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

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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

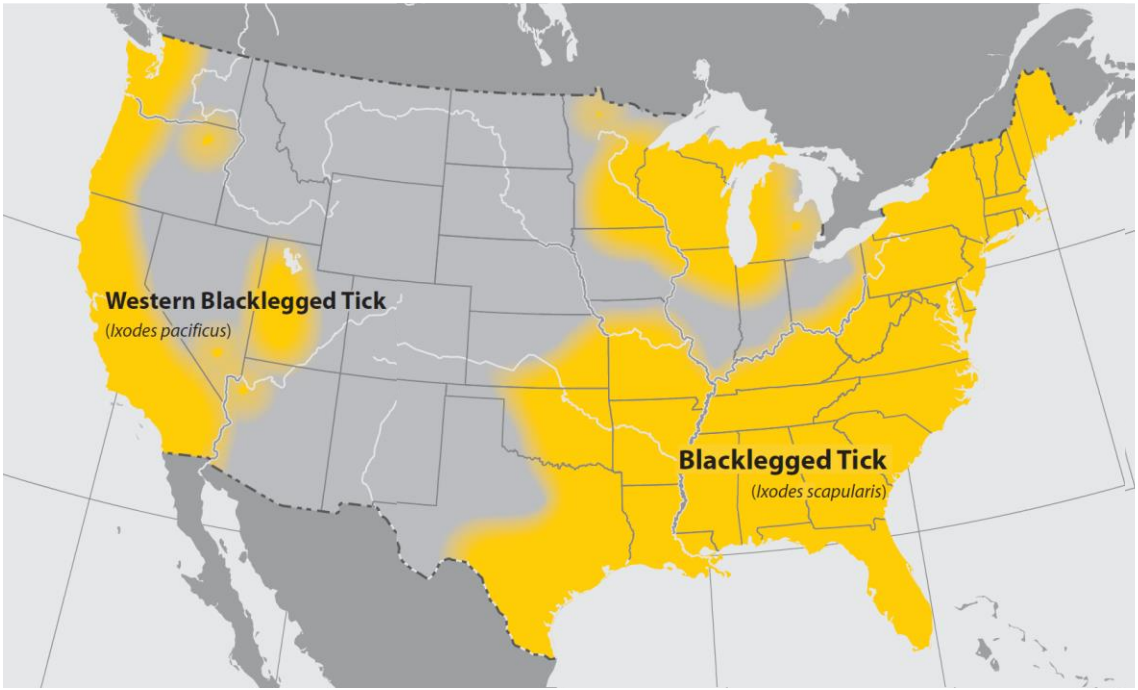
Lyme Disease

- *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



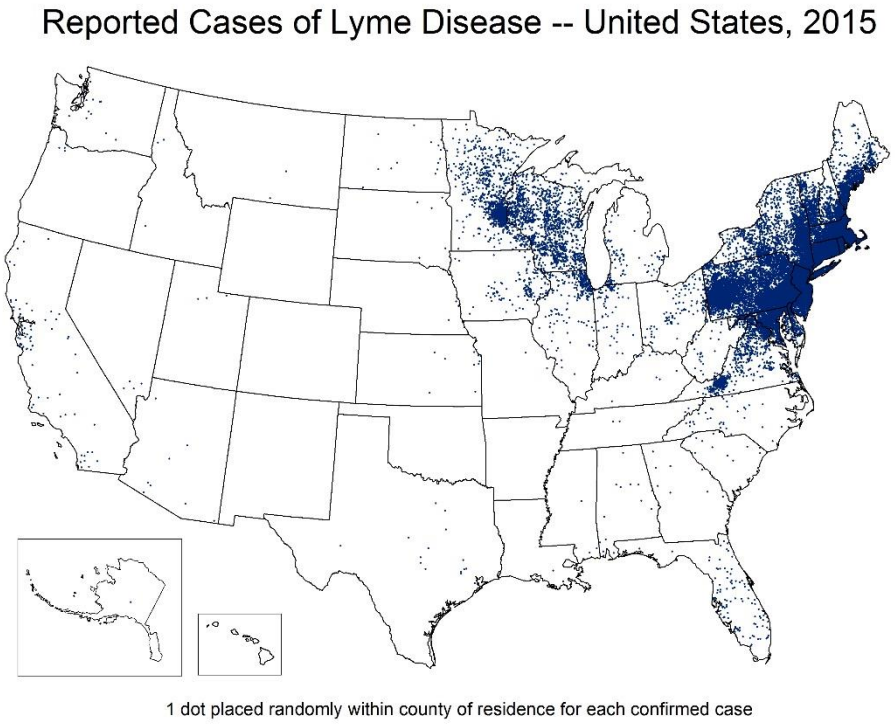


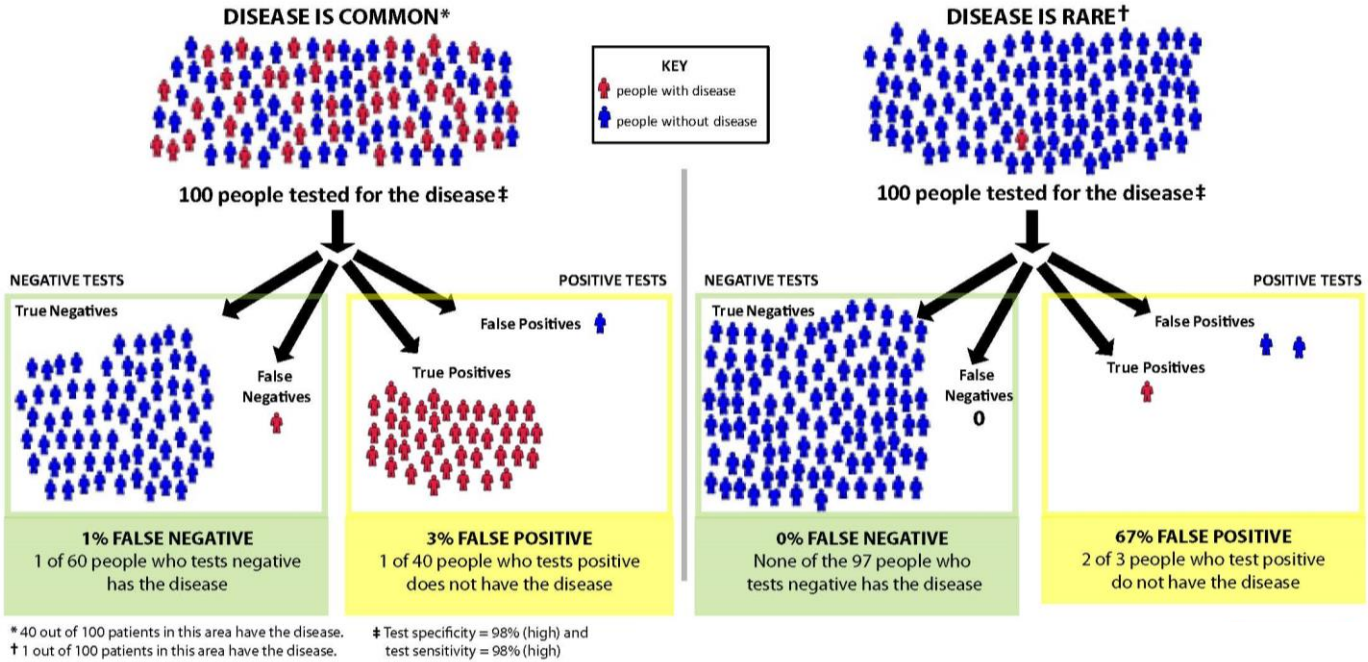
Geographic distribution of tick vectors



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





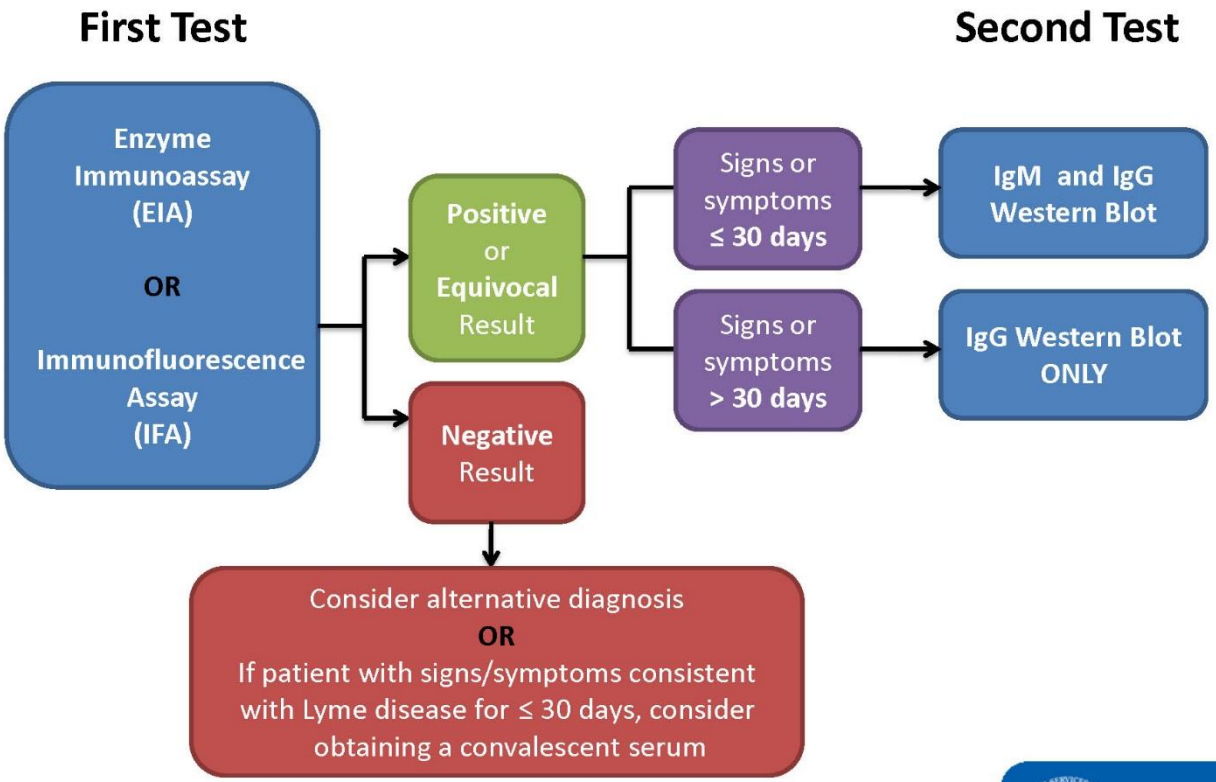
* 40 out of 100 patients in this area have the disease.
† 1 out of 100 patients in this area have the disease.

‡ 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



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**

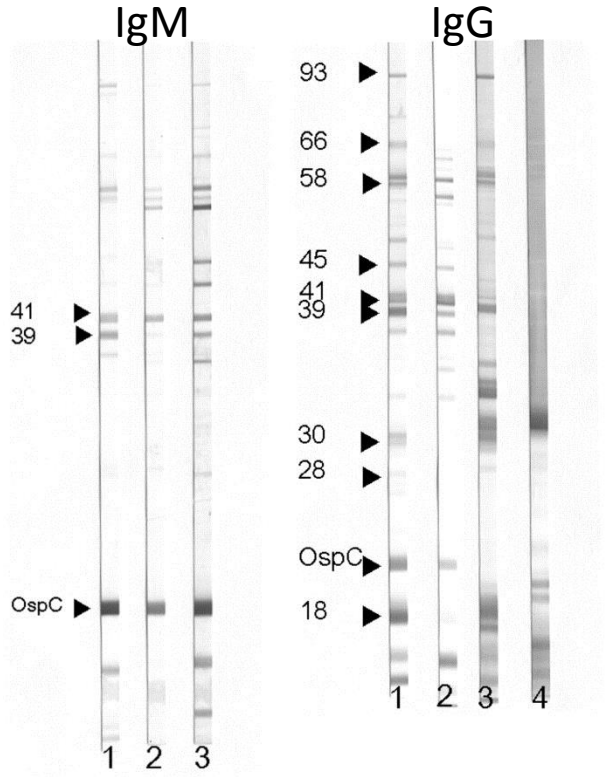
Lyme, STARI, or other?

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

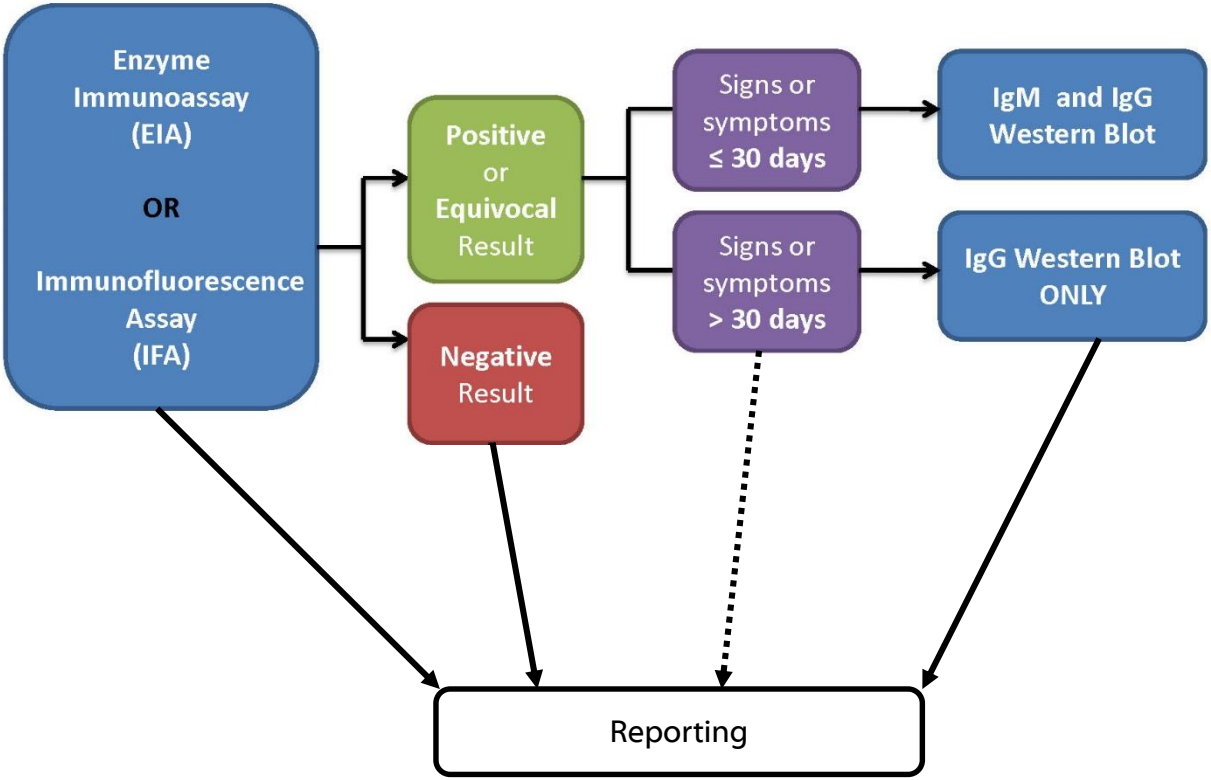
- IgM Western blot
  - Useful for diagnosing early disease
  - Positive if 2 of 3 specific bands are reactive
- IgG Western blot
  - Positive if 5 of 10 specific bands are reactive

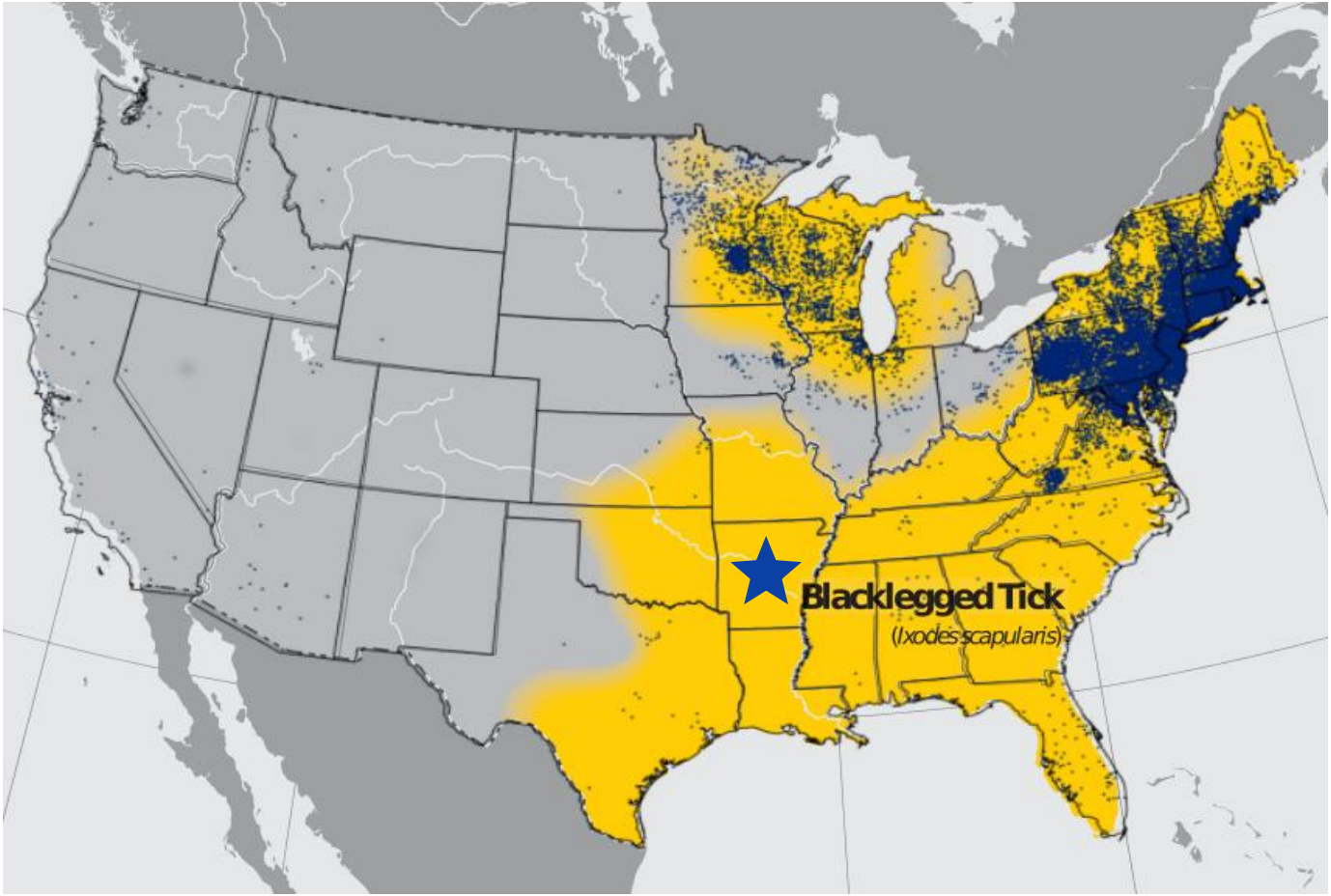


Aguero-Rosenfeld et al. Clin Microbiol Rev 2005;18:484-509.

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

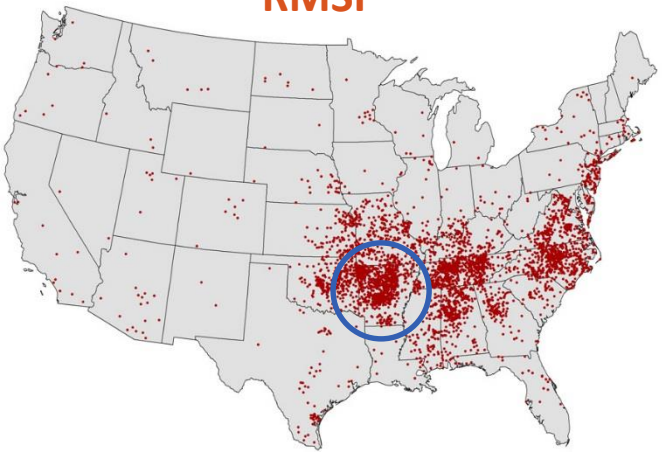



Blacklegged Tick
(Ixodes scapularis)

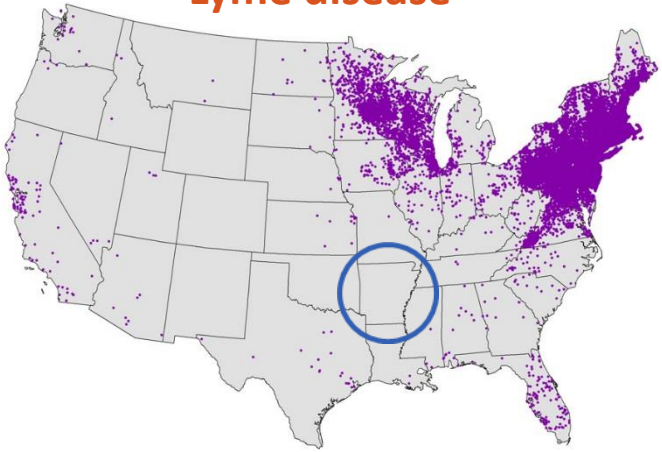
Northern vs. Southern *I. scapularis*

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

RMSF



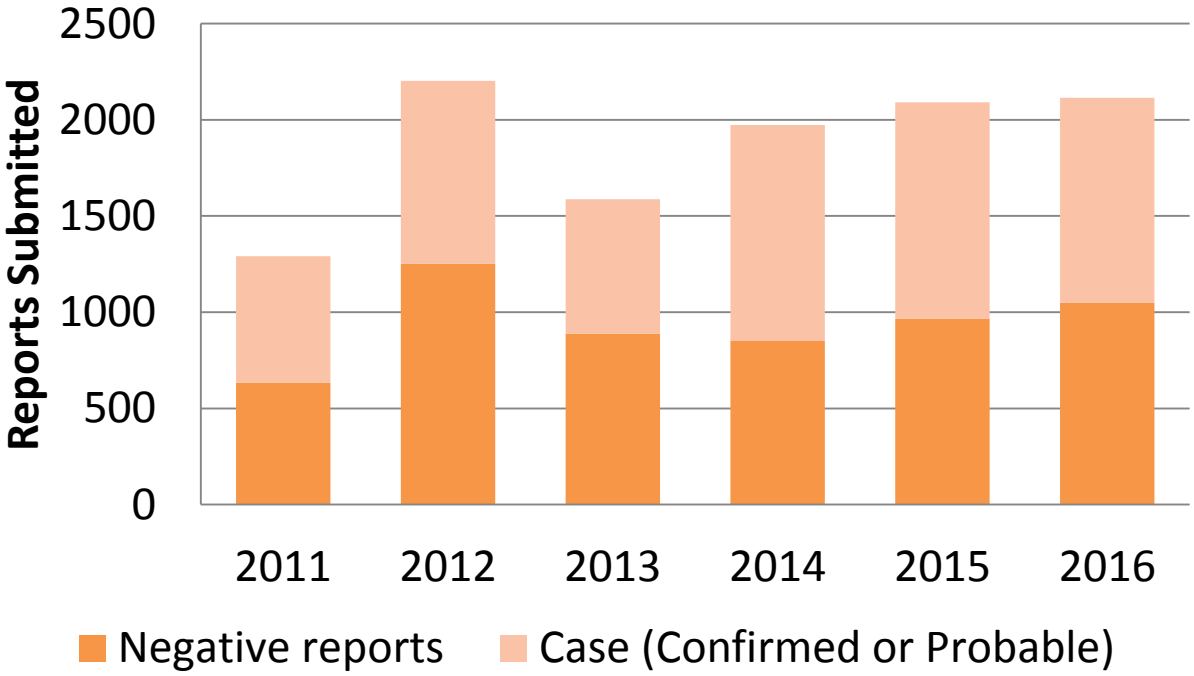
Lyme disease



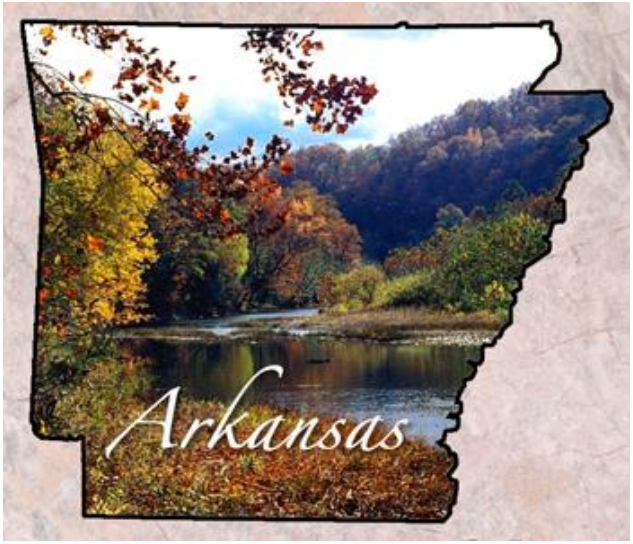
Ehrlichiosis

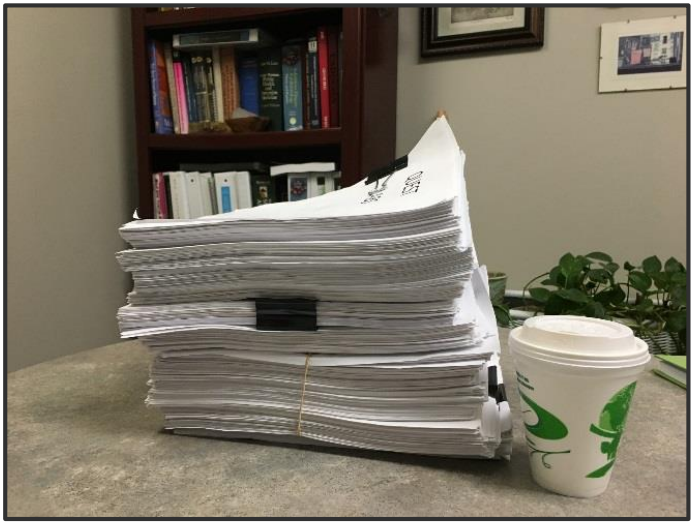
Tularemia

Human tickborne disease surveillance — Arkansas, 2011–2016

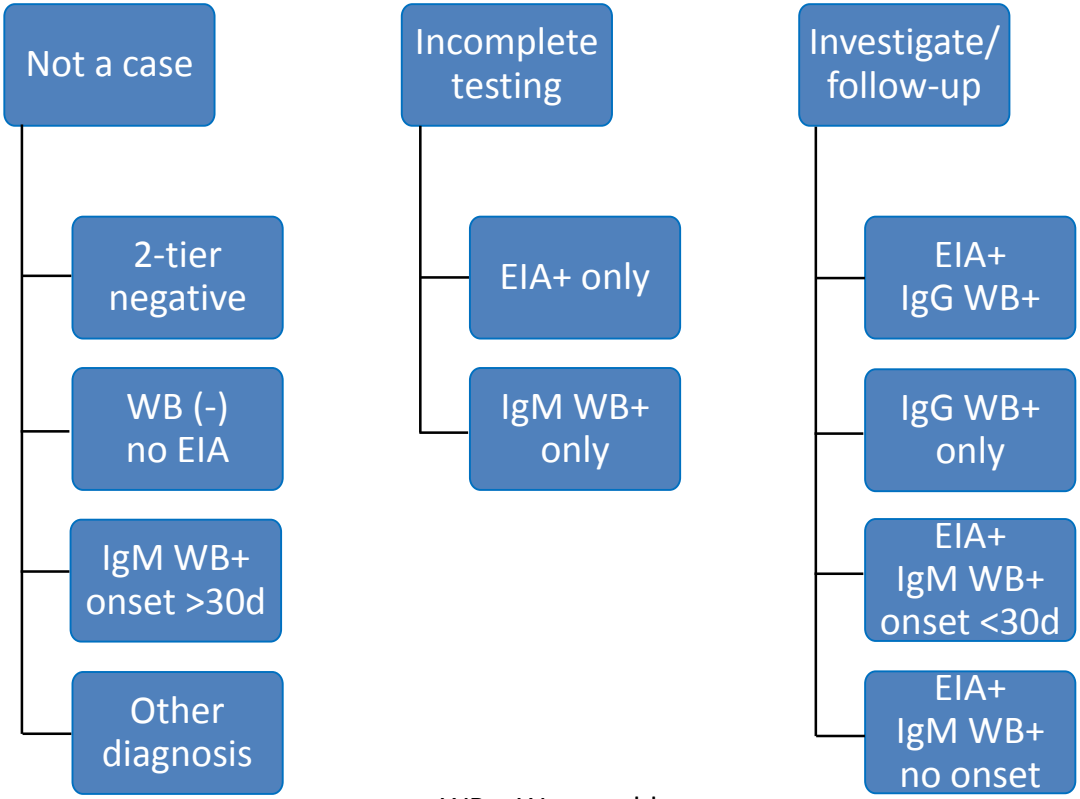


Lyme disease surveillance in Arkansas



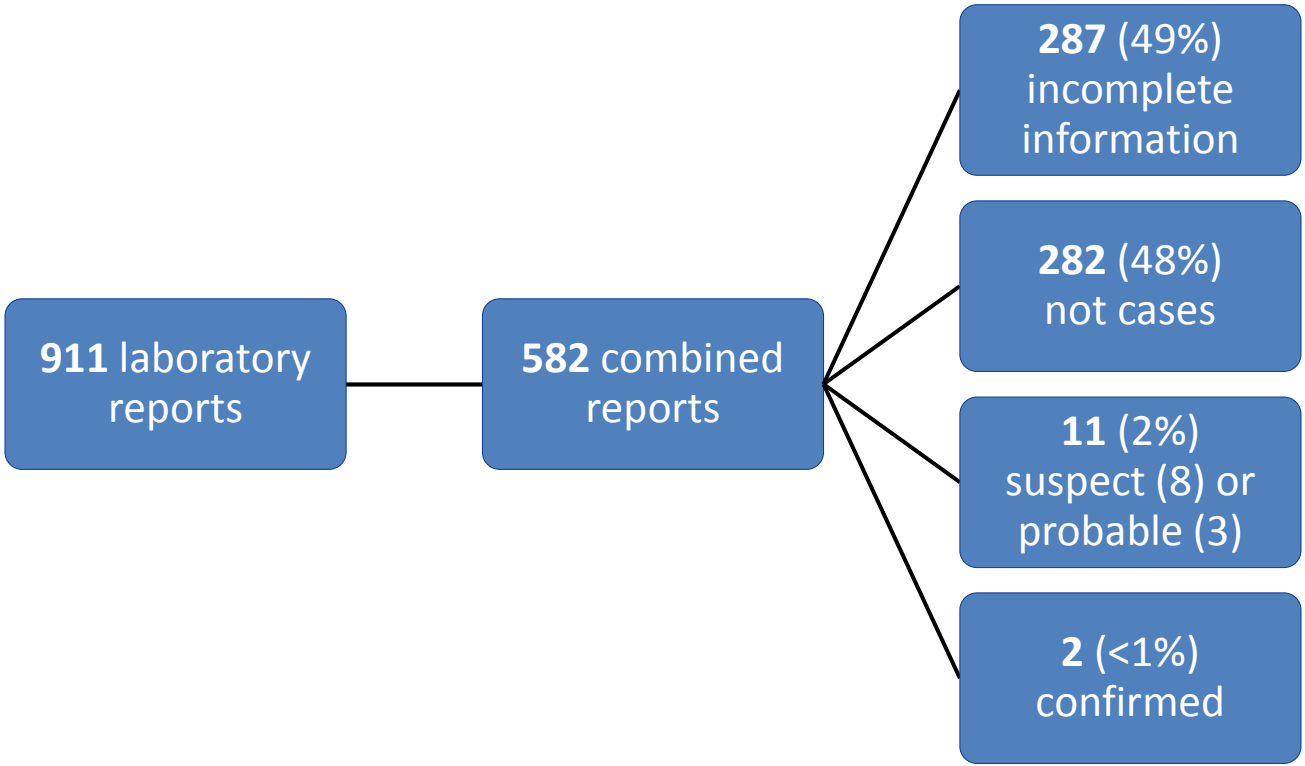


Laboratory report sorting methods



WB = Western blot

Preliminary results of sorting and follow-up



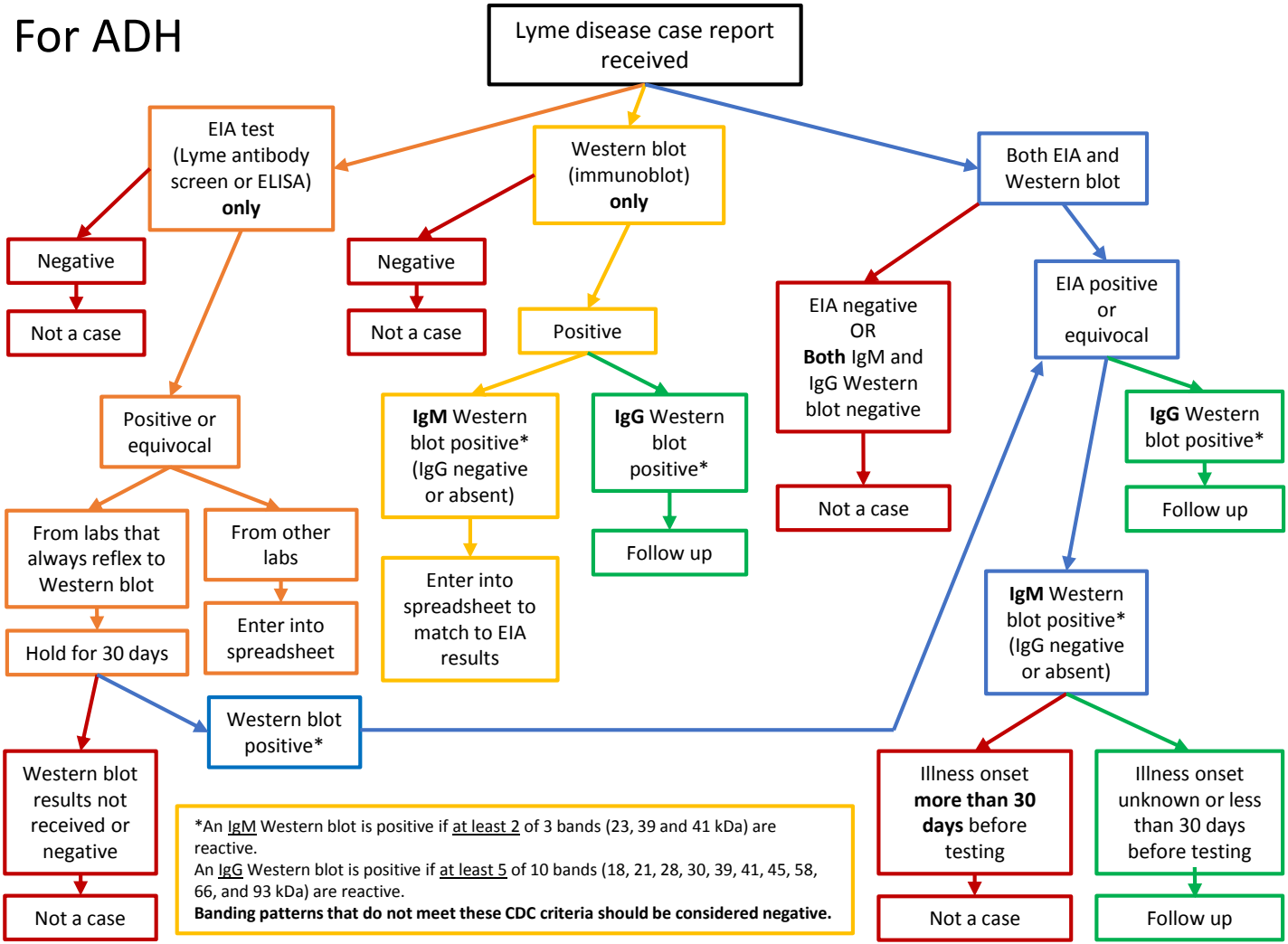
Conclusions

- 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

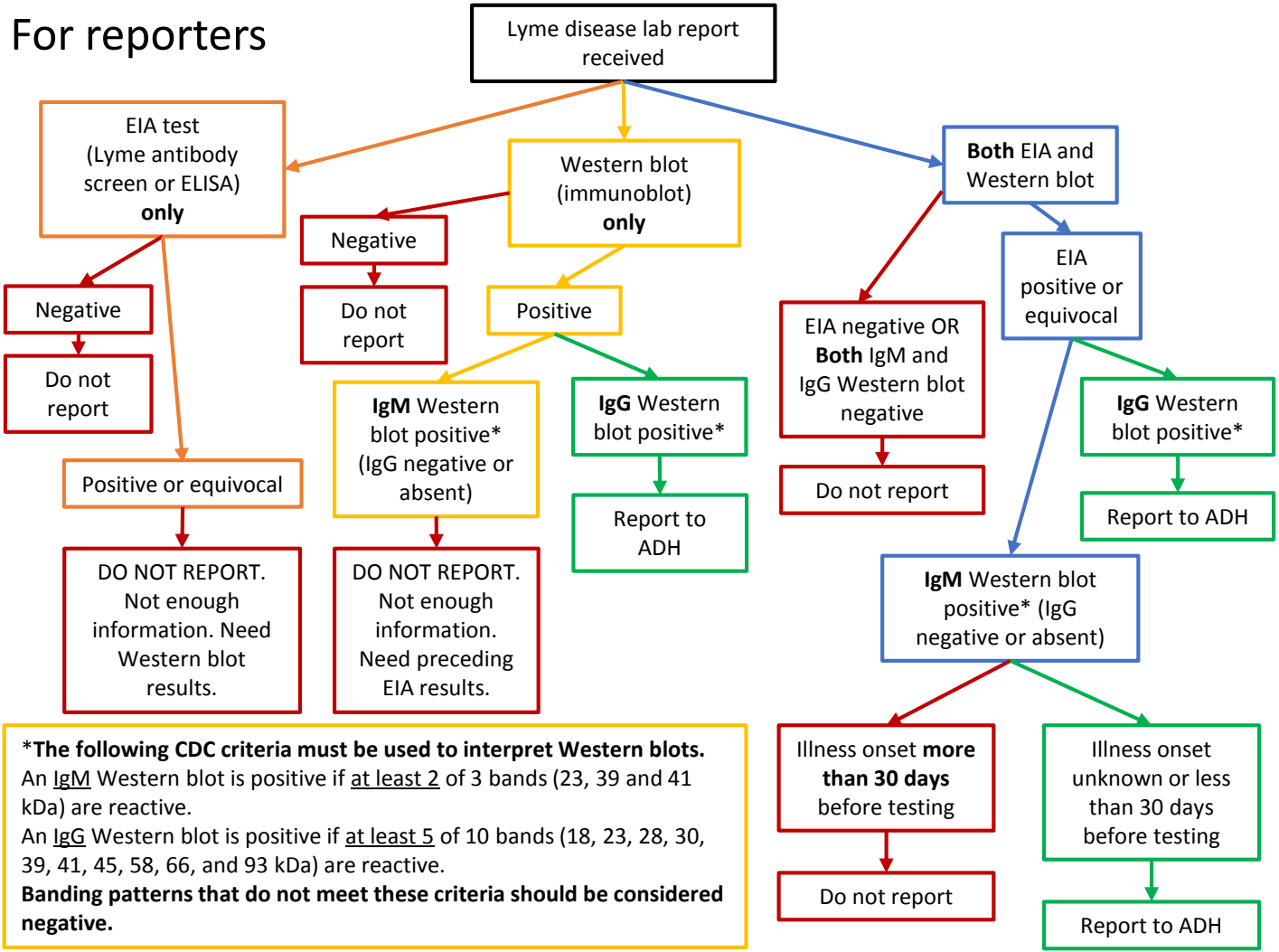


*An IgM Western blot is positive if at least 2 of 3 bands (23, 39 and 41 kDa) are reactive.
An IgG Western blot is positive if at least 5 of 10 bands (18, 21, 28, 30, 39, 41, 45, 58, 66, and 93 kDa) are reactive.
Banding patterns that do not meet these CDC criteria should be considered negative.

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



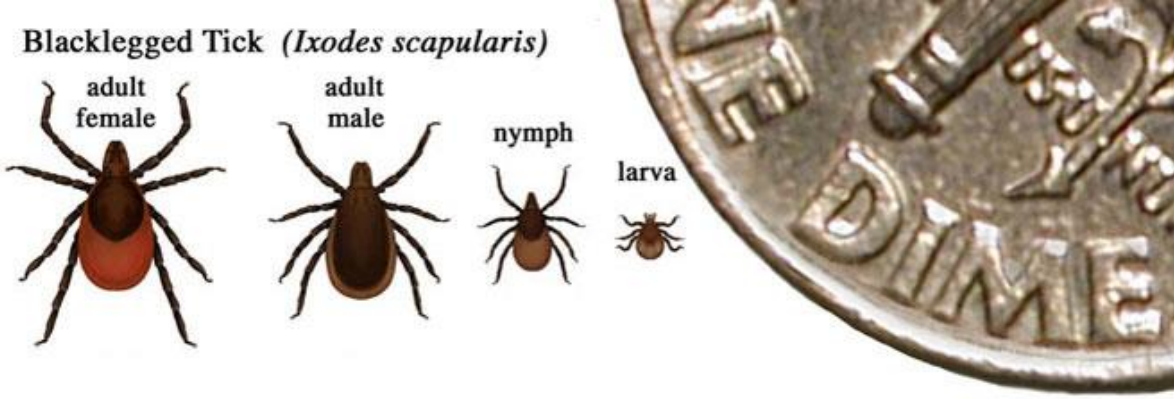
***The following CDC criteria must be used to interpret Western blots.**
An IgM Western blot is positive if at least 2 of 3 bands (23, 39 and 41 kDa) are reactive.
An IgG Western blot is positive if at least 5 of 10 bands (18, 23, 28, 30, 39, 41, 45, 58, 66, and 93 kDa) are reactive.
Banding patterns 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)



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.