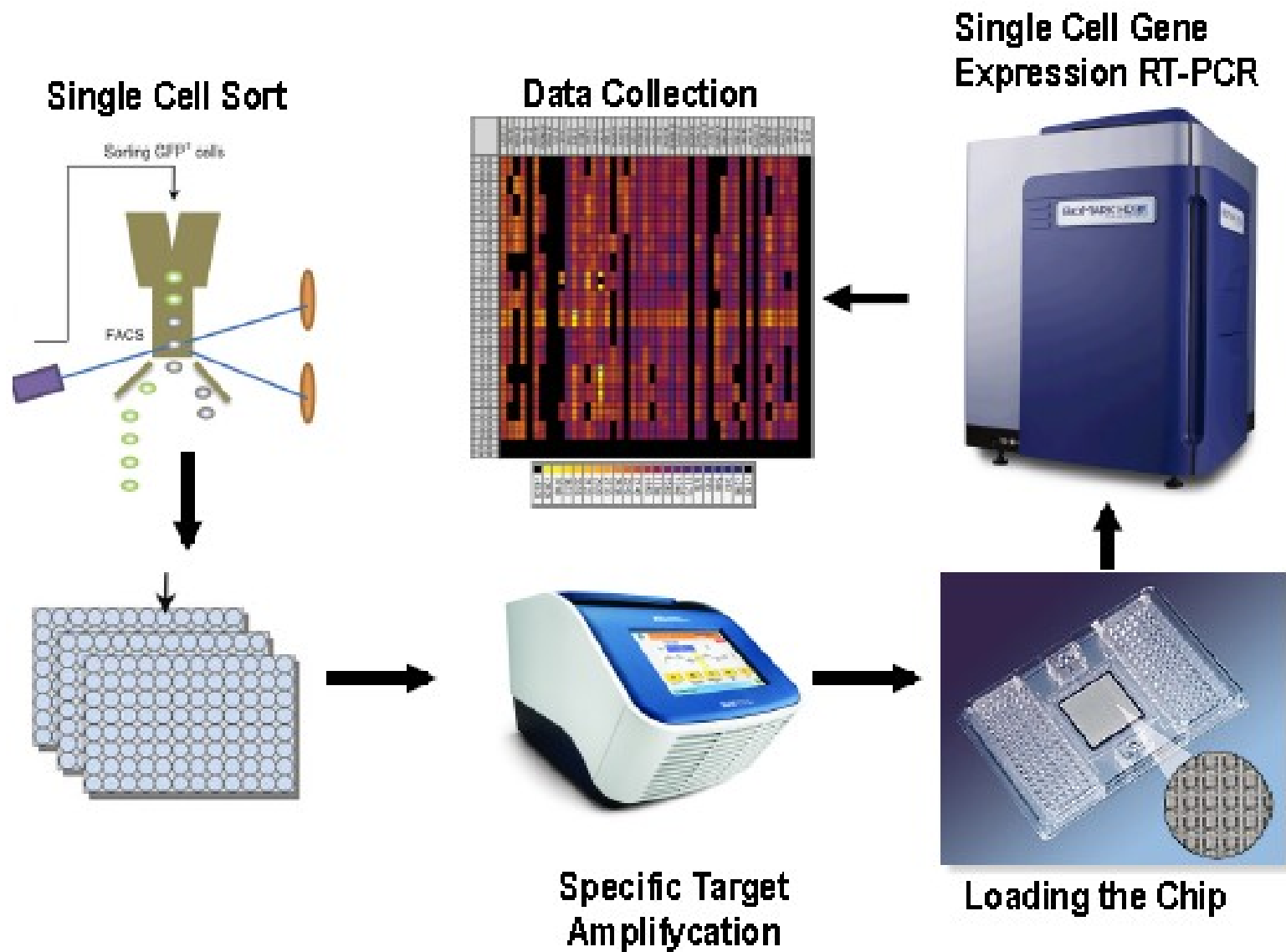
- Multiple antigens recognized
- Highly variable receptors
- Low affinity receptors
- Slow response
- Memory

## Innate Immune Response

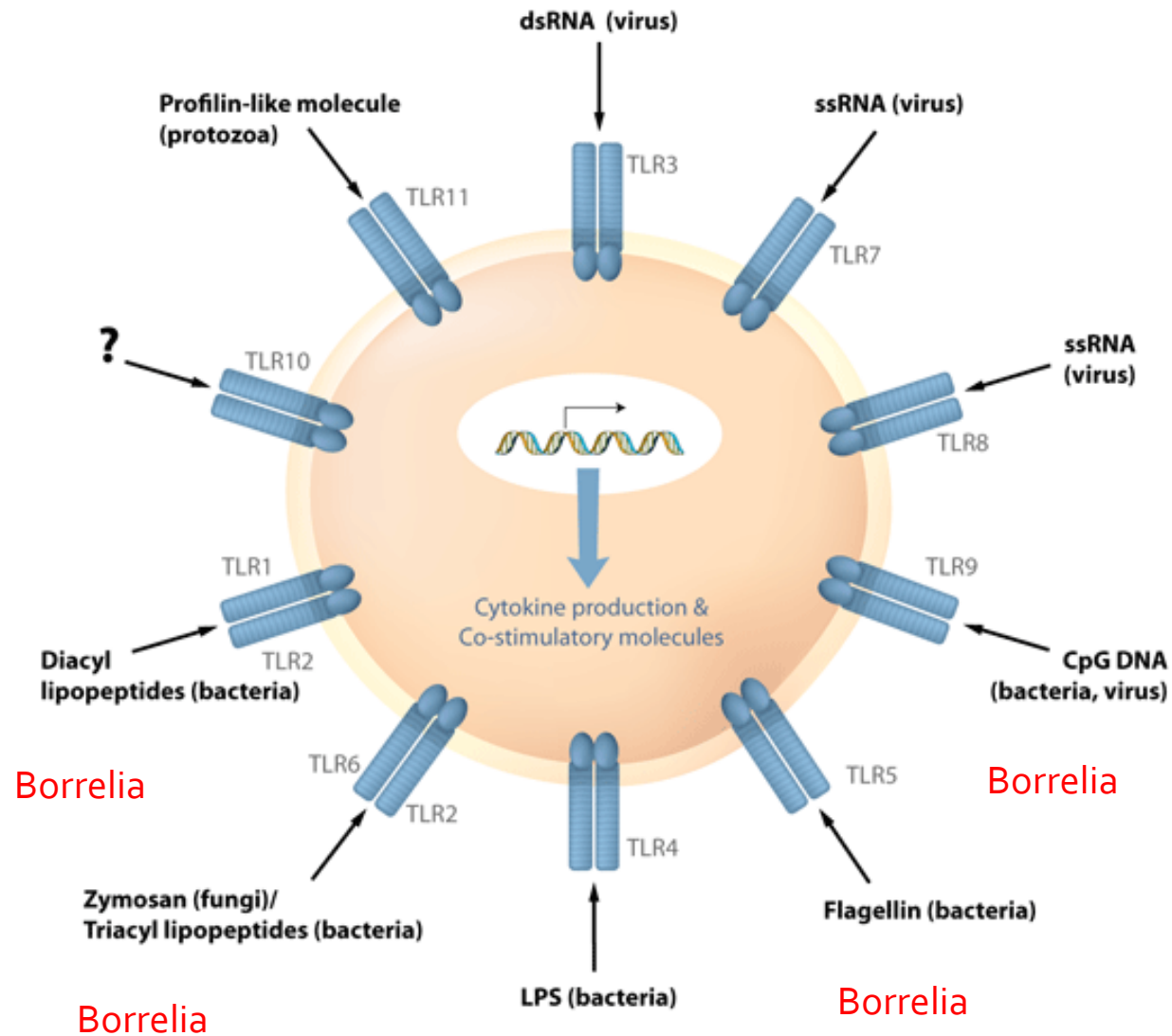


- Limited antigens recognized
- Non-variable receptors
- High affinity receptors
- Fast response
- No memory

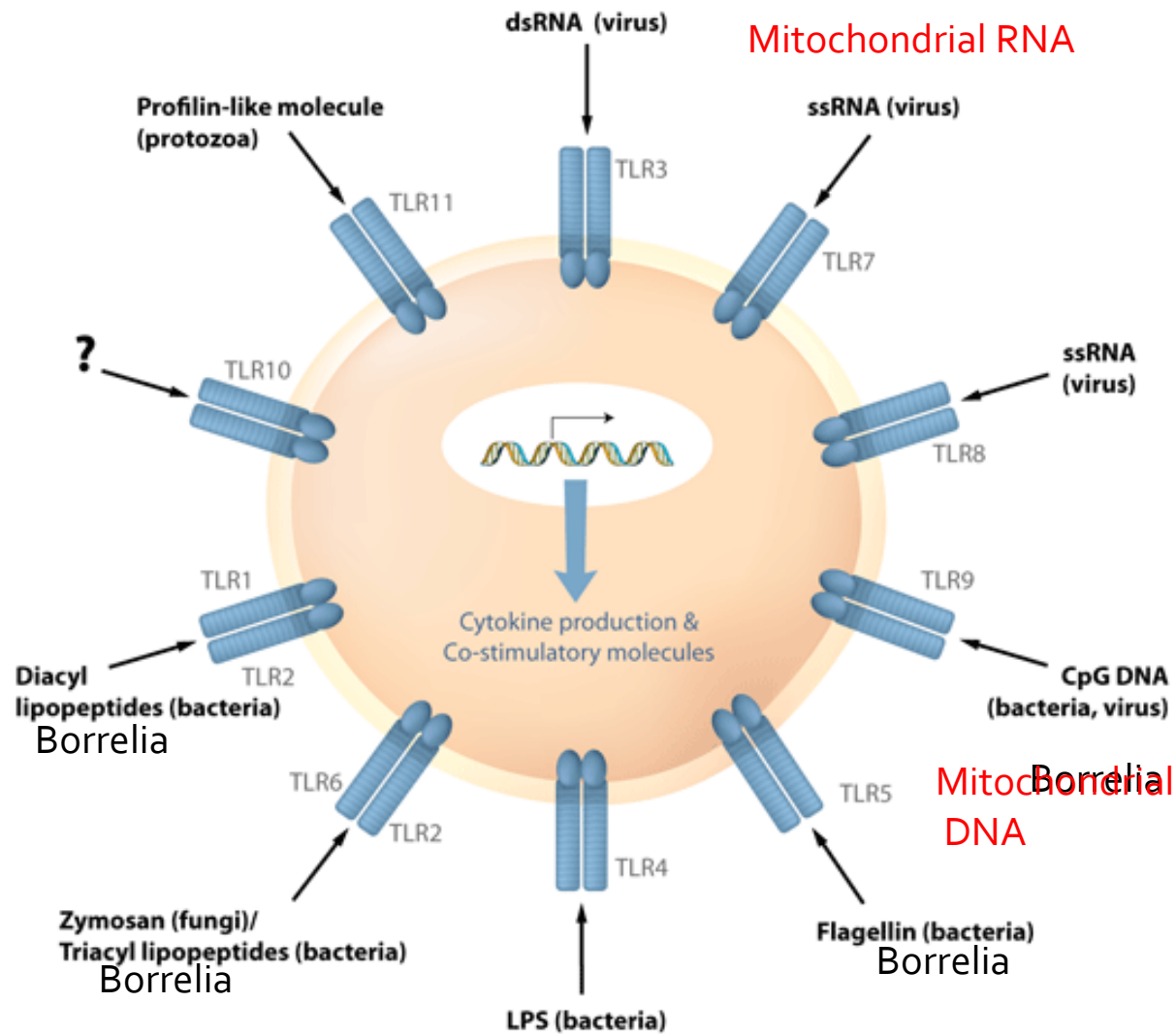




# TLR Ligands (Pathogen-Associated molecular Patterns, PAMPs)

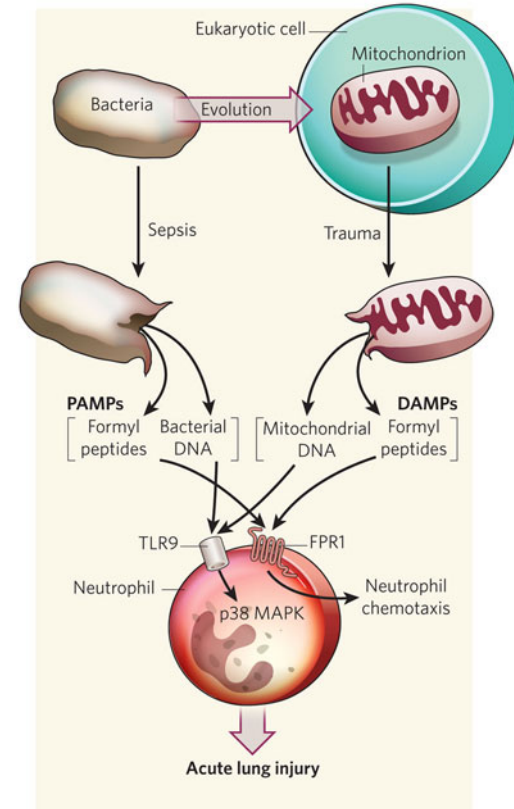


TLR Ligands  
(Pathogen-Associated molecular Patterns, PAMPs)  
(Damage-Associated Molecular Patterns, DAMPS)



Mitochondrial RNA

Mitochondrial DNA



# References

1. Steere, A. C. C., Malawista, S. E., Snyderman, D. R. & Andiman, W. A. A cluster of arthritis in children and adults in Lyme, Connecticut. *Arthritis Rheum.* 20, 7–17 (1977).
2. Marshall, W. F. et al. Detection of *Borrelia burgdorferi* DNA in museum specimens of *Peromyscus leucopus*. *J. Infect. Dis.* 170, 1027–1032 (1994).
3. Humphrey, P. T., Caporale, D. A. & Brisson, D. Uncoordinated phylogeography of *Borrelia burgdorferi* and its tick vector, *Ixodes scapularis*. *Evolution* 64, 2653–2663 (2010).
4. Biology of Ticks. Volume 2. Second Edition. Edited by Daniel E. Sonenshine and R. Michael Roe. Oxford and New York: Oxford University Press. xv + 540 p.
5. Steere, A.C., Franc. S., Wormser, G.P. Hu, L.T., Branda, J.A., Hovius, J.W.R., Li, X. and P.S. Mead. Lyme borreliosis. *Nature Reviews Disease Primers* 2, 2-18 (2016).
6. Ostfeld, R.S. Lyme disease: the ecology of a complex system. Oxford University Press, 2011. 216 p.

# QUESTIONS?

---