

Lyme Disease Testing and Surveillance in Low-incidence States: a Case Study in Arkansas

Elizabeth Dietrich, PhD

Susan Weinstein, DVM, MPH

Natalie Kwit, DVM, MPH

Centers for Disease Control and Prevention
Arkansas Department of Health

May 18th, 2017



Session Objectives

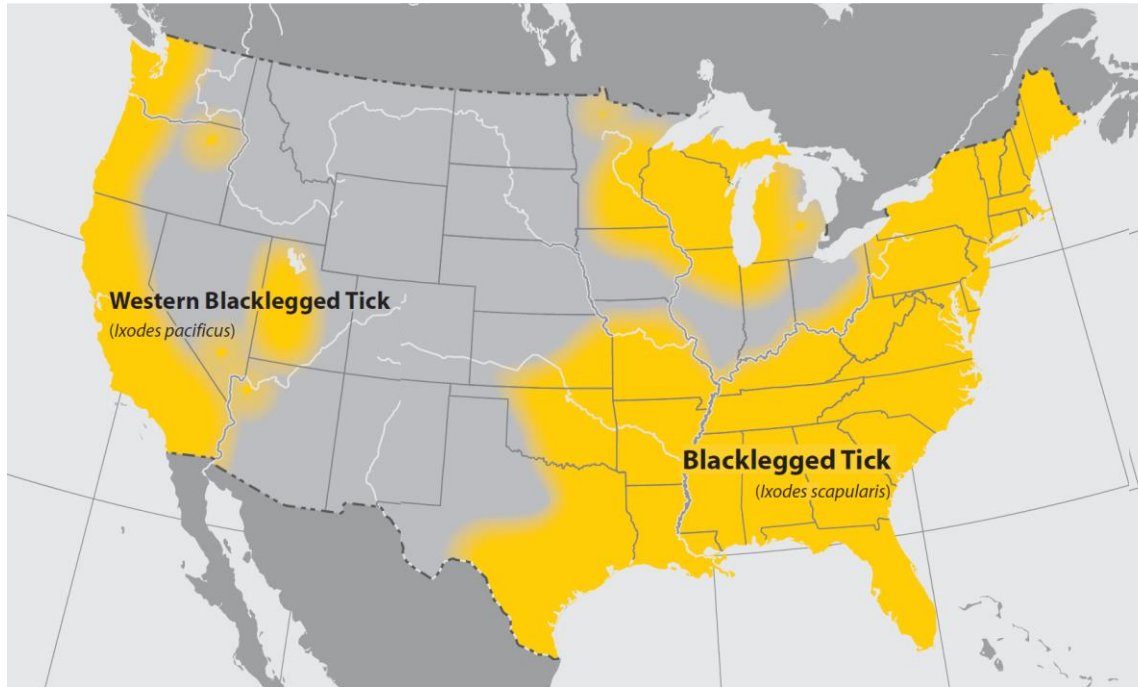
- Lyme disease background
 - Geographic distribution
 - Review of diagnostics and case definition
- Specific background and challenges in Arkansas
- Epi-Aid findings
 - Practical recommendations
 - Resources

Lyme Disease

- *Borrelia burgdorferi*, *B. mayonii*
- *Ixodes* spp. ticks
- Clinical features
 - Fever, headache, fatigue, muscle aches
 - Erythema migrans (EM) rash
 - Disseminated disease
 - Arthritis, carditis, meningitis, facial palsy



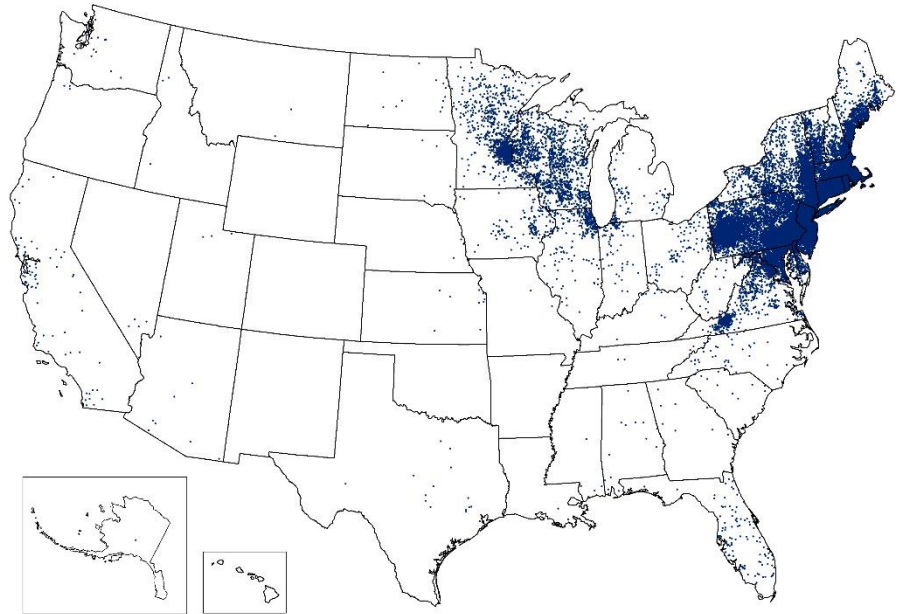
Geographic distribution of tick vectors



95% of Lyme disease cases from 14 states

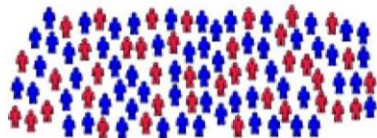
- Connecticut
- Delaware
- Maine
- Maryland
- Massachusetts
- Minnesota
- New Hampshire
- New Jersey
- New York
- Pennsylvania
- Rhode Island
- Vermont
- Virginia
- Wisconsin

Reported Cases of Lyme Disease -- United States, 2015



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

DISEASE IS COMMON*



100 people tested for the disease‡

NEGATIVE TESTS

True Negatives



1% FALSE NEGATIVE

1 of 60 people who tests negative has the disease

False Negatives

POSITIVE TESTS

False Positives



True Positives



3% FALSE POSITIVE

1 of 40 people who tests positive does not have the disease

KEY

people with disease
people without disease

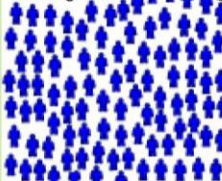
DISEASE IS RARE†



100 people tested for the disease‡

NEGATIVE TESTS

True Negatives



0% FALSE NEGATIVE

None of the 97 people who tests negative has the disease

False Negatives
0

POSITIVE TESTS

False Positives



True Positives



67% FALSE POSITIVE

2 of 3 people who test positive do not have the disease

* 40 out of 100 patients in this area have the disease.

† 1 out of 100 patients in this area have the disease.

‡ Test specificity = 98% (high) and

test sensitivity = 98% (high)

Haiku for diagnostic testing

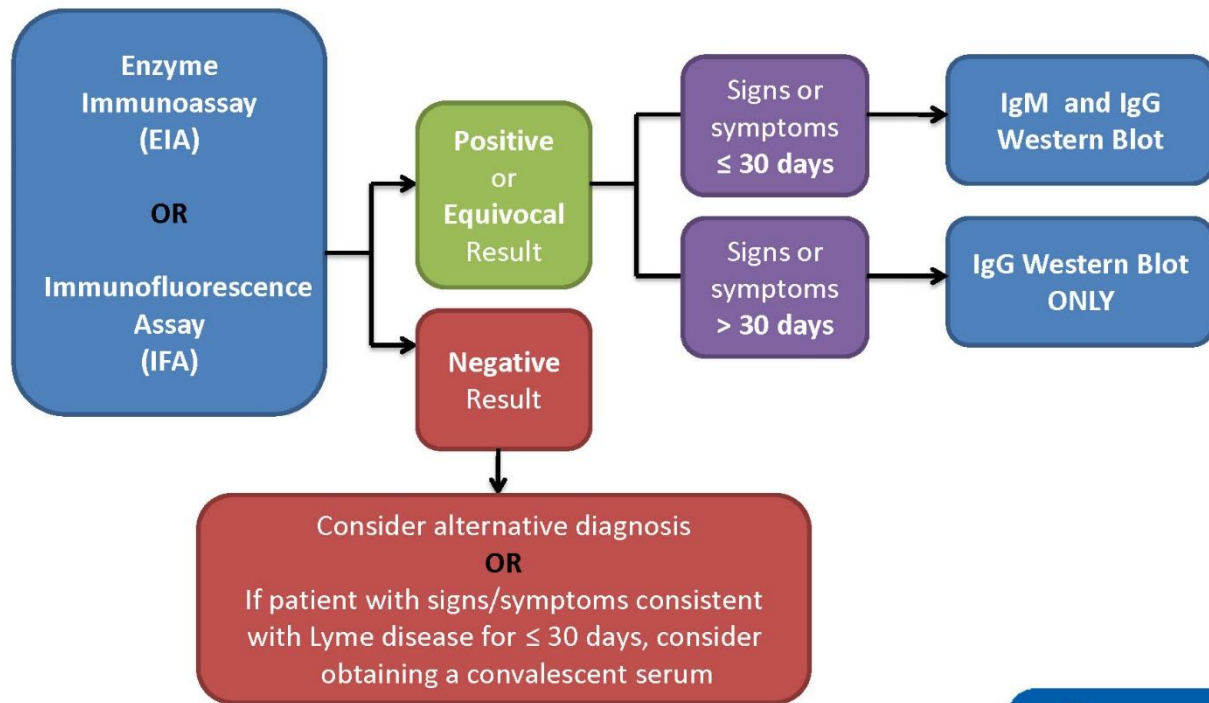


*Where disease is rare
Positives mostly deceive
Even with good tests*

Two-Tiered Testing for Lyme Disease

First Test

Second Test



Laboratory and clinical criteria for Lyme disease surveillance

- Laboratory criteria
 - ✓ Culture for *B. burgdorferi*
 - ✓ **OR** two-tiered test
 - ✓ **OR** single-tier IgG WB test for LD
- Clinical criteria
 - ✓ Erythema migrans
 - ✓ **OR** late manifestation
- Exposure criteria
 - ✓ Tick habitat ≤ 30 days before EM onset
 - ✓ **High vs. low incidence state**

Lyme, STARI, or other?

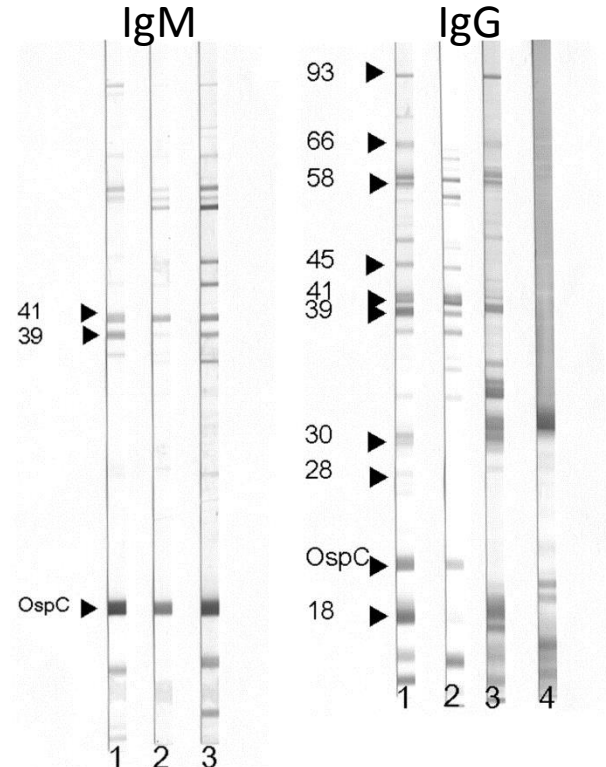


2017 Lyme disease surveillance case definition

- Confirmed
 - A case of **EM** with **exposure** in a **high incidence state**, OR
 - A case of **EM** with **exposure** in a **low incidence state** + **laboratory evidence** of infection, OR
 - Any case with at least one **late manifestation** that has **laboratory evidence** of infection
- Probable
 - Any other case of **physician-diagnosed Lyme disease** that has **laboratory evidence** of infection
- Suspect
 - A case of **EM** where there is no known exposure and no laboratory evidence of infection, OR
 - A case with **laboratory evidence of infection** but **no clinical information** available

Lyme disease Western blot interpretation

- IgM Western blot
 - Useful for diagnosing early disease
 - Positive if 2 of 3 specific bands are reactive
- IgG Western blot
 - Positive if 5 of 10 specific bands are reactive



TEST PROCEDURE	TEST RESULT	UNITS	REFERENCE RANGE
LYME DISEASE (IGG),WB	NEGATIVE		NEGATIVE U

IGG WESTERN BLOTS WHICH HAVE 5 (OR MORE) OF THE 10
SIGNIFICANT BANDS ARE CONSIDERED POSITIVE FOR SPECIFIC
ANTIBODY TO B.BURGDORFERI. (PROCEEDINGS OF THE SECOND
CONFERENCE OF LYME DISEASE. DEARBORN, MICHIGAN, 1994.)

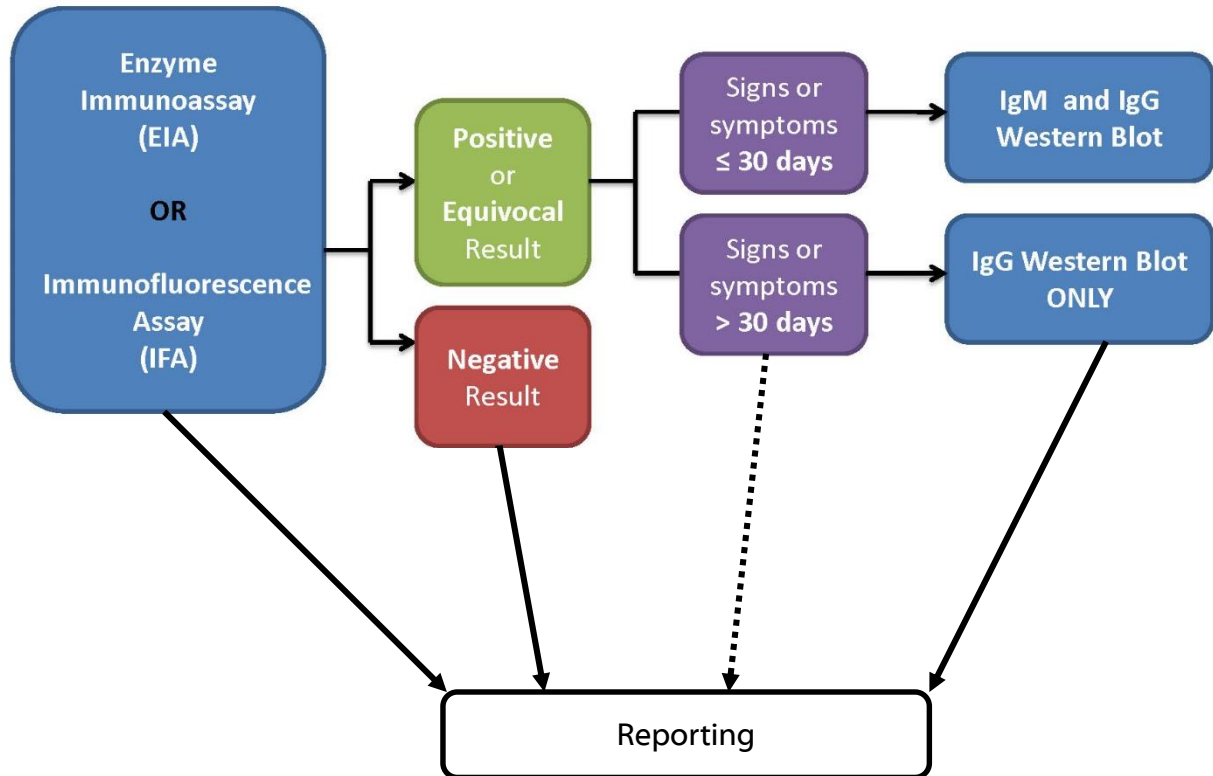
18 KD (IGG) BAND		NONREACTIVE	NONREACTIVE U
23 KD (IGG) BAND		NONREACTIVE	NONREACTIVE U
28 KD (IGG) BAND		NONREACTIVE	NONREACTIVE U
30 KD (IGG) BAND		NONREACTIVE	NONREACTIVE U
39 KD (IGG) BAND		NONREACTIVE	NONREACTIVE U
41 KD (IGG) BAND	REACTIVE		NONREACTIVE U
45 KD (IGG) BAND	REACTIVE		NONREACTIVE U
58 KD (IGG) BAND		NONREACTIVE	NONREACTIVE U
66 KD (IGG) BAND	REACTIVE		NONREACTIVE U
93 KD (IGG) BAND		NONREACTIVE	NONREACTIVE U

LYME DISEASE (IGM),WB	NEGATIVE		NEGATIVE U
-----------------------	----------	--	------------

IGM WESTERN BLOTS WHICH HAVE 2 (OR MORE) OF THE 3
SIGNIFICANT BANDS ARE CONSIDERED POSITIVE FOR SPECIFIC
ANTIBODY TO B.BURGDORFERI. (PROCEEDINGS OF THE SECOND
CONFERENCE OF LYME DISEASE. DEARBORN, MICHIGAN, 1994.)

23 KD (IGM) BAND		NONREACTIVE	NONREACTIVE U
39 KD (IGM) BAND		NONREACTIVE	NONREACTIVE U
41 KD (IGM) BAND		NONREACTIVE	NONREACTIVE U

Issues with reporting of two-tiered tests

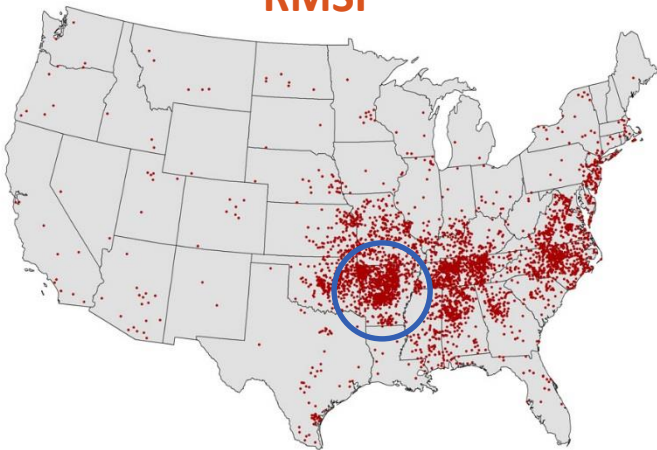




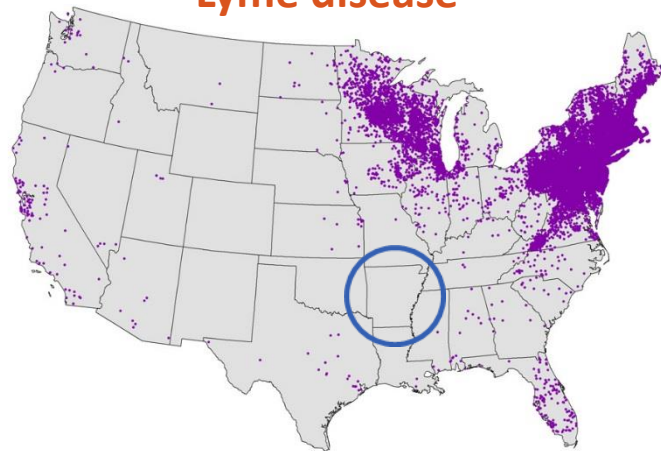
Northern vs. Southern *I. scapularis*

	Northern	Southern	Reference
Found on humans?	Frequently	Rarely	Stromdahl and Hickling 2012
Collected by drag sampling	Frequently	Rarely	Diuk-Wasser <i>et al.</i> 2006
Most common host of larvae	Mice	Lizards	Apperson <i>et al.</i> 1993
Questing behavior	On stems	In leaf litter	Arsnoe <i>et al.</i> 2015

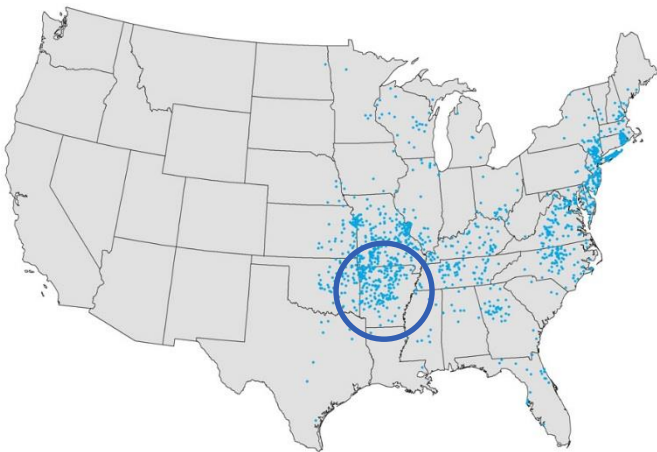
RMSF



Lyme disease



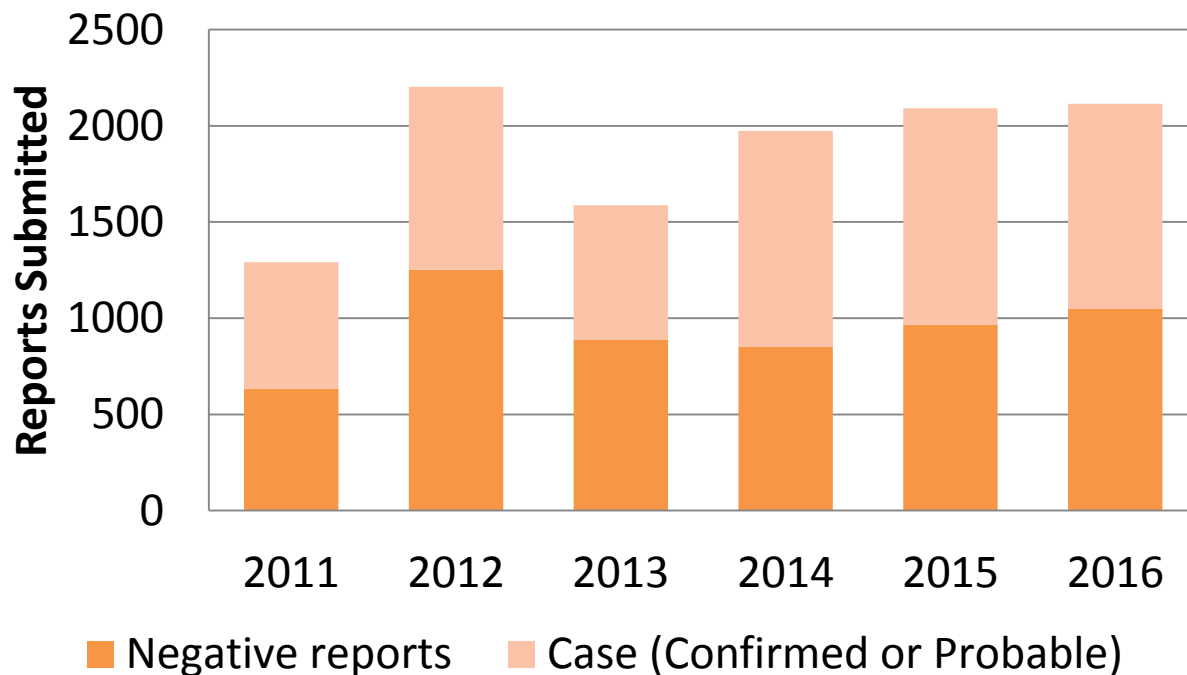
Ehrlichiosis



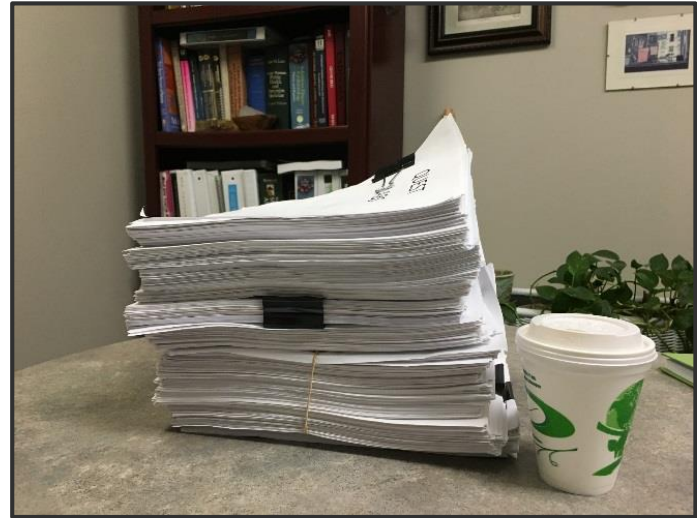
Tularemia



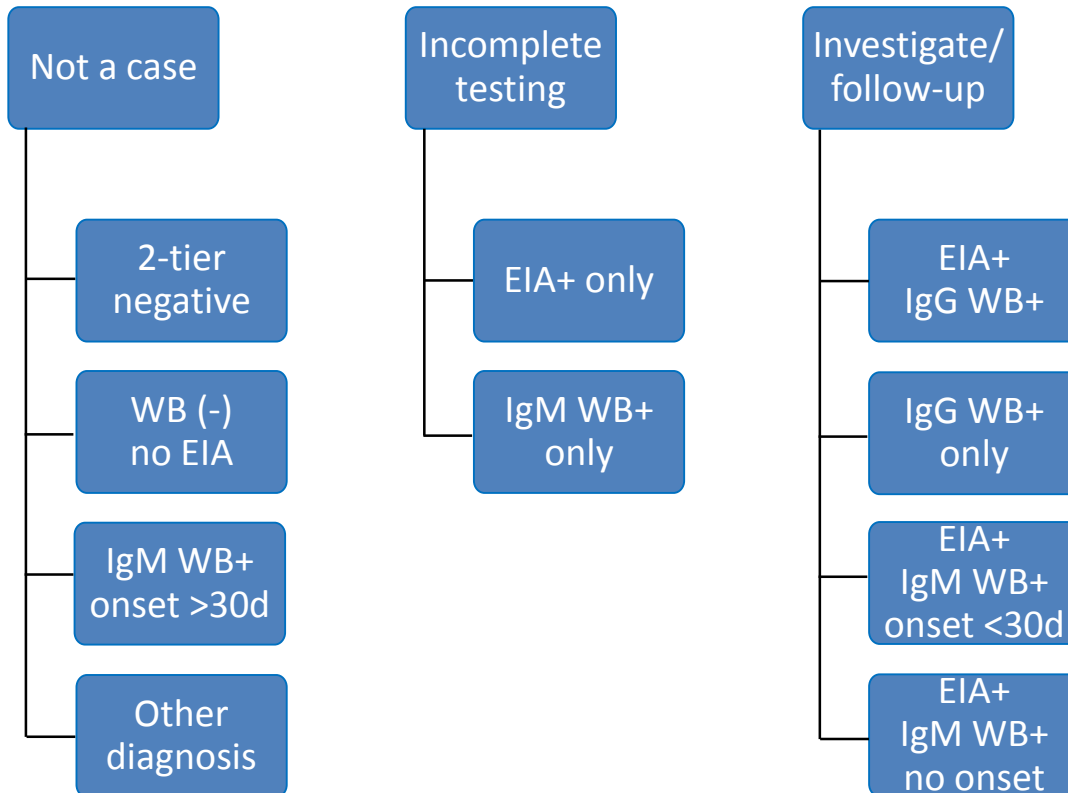
Human tickborne disease surveillance — Arkansas, 2011–2016



Lyme disease surveillance in Arkansas

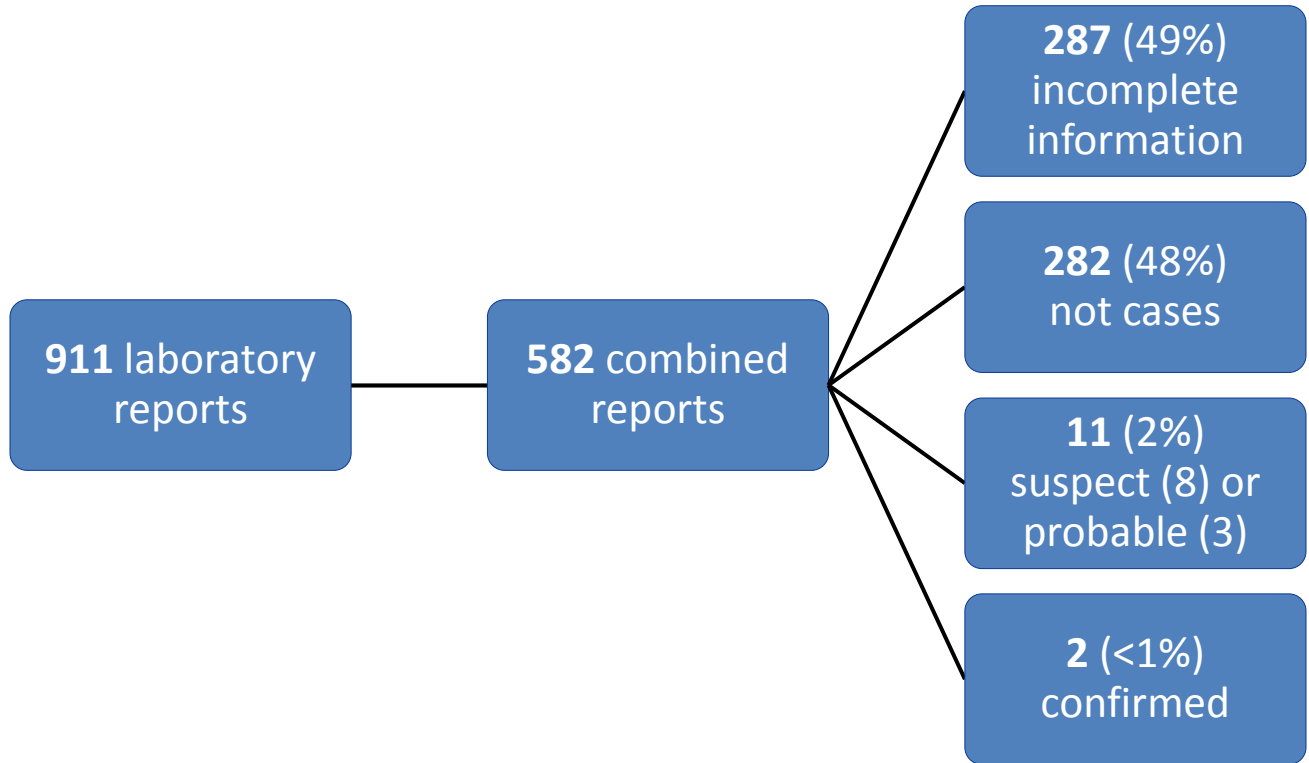


Laboratory report sorting methods



WB = Western blot

Preliminary results of sorting and follow-up



Conclusions

- Two confirmed, travel-associated infections in 2015–2016
- Locally-acquired infection rare or does not occur in AR
- Prioritization for follow-up is key

Recommendations → Optimizing internal ADH processes

- Prioritize follow-up on case reports
 - “Follow-up” category then “not enough information”
 - Not all laboratories are created equal
- Enter partial reports into spreadsheet or database
- Consider updating case report form
 - Include fields specific to two-tiered testing
 - Instructions on when to report
- Consider using an algorithm to prioritize cases for follow-up

For ADH

Lyme disease case report received

EIA test
(Lyme antibody screen or ELISA)
only

Negative

Not a case

Positive or equivocal

From labs that always reflex to Western blot

From other labs

Hold for 30 days

Enter into spreadsheet

Western blot results not received or negative

Not a case

Western blot
(immunoblot)
only

Negative

Not a case

Positive

IgM Western blot positive*
(IgG negative or absent)

Enter into spreadsheet to match to EIA results

IgG Western blot positive*

Follow up

Both EIA and Western blot

EIA negative OR
Both IgM and IgG Western blot negative

Not a case

EIA positive or equivocal

IgG Western blot positive*

Follow up

IgM Western blot positive*
(IgG negative or absent)

Illness onset **more than 30 days** before testing

Not a case

Illness onset unknown or less than 30 days before testing

Follow up

*An **IgM** Western blot is positive if at least 2 of 3 bands (23, 39 and 41 kDa) are reactive.
An **IgG** Western blot is positive if at least 5 of 10 bands (18, 21, 28, 30, 39, 41, 45, 58, 66, and 93 kDa) are reactive.
Banding patterns that do not meet these CDC criteria should be considered negative.

Recommendations → Optimizing external processes

- Communicate reporting needs to commercial and reference labs
 - Request that incomplete information not be reported
 - Request that labs not offer single tier tests
- Provide targeted educational materials for:
 - Providers who order tests incorrectly
 - Reporters such as infection prevention nurses

For reporters

Lyme disease lab report received

EIA test
(Lyme antibody screen or ELISA)
only

Negative

Do not report

Positive or equivocal

DO NOT REPORT.
Not enough information. Need Western blot results.

Western blot
(immunoblot)
only

Negative

Do not report

Positive

IgM Western blot positive*
(IgG negative or absent)

DO NOT REPORT.
Not enough information. Need preceding EIA results.

IgG Western blot positive*

Report to ADH

Both EIA and Western blot

EIA positive or equivocal

EIA negative OR
Both IgM and IgG Western blot negative

Do not report

IgG Western blot positive*

Report to ADH

IgM Western blot positive* (IgG negative or absent)

Illness onset **more than 30 days** before testing

Do not report

Illness onset unknown or less than 30 days before testing

Report to ADH

***The following CDC criteria must be used to interpret Western blots.**

An **IgM** Western blot is positive if at least 2 of 3 bands (23, 39 and 41 kDa) are reactive.

An **IgG** Western blot is positive if at least 5 of 10 bands (18, 23, 28, 30, 39, 41, 45, 58, 66, and 93 kDa) are reactive.

Banding patterns that do not meet these criteria should be considered negative.

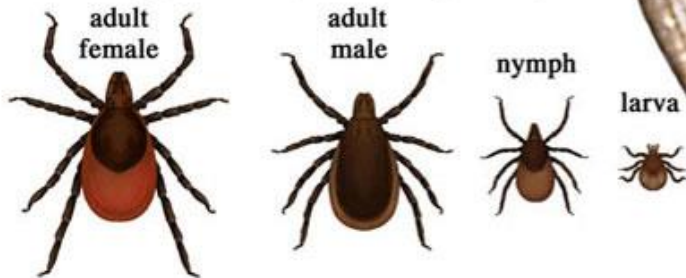
What can we do to help?

- Consultation regarding physician and public inquiries
- Interpretation of laboratory reports
- Reference testing for diagnostic specimens
- Provide diagnostic and reporting algorithms or feedback

Contact information and resources

- CDC Division of Vector-Borne Diseases: (970) 221-6400
- BZB_Public@cdc.gov
- [Concerns Regarding a New Culture Method for *Borrelia burgdorferi* Not Approved for the Diagnosis of Lyme Disease](#) (Nelson *et al.* 2014. MMWR)
- [Current Guidelines, Common Clinical Pitfalls, and Future Directions for Laboratory Diagnosis of Lyme Disease, United States](#) (Moore *et al.* 2016. EID)

Blacklegged Tick (*Ixodes scapularis*)



Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.