Vectorborne Disease Surveillance Update

6 April 2017

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All data provisional; final reported case counts subject to change

Objectives / Overview

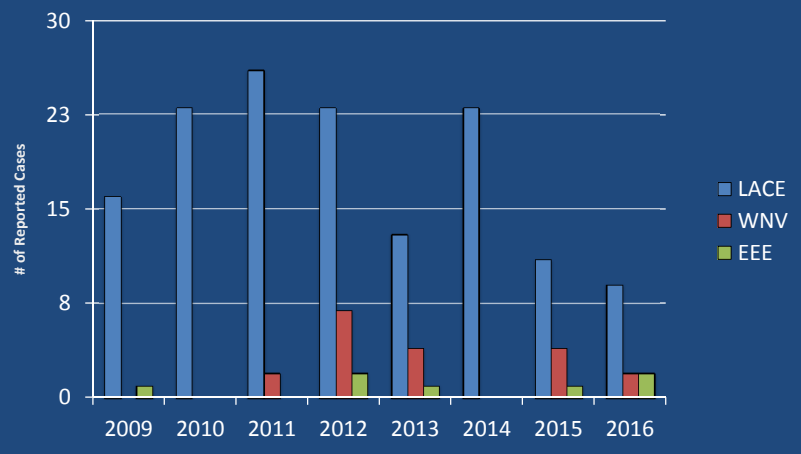
- Discuss vectorborne disease surveillance data
- Explain seasonal and geographic distribution
- Describe classification process using case definition
- Interpret laboratory data

Neuroinvasive Arboviral Infections

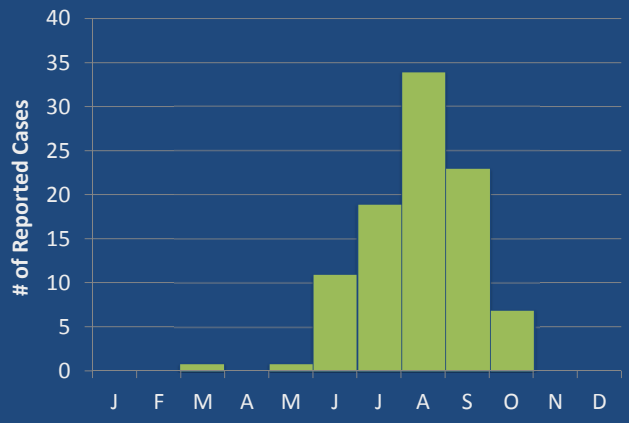
	Reportable	1° Vector	Geography	Genus	Reservoir
La Crosse	Y*	*Aedes* spp	Western NC	Bunyavirus	Small rodents
Eastern Equine Encephalitis	Y*	*Culex* spp	Piedmont and Coastal NC	Alphavirus	Birds
West Nile	Y*	*Culex* spp	Statewide	Flavivirus	Birds
Powassan	Y* **	*Ixodes* spp	Upper Midwest & New England	Flavivirus	Small rodents
St. Louis	Y* **	*Culex* spp	Ohio-Mississippi River Basin	Flavivirus	Songbirds; blue jay, robin
Japanese Encephalitis	Y* **	*Culex* spp	Eastern Asia	Flavivirus	Pigs, wading birds

* Per 10A NCAC 41A .0101 arboviral encephalitis (neuroinvasive disease) is reportable
** Transmission not documented in NC

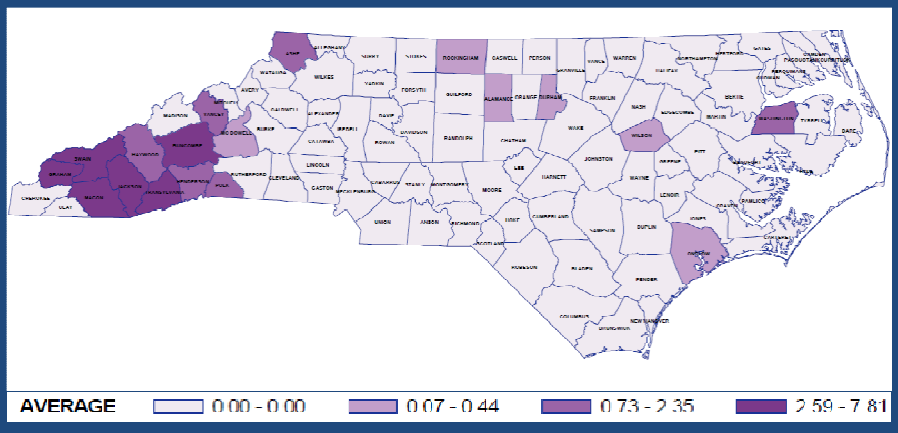
Confirmed and Probable Endemic Arboviral Conditions by Year Onset, NC



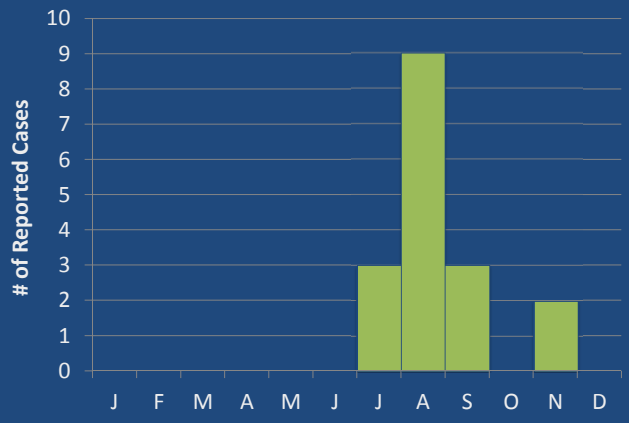
Confirmed and Probable Reported LACE Cases by Month Illness Onset, NC, 2011-2015 (n=96)



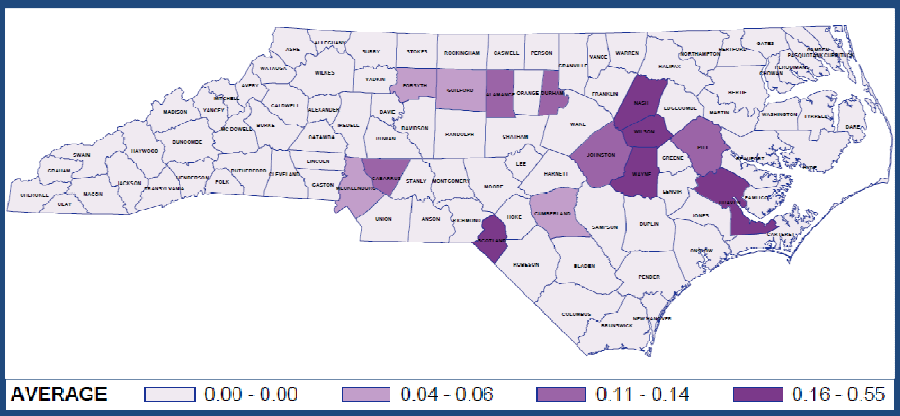
Encephalitis, arboviral, LAC Average Incidence by County, 2011 - 2015



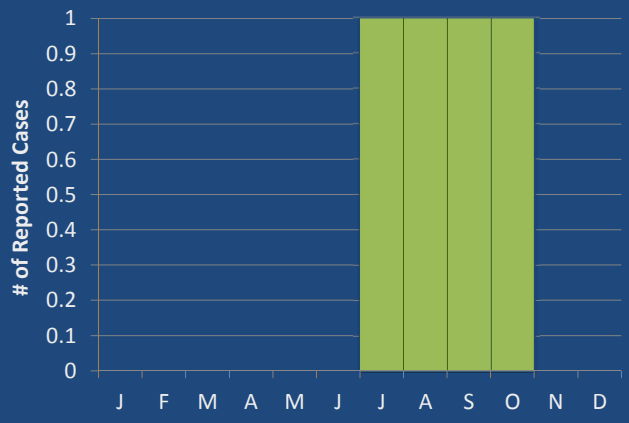
Confirmed and Probable Reported WNV Cases by Month Illness Onset, NC, 2011-2015 (n=17)



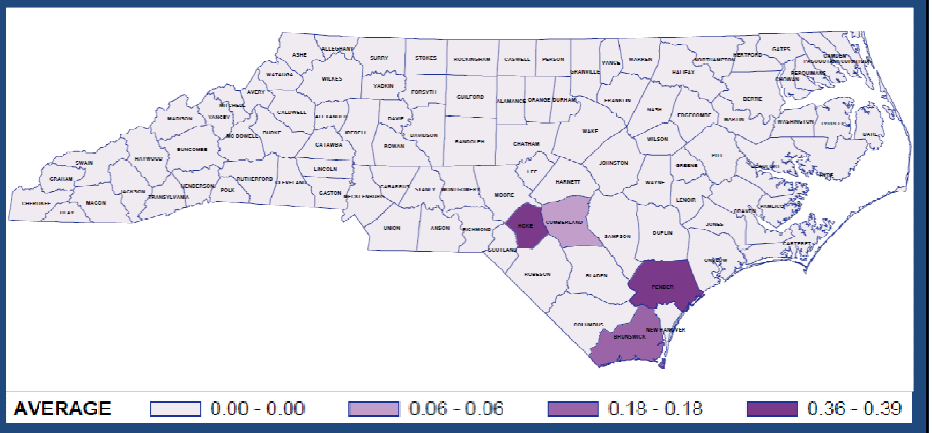
Encephalitis, arboviral, WNV Average Incidence by County, 2011 - 2015



Confirmed and Probable Reported EEE Cases by Month Illness Onset, NC, 2011-2015 (n=4)



Encephalitis, arboviral, EEE Average Incidence by County, 2011 - 2015

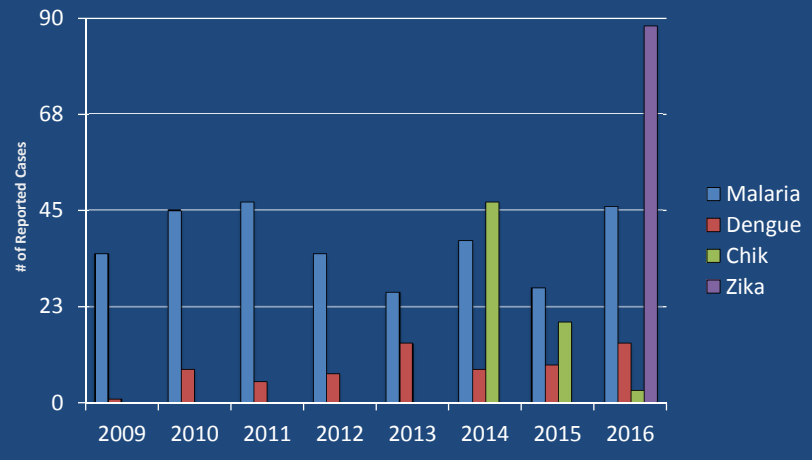


Other Mosquito Borne Infections

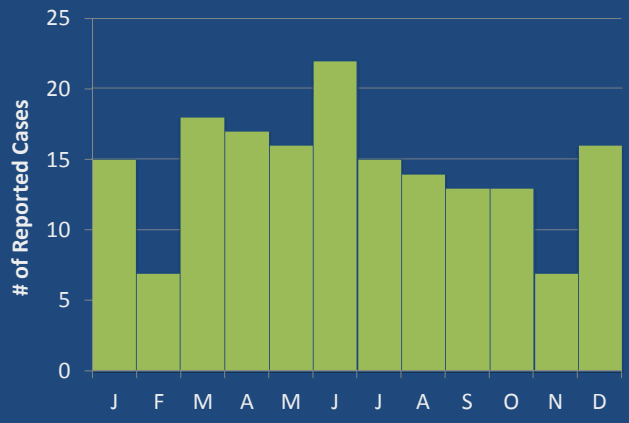
	Reportable	1° Vector	Geography	Genus	Reservoir
Dengue	Y* **	*Aedes* aegypti	Multiple Continents	Flavivirus	Human & NHP
Chikungunya	Y* **	*Aedes* aegypti	Multiple Continents	Alphavirus	Human & NHP
Zika	Y* **	*Aedes* aegypti	Multiple Continents	Flavivirus	Human & NHP
Yellow Fever	Y* **	*Aedes* aegypti	Multiple Continents	Flavivirus	Human & NHP
Malaria	Y* **	*Anopheles* spp	Multiple Continents	Plasmodium	Human

* Per 10A NCAC 41A .0101 each condition is individually reportable
** Transmission not documented in NC

Confirmed and ProbableTravel Associated Mosquito Borne Disease Cases by Year Onset, NC



Confirmed Reported Malaria Cases by Month Illness Onset, NC, 2011-2015 (n=173)

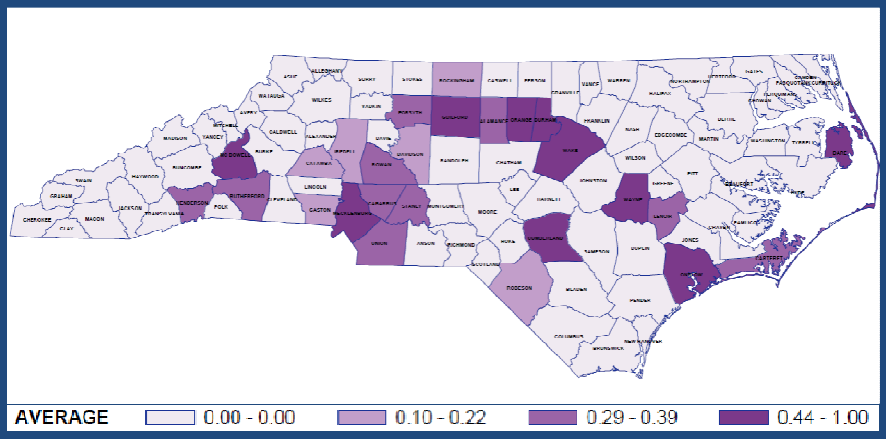


Malaria Results in NCEDSS

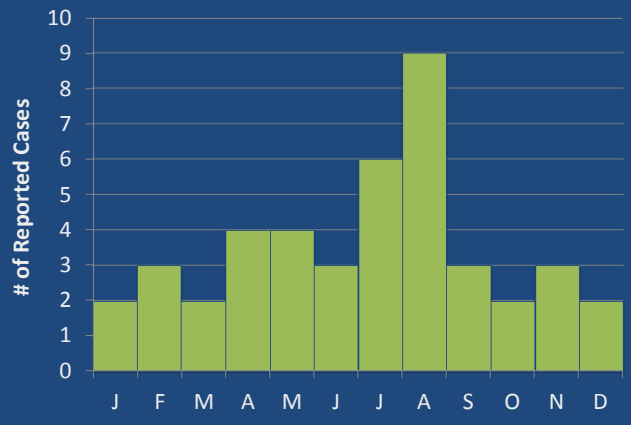
Test: Malaria Smear Bld || Microscopic observation: Malaria smear
Result: Plasmodium species
Result Local Desc: Malaria Smear
Comments: Plasmodium Falciparum 0.8% Parasitemia

Test:P falciparum DNA Bld Ql PCR || Plasmodium falciparum DNA: Probe.amp.tar
Result: Positive
Test Local Desc: P. falciparum
Test Local Code: 139481
Result Status: Final Results
Result Local Desc: Positive
Result Local Code: P
Comments: Positive

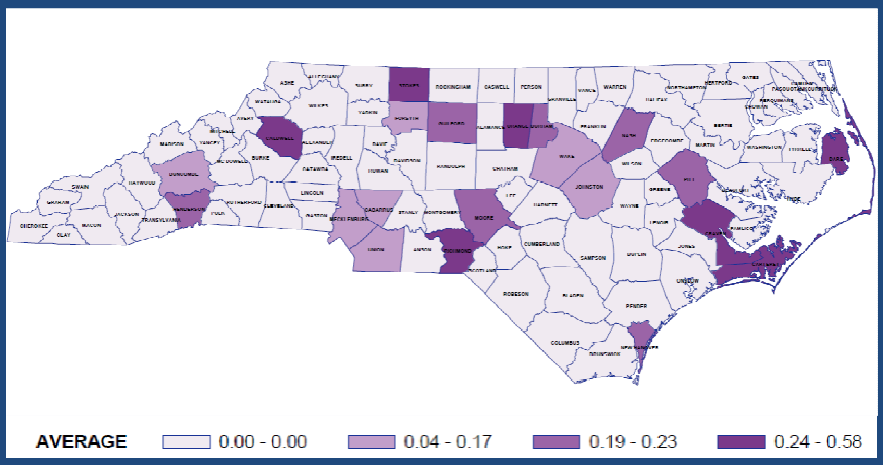
Malaria Average Incidence by County, 2011 - 2015



Confirmed and Probable Reported Dengue Cases by Month Illness Onset, NC, 2011-2015 (n=43)



Dengue Average Incidence by County, 2011 - 2015



Zika Virus Emergency Use Authorization

- An EUA is a tool that FDA can use to allow the use of certain medical products for emergencies based on scientific data. The U.S. Secretary of Health and Human Services (HHS) has declared that circumstances exist to allow the emergency use of authorized diagnostic tests for Zika virus infection
- There are no commercially available diagnostic tests cleared by FDA for the detection of Zika virus. FDA encourages commercial diagnostic developers and researchers developing laboratory developed tests for Zika virus to submit an EUA request. FDA will work interactively with developers to support such requests
- The assay is intended for use with specimens collected from individuals meeting CDC Zika virus clinical criteria (e.g., clinical signs and symptoms associated with Zika virus infection) and/or CDC Zika virus epidemiological criteria (e.g., history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiologic criteria for which Zika virus testing may be indicated as part of a public health investigation).

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Current Zika FDA EUAs

- Abbott RealTi*m*e Zika (Abbott Molecular Inc.)
- Zika Virus Detection by RT-PCR Test (ARUP Laboratories)
- *Sentosa*® SA ZIKV RT-PCR Test (Vela Diagnostics USA, Inc.)
- LightMix® Zika rRT-PCR Test (Roche Molecular Systems, Inc.)
- ZIKV Detect™ IgM Capture ELISA (InBios International, Inc.)
- xMAP® MultiFLEX™ Zika RNA Assay (Luminex Corporation)
- VERSANT® Zika RNA 1.0 Assay (kPCR) Kit (Siemens Healthcare Diagnostics Inc .)
- Viracor-IBT Laboratories, Inc.'s Zika Virus Real-time RT-PCR Test
- Aptima® Zika Virus Assay (Hologic, Inc.)
- RealStar® Zika Virus RT-PCR Kit U.S. (altona Diagnostics)
- Zika Virus RNA Qualitative Real-Time RT-PCR (Focus Diagnostics)
- Zika MAC-ELISA (CDC)
- Trioplex Real-time RT-PCR Assay (CDC)

- http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika

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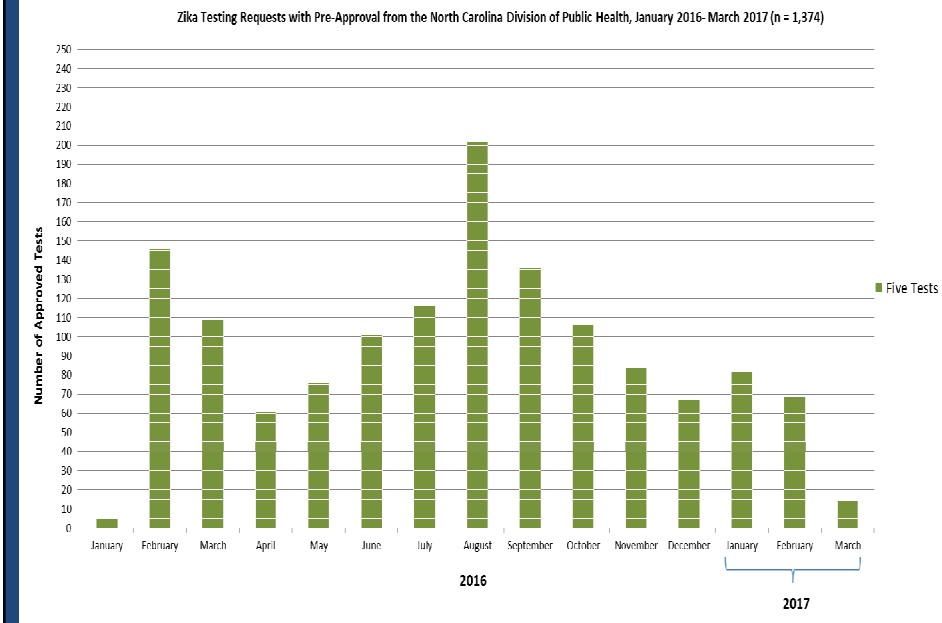


It's not just RMSF…

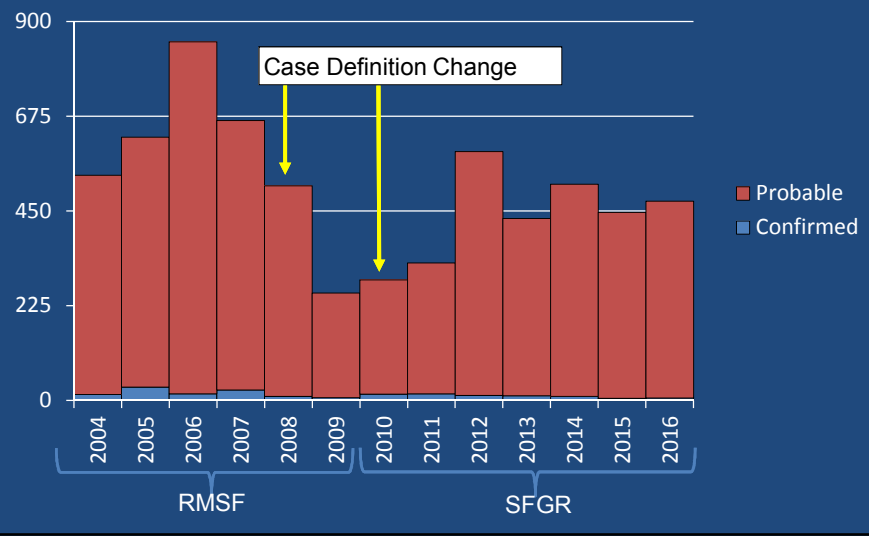
Tick-Borne Diseases in North Carolina:
Is "*Rickettsia amblyommii*" a Possible Cause of Rickettsiosis Reported as Rocky Mountain Spotted Fever?

VECTOR-BORNE AND ZOONOTIC DISEASES
Volume 8, Number 5, 2008

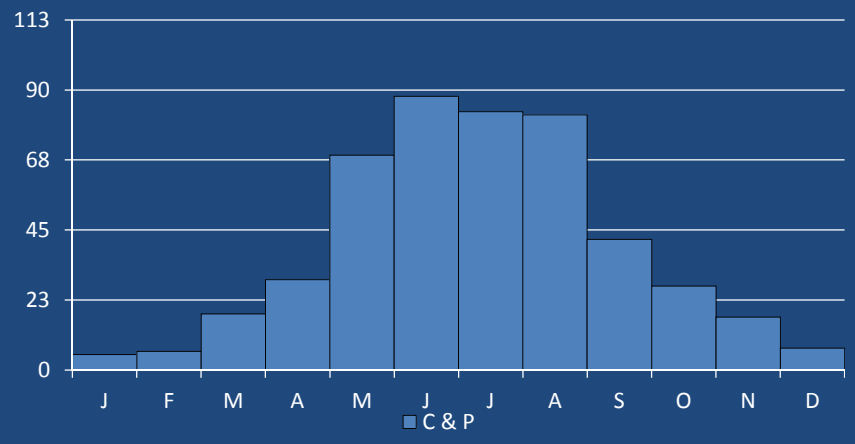
Rickettsia parkeri: A Newly Recognized Cause of Spotted Fever Rickettsiosis in the United States

Clinical Infectious Diseases 2004; 38:805–11

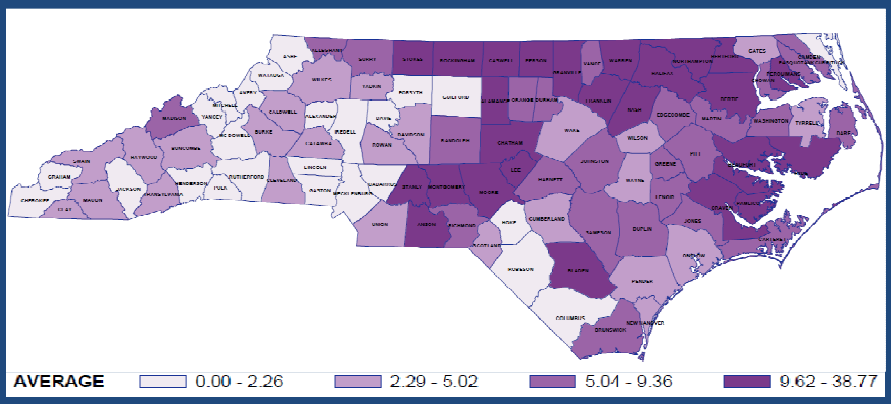
Rickettsia spp. Cases by Year, NC



Confirmed and Probable SFGR Cases by Month Illness Onset, NC, 2016 (n=473)



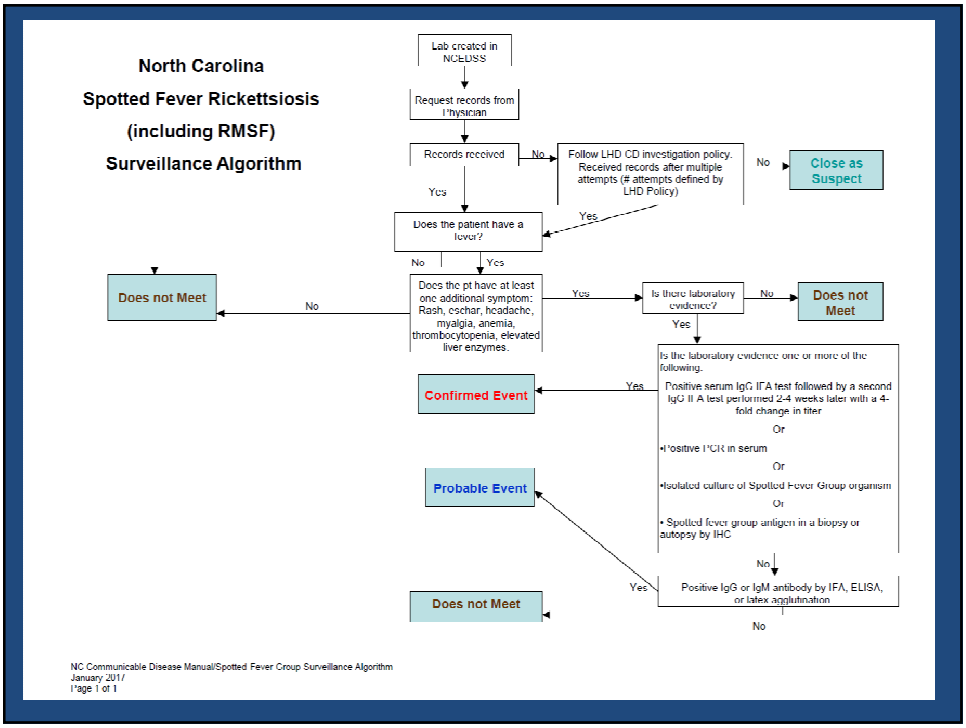
Spotted Fever Group Rickettsia Average Incidence by County, 2011 - 2015



SFGR Event Investigation Details

Year	Total Events Created for Investigation	Events Created by Electronic Lab Report (ELR)	% of Total Events Created by ELR	% of Total Events Resulting in C / P Case Classification
2016*	2119	1790	84%	23% (477/2119)
2013**	1532	1184	77%	27% (420/1532)
2009**	1116	261	23%	23% (255/1116)

*Data extracted from NC EDSS "TATP – Source of Event CD" and "event line list – deidentified" reports on 25 JAN 2017
**Data extracted from NC EDSS "TATP – Source of Event CD" and "event line list – deidentified" reports on 6 FEB 2014

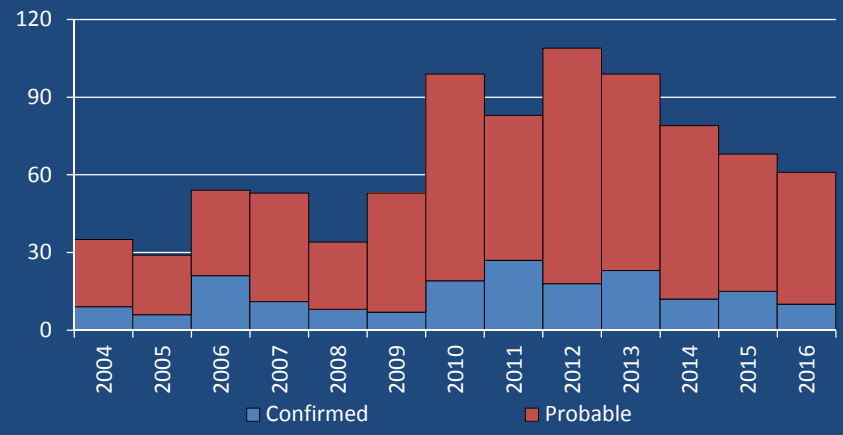


Confirmed RMSF IFA in NCEDSS; LabCorp

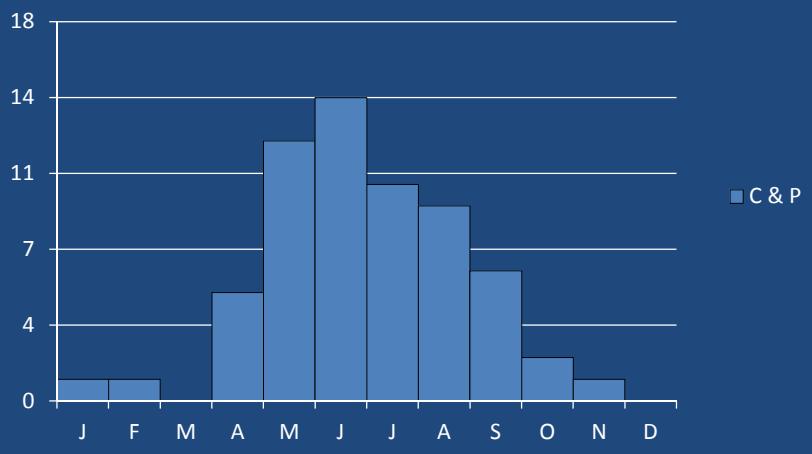
Test: R rickettsi IgG Titr Ser IF || Rickettsia rickettsii Ab.IgG: IF
Result Value: 1:64
Ref Range: Neg <1:64
Test Local Desc: RMSF, IgG, IFA
Test Local Code: 016174
Result Status: Final Results
Comments: Negative <1:64 Positive 1:64 Recent/Active >1:64 . Titers of 1:64 are suggestive of past or possible current infection. Titers >1:64 are suggestive of recent or active infection. Approximately 9% of specimens positive by EIA screen are negative by IFA. **Result Date: 08/11/2016**

Test: R rickettsi IgG Titr Ser IF || Rickettsia rickettsii Ab.IgG: IF
Result Value: 1:256
Ref Range: Neg <1:64
Test Local Desc: RMSF, IgG, IFA
Test Local Code: 016174
Result Status: Final Results
Comments: Negative <1:64 Positive 1:64 Recent/Active >1:64 . Titers of 1:64 are suggestive of past or possible current infection. Titers >1:64 are suggestive of recent or active infection. Approximately 9% of specimens positive by EIA screen are negative by IFA. **Result Date: 08/30/2016**

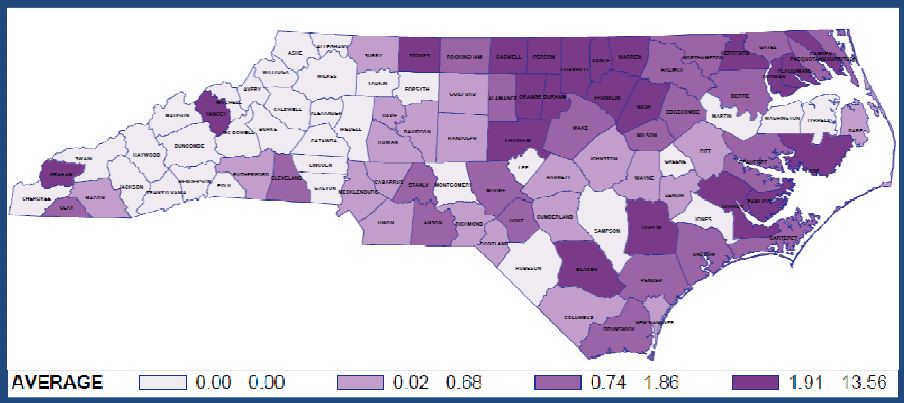
HME Cases by Year, NC



Confirmed and Probable HME Cases by Month Illness Onset, NC, 2016 (n=61)



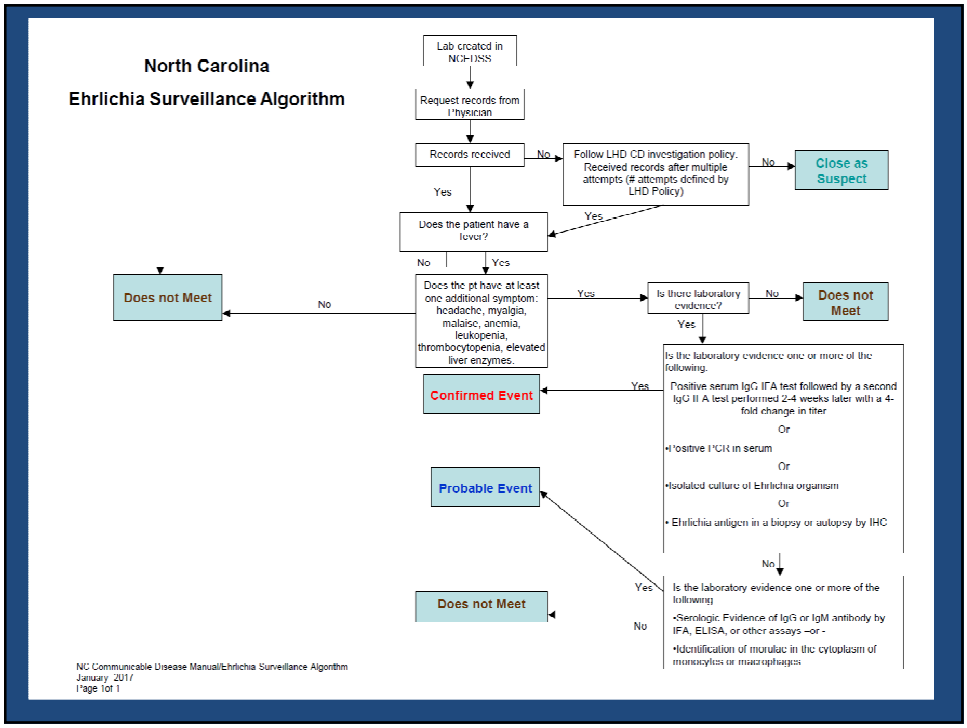
Human Monocytic Ehrlichiosis Average Incidence by County, 2011 - 2015

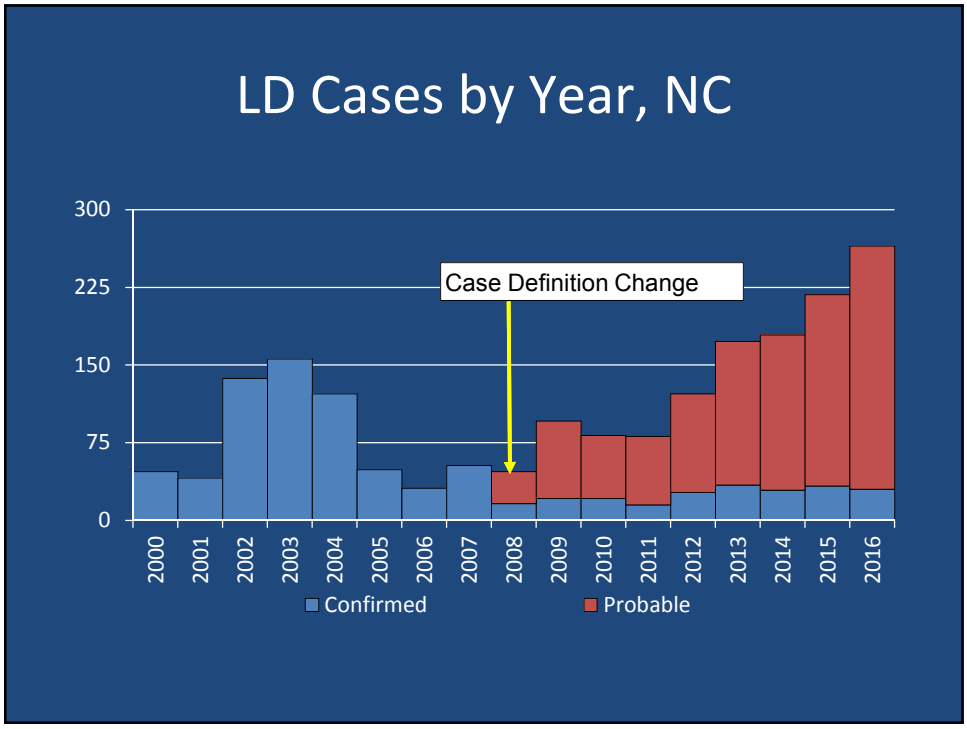


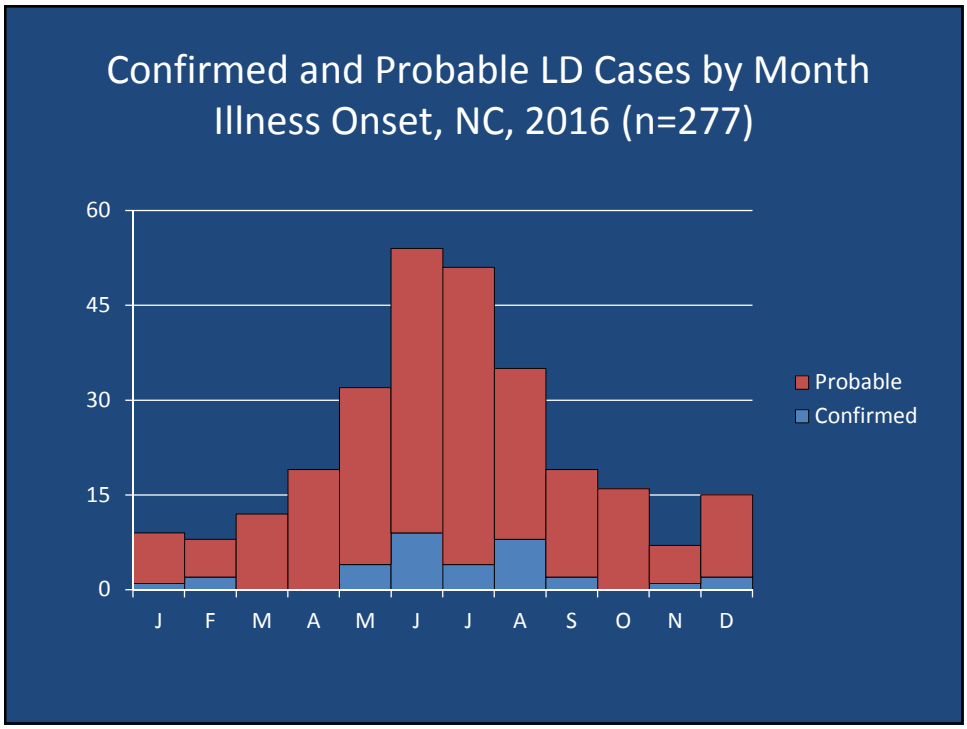
HME Event Investigation Details

Year	Total Events Created for Investigation	Events Created by Electronic Lab Report	% of Total Events Created by ELR	% of Total Events Resulting in C / P Case Classification
2016*	217	185	85%	28% (61/217)
2013**	218	174	80%	35% (76/218)
2009**	196	11	6%	27% (53/196)

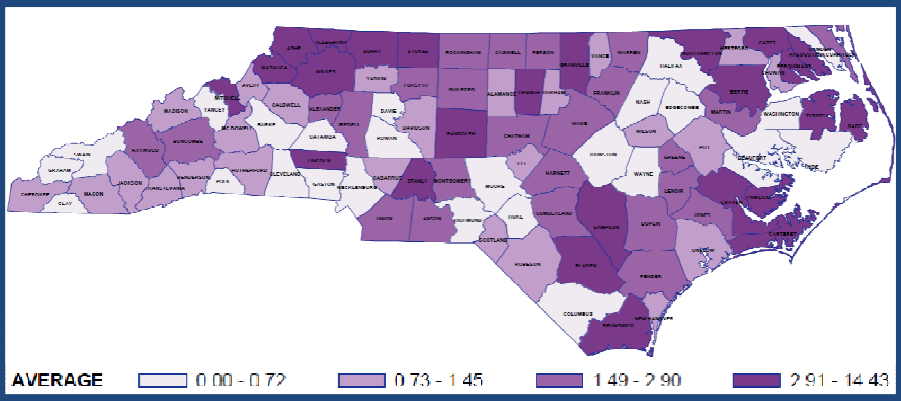
*Data extracted from NC EDSS "TATP – Source of Event CD" and "event line list – deidentified" reports on 25 JAN 2017
**Data extracted from NC EDSS "TATP – Source of Event CD" and "event line list – deidentified" reports on 6 FEB 2014




LD Cases by Year, NC
300
225
150
75
0
Case Definition Change
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
Confirmed
Probable


Confirmed and Probable LD Cases by Month Illness Onset, NC, 2016 (n=277)
60
45
30
15
0
J
F
M
A
M
J
J
A
S
O
N
D
Probable
Confirmed

Lyme Disease Average Incidence by County, 2011 - 2015



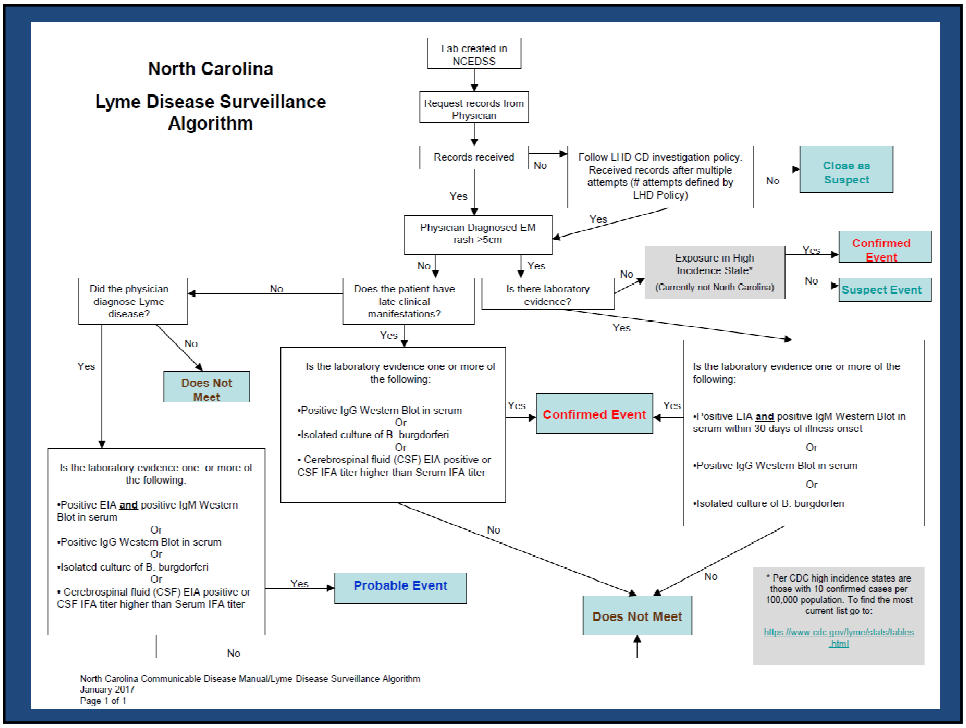
LD Event Investigation Details

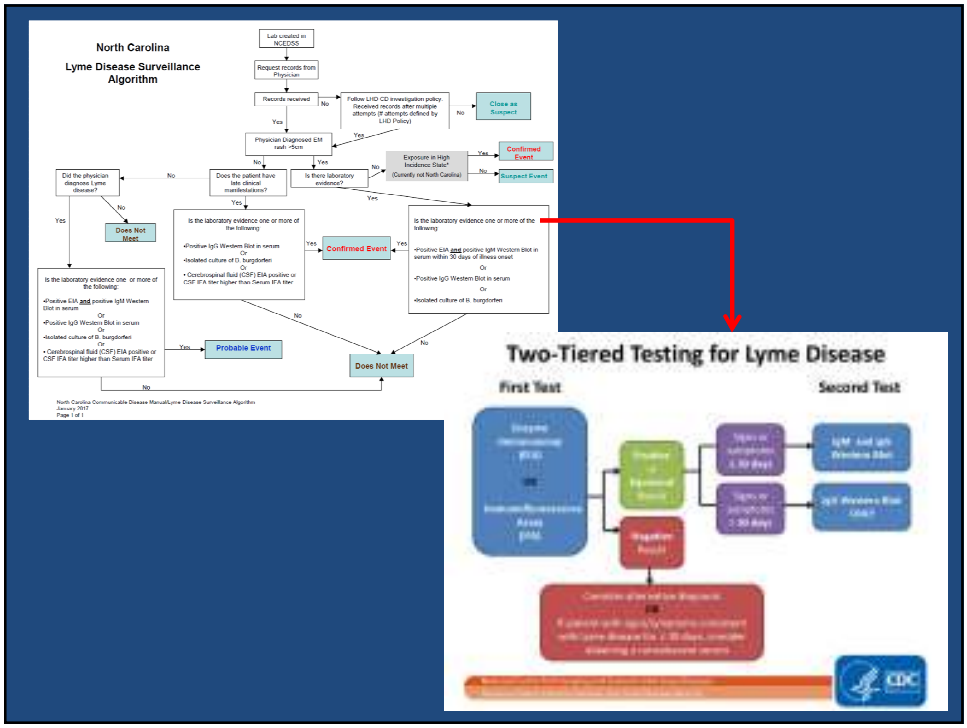
Year	Total Events Created for Investigation	Events Created by Electronic Lab Report	% of Total Events Created by ELR	% of Total Events Resulting in C / P Case Classification
2016*	1243	1055	85%	22% (277/1243)
2013**	1172	972	83%	15% (173/1172)
2009**	1704	1513	89%	5% (96/1704)

*Data extracted from NC EDSS "TATP – Source of Event CD" and "event line list – deidentified" reports on 25 JAN 2017
**Data extracted from NC EDSS "TATP – Source of Event CD" and "event line list – deidentified" reports on 6 FEB 2014

CSTE 16-ID-10

- We propose to change the exposure criteria for the Lyme disease case definition to consider whether the exposure occurred in a state that consistently reports a high incidence of Lyme disease vs. in a state where Lyme disease is less frequently reported.
- In states with a high incidence rate of Lyme disease, an erythema migrans rash and exposure to potential tick habitats will be sufficient to confirm Lyme disease; in states where Lyme disease is less frequently reported, case confirmation will require both clinical and laboratory evidence of infection.
- In this position statement, we designate a state as high or low incidence based on a cutoff of 10 reported Lyme disease cases per 100,000 persons.





ELISA: Enzyme-Linked ImmunoSorbent Assay

- Measures a person's antibody (or immune response) to the bacteria that cause Lyme disease
- Very "sensitive", meaning that when they are used properly, almost everyone with Lyme disease will test positive
- Not "specific"
  - For this reason, doctors want to verify any "positive" or "equivocal" (indeterminate) ELISA results by performing an immunoblot test such as a Western blot.
  - The Western blot or other FDA-approved type of immunoblot can help distinguish patients who have Lyme disease from those with other conditions

LabCorp EIA result in NCEDSS

Tests
Test: B burgdor IgM Ser EIA-aCnc
Result Value: 6.17
Result Units: index
Ref Range: 0.00-0.79
Test Local Desc: Lyme Disease Ab, Quant, IgM
Test Local Code: 161998
Result Status: Final Results
Comments: Negative <0.80 Equivocal 0.80 - 1.19 Positive >1.19 . IgM levels may peak at 3-6 weeks post infection, then gradually decline.

Western Blots / Immuno Blots

- Looks for antibodies the body makes against different molecules, or "antigens," that are part of *Borrelia burgdorferi*
- Detects two different classes of antibodies: IgM and IgG
  - IgM antibodies are made sooner, so testing for them can be helpful for identifying patients during the first few weeks of infection
    - IgM antibodies is that they are more likely to give false positive results.
  - IgG antibodies are more reliable, but can take 4-6 weeks for the body to produce in large enough quantities for the test to detect them

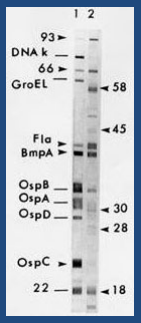
Lyme disease WB → Tier Two

IgM: 2 of the 3 following bands must be present to be considered positive
24 kDa (OspC)
39 kDa (BmpA)
41 kDa (Fla)

A positive IgM immunoblot is only meaningful during the first 4 weeks of illness

IgG: 5 of the following 10 bands must be present to be considered positive
18 kDa
21 kDa (OspC)
28 kDa
30 kDa
39 kDa (BmpA)
41 kDa (Fla)
45 kDa
58 kDa (not GroEL)
66 kDa
93 kDa

By 4 – 6 weeks post infection the IgG WB is virtually always positive



LabCorp WB result in NCEDSS

Test: B burgdor IgG Patrn Ser IB-Imp || Borrelia burgdorferi Ab.IgG band pattern: IB
Result: Positive
Ref Range: Positive: 5 of the following
Test Local Desc: Lyme IgG WB Interp.
Test Local Code: 163640
Result Status: Final Results
Result Local Desc: Positive
Result Local Code: P
Comments: Positive . Positive: 5 of the following Borrelia-specific bands: 18,23,28,30,39,41,45,58, 66, and 93. Negative: No bands or banding patterns which do not meet positive criteria.

Rules for Understanding WB Testing

- The immunoblot should not be run without first performing an ELISA
- The immunoblot should not be run if the ELISA is negative
- A positive IgM immunoblot is only meaningful during the first 4 weeks of illness
- If the patient has been ill for longer than 4-6 weeks and the IgG immunoblot test is negative, the case definition requirements for laboratory evidence of infection are NOT fulfilled

Note PCR is NOT an Accepted Test for LD Surveillance

- *B. burgdorferi* initially disseminates from the site of an infected tick bite via the blood, but the bloodborne phase is relatively brief and the concentration of spirochetes is quite low.
- This test is not clinically useful for LD diagnosis
- There are no PCR-based assays for the diagnosis of Lyme disease cleared by the US FDA
- Two-tiered serology remains the mainstay of laboratory testing for Lyme disease
- See: http://www.medscape.com/viewarticle/764501 for more information

Contributions From

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