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Vectorborne Zoonoses: Break-out Session

Epidemiology and Laboratory Capacity Workshop – Oct. 2018

DSHS Zoonosis Control Branch

Session Topics

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- NEDSS case investigation tips
- Lyme disease
- Rickettsial diseases
- Arboviral diseases

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Don't be a Reject!

Helpful tips to keep your notification from being rejected

ELC breakout session
October 3, 2018

Kamesha Owens, MPH
Zoonosis Control Branch
Texas Department of State Health Services

Objectives

- Rejection Criteria
- How to document in NBS (NEDSS)
- How to Report

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Rejection Criteria

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Missing/incorrect information:

- Incorrect case status or condition selected
- Full Name
- Date of Birth
- Address
- County
- Missing laboratory data

Rejection Criteria
continued

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- Inconsistent information
  - e.g. Report date is a week before onset date
- Case investigation form not received by ZCB within 14 days of notification
  - ZCB recommends that notification not be created until the case is closed and the investigation form has been submitted

Rejection Criteria
continued

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- Condition-specific information necessary to report the case is missing:
  - Travel history for Zika and other non-endemic conditions
  - Evidence of neurological disease for WNND case
  - Supporting documentation for Lyme disease case determination

How to Document in NBS (NEDSS)

Do	Don't
Add detailed comments in designated comments box under case info tab. (**strongly recommended** not required)	**Leave us guessing!** If you decide not to enter comments, please make sure information on paper form is **legible**.
Ensure all fields required to be entered are filled in or selected. • **Check your dates** (Onset date, date of report, etc.) to ensure the timeline reflected makes sense and is accurate.(See DEG for details)	Leave important fields blank, i.e. symptoms, lab results, date of report, etc.
Check NBS entry against paper form to make sure the information is the same.	Leave out **Condition-specific** information necessary to report a case (i.e. travel dates and history for Zika cases).
Enter a comment in **ALL positive ELRs** for non-cases explaining why the case-patient does not meet case definition or is "lost to follow-up" (LTF) unless the ELRs are associated with an NBS investigation.	Leave positive ELRs comments section blank or not associate relevant appropriate labs to case investigations.

Reporting Zoonoses

- **For LHDs:** Scan and attach, fax, or send via secure e-mail the completed investigation form with relevant lab reports to your Regional ZC office for review
  - After review, the Regional ZC staff will forward to ZCB Central Office for final review and approval

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Reporting Zoonoses

For ZC Regional Staff:

Scan and attach, fax, or send via secure e-mail completed case investigation form with relevant lab reports to Central Office ZCB epidemiologists for review and approval

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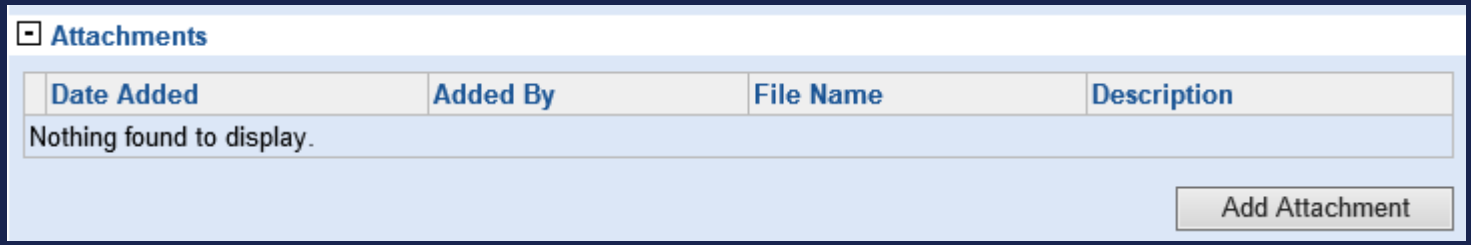
Attaching Documents in NEDSS

- **Not all Conditions allow this**
- **Scan/Save** the completed form and laboratory reports as a pdf
- **Attach** the document under the Supplemental Info tab of the case investigation
  - Scroll down until you see "Attachments" under the "Notes and Attachments" section, then click on the button that is labeled "Add Attachment"



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Resources

- TDSHS Zoonosis website: http://www.dshs.texas.gov/idcu/health/zoonosis/
- IDCU: http://www.dshs.texas.gov/idcu/default.shtm
- NBS Data Entry Guide (DEG): https://txnedss.dshs.state.tx.us:8009/PHINDox/UserResources/
- Epi Case Criteria Guidelines (ECCG): https://txnedss.dshs.state.tx.us:8009/PHINDox/UserResources/

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Lyme Disease Case Classification and Two-Tiered Testing

Bonny Mayes, MA, RYT

Epidemiologist

Zoonosis Control Branch

Department of State Health Services

Austin, Texas

Lyme Disease

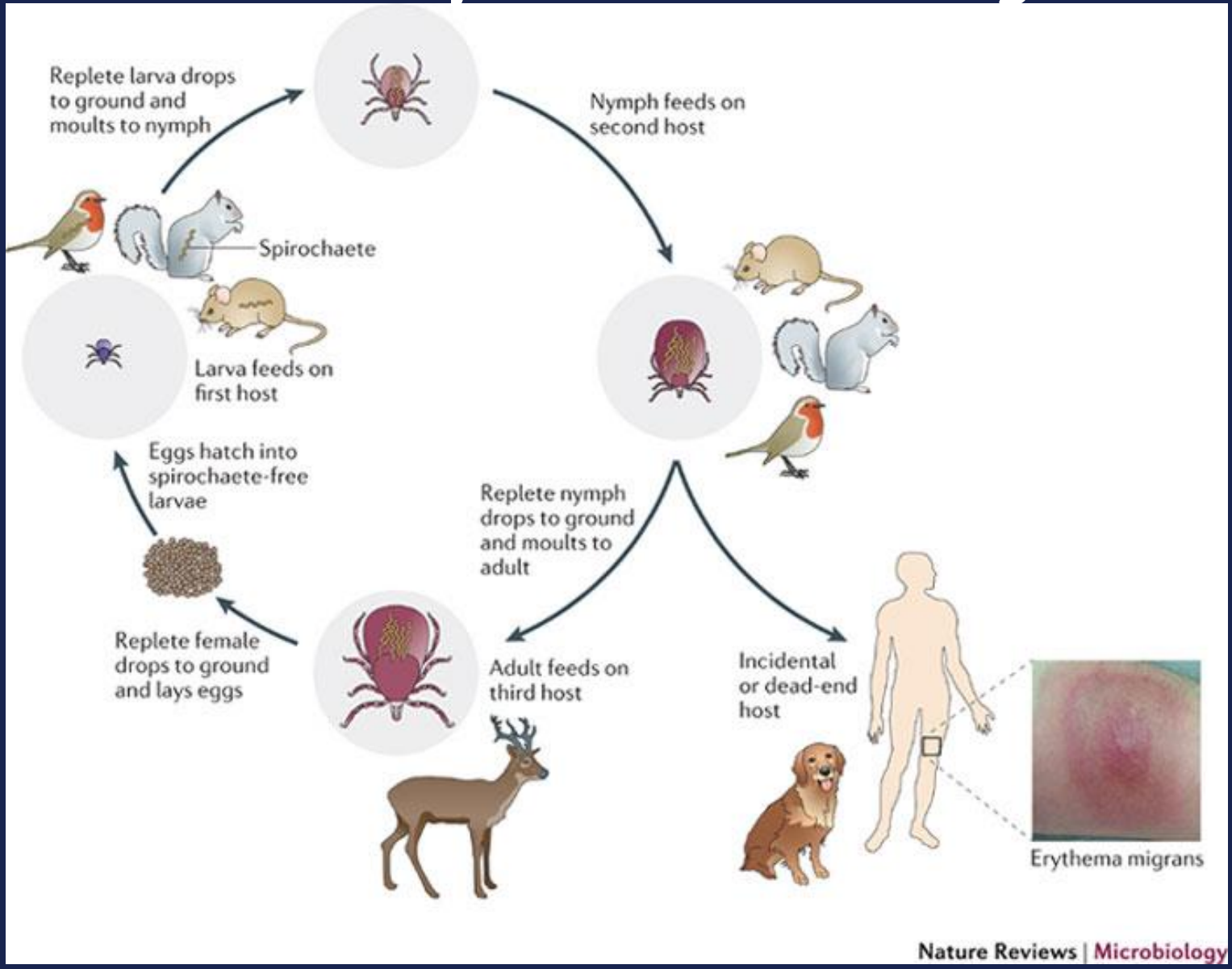
Causative Agent: Spirochete bacterium *Borrelia burgdorferi* sensu stricto in US (5 other *Borrelia* sp in Europe or Asia)

Vectors: Blacklegged tick (deer tick), *Ixodes scapularis,* and western blacklegged tick, *Ixodes pacificus,* on Pacific Coast

Incubation Period: 3-32 days after exposure (mean 7-10 days) for EM rash and/or flu-like symptoms

Transmission: Transmission generally does not occur until after tick has been attached for at least 36 hours

The Enzootic Cycle of *Borrelia burgdorferi*



www.nature.com/nrmicro/journal/v10/n2/fig tab/nrmicro2714 F1.html

Lyme Disease
Clinical Presentation

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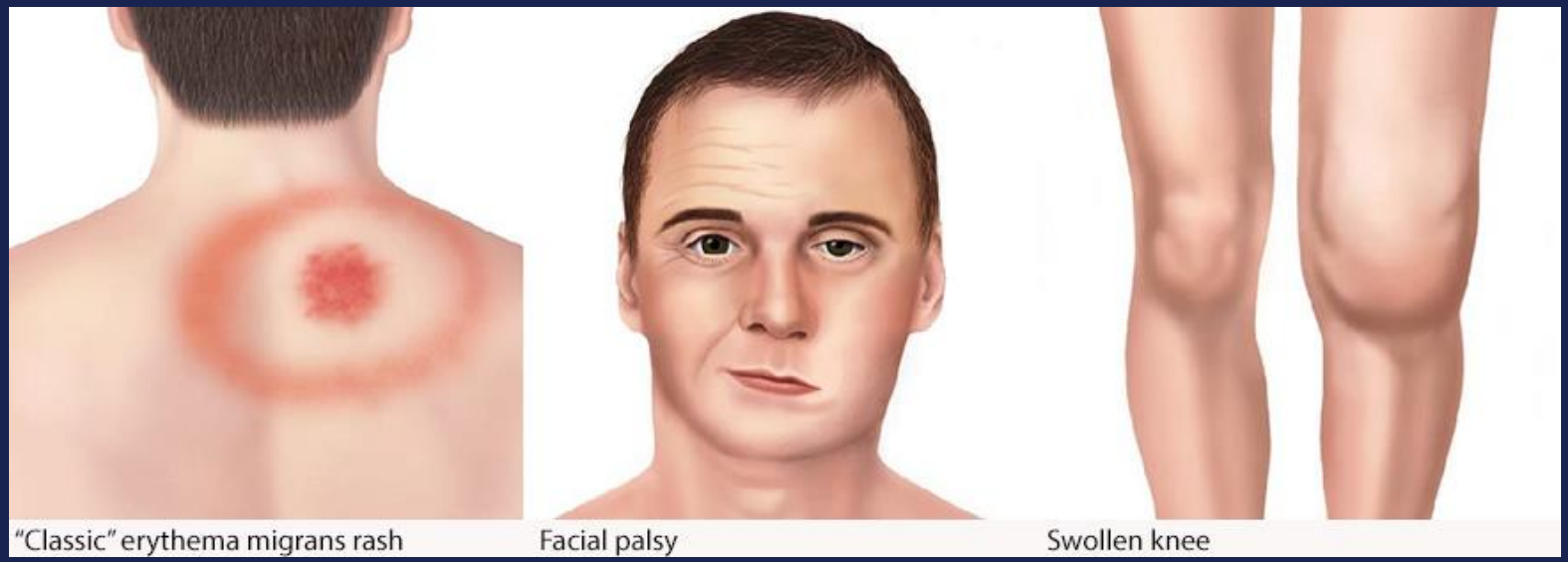
A systemic, tickborne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The best clinical marker for the disease is the initial skin lesion, erythema migrans (EM). For most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia.



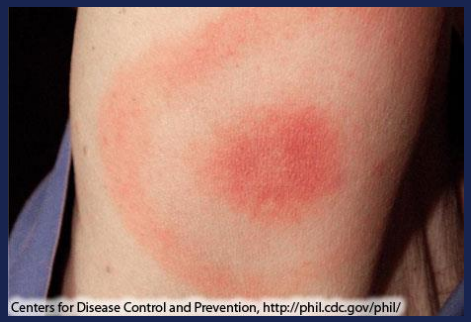
www.cdc.gov/lyme/signs_symptoms/index.html

Erythema Migrans (EM) Rash

www.cdc.gov/lyme/signs_symptoms/index.html

- Occurs in approximately 70 to 80 percent of infected persons
- Begins at the site of a tick bite after a delay of 3 to 30 days (average is about 7 days)
- Expands gradually over a period of days reaching up to 12 inches or more (30 cm) in diameter
- May feel warm to the touch but is rarely itchy or painful
- Sometimes clears as it enlarges, resulting in a target or "bull's eye" appearance
- May appear on any area of the body
- **Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM!**

Lyme Disease rashes and Look alikes:
www.cdc.gov/lyme/signs_symptoms/rashes.html



"classic" Lyme disease rash

Itchy rash due to insect bites

Lyme Disease
2018 Case Definition/Case Classification

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Confirmed: A case with physician diagnosed EM ≥ 5 cm in size with an **exposure** in a **high-incidence** state or country*,
OR a case of physician diagnosed EM ≥ 5 cm in size with laboratory confirmation with an exposure in a **low-incidence** state or country*,
OR a case with at least one late manifestation that has laboratory confirmation.

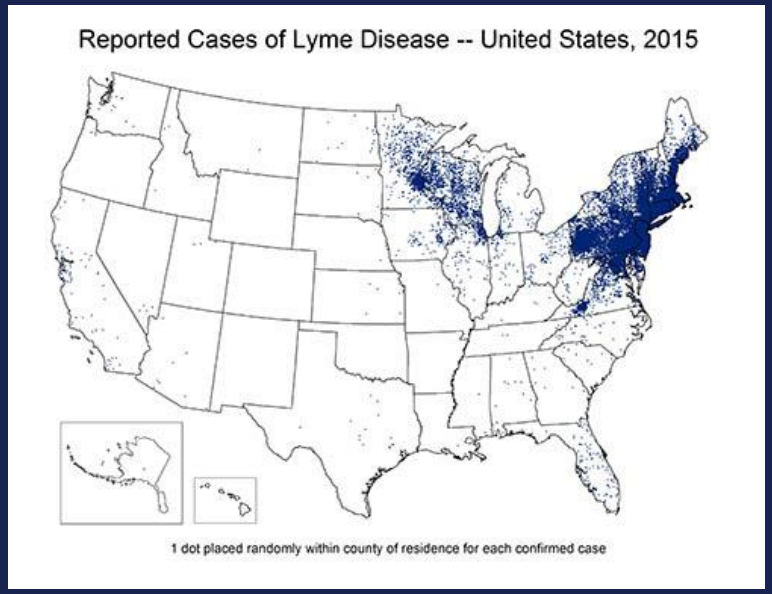
*Exposure is defined as having been (≤ 30 days before onset of EM) in wooded, brushy, or grassy areas (i.e., potential tick habitats). An exposure in a high-incidence state is defined as exposure in a state with an average Lyme disease incidence of at least 10 confirmed cases/100,000 persons for the previous three reporting years. A low-incidence state is defined as a state with disease incidence of <10 confirmed cases/100,000 persons for the previous three reporting years.
www.cdc.gov/lyme/stats/tables.html

Texas is considered a low incidence state for Lyme disease!

Lyme Disease
High Incidence Areas

- Most commonly reported vector-borne illness in the United States
- Does **not** occur nationwide and is concentrated heavily in the northeast and upper Midwest

High Incidence States:
Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, Wisconsin



www.cdc.gov/lyme/stats/index.html

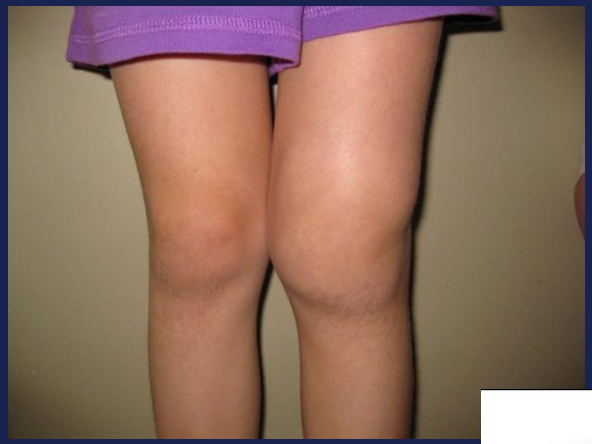
Outside of the US

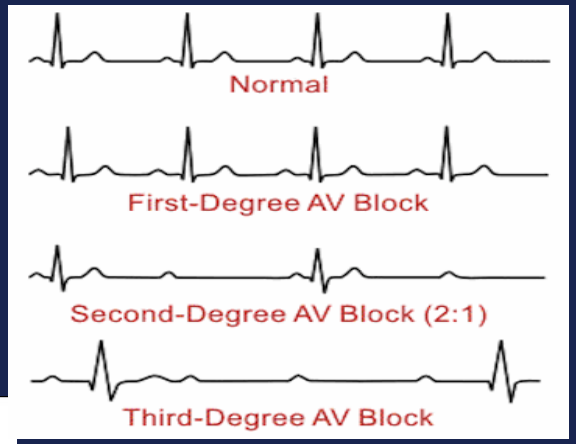
Lyme disease is common in some forested areas in Europe. Countries with highest reported incidence include **Germany, Austria, Slovenia, and Sweden.***

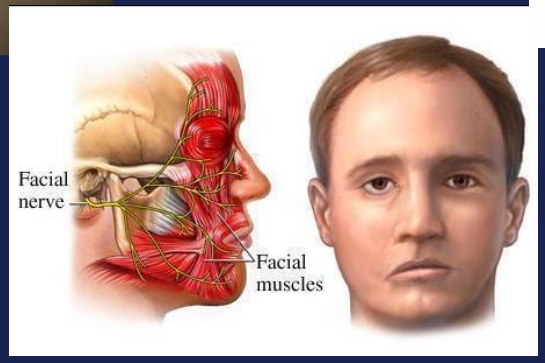
*Infectious Disease Clinics of North America, Vol. 22/Ed. 2, Fish AE, Pride YB, Pinto DS, Lyme carditis, 275-288

Lyme Disease
2018 Case Definition/Case Classification

Confirmed: A case with physician diagnosed EM ≥ 5 cm in size with an exposure in a high incidence state or country,
OR a case of physician diagnosed EM ≥ 5 cm in size with laboratory confirmation with an exposure in a low incidence state or country,
OR a case with at least one **late manifestation*** that has laboratory confirmation.







Lyme Disease
2018 Case Definition/Case Classification

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*For purposes of surveillance, late manifestations include any of the following **when an alternate explanation is not found:**
wwwn.cdc.gov/nndss/conditions/lyme-disease/case-definition/2017/

- **Musculoskeletal system**: recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints.
  - ***NOT:*** *chronic progressive arthritis not preceded by brief attacks; chronic symmetrical polyarthritis or arthralgia, myalgia, or fibromyalgia syndromes alone*

- **Nervous system**: any of the following, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (can be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis.
  - ***NOT:*** *headache, fatigue, paresthesia, or mildly stiff neck alone*

- **Cardiovascular system**: acute onset of high grade (2nd or 3rd degree) atrioventricular conduction defects that resolve in days to weeks and are sometimes associated with myocarditis.
  - ***NOT:*** *palpitations, bradycardia, bundle branch block, or myocarditis alone*

Lyme Disease
2018 Case Definition/Case Classification

***Probable**:* Any other clinically compatible* case of physician-diagnosed Lyme disease that has laboratory confirmation

**fever, chills, headache, fatigue, muscle & joint aches, swollen lymph nodes, EM rash*

Suspect: A case of EM with no known exposure and no laboratory evidence of infection, **OR** a case with laboratory evidence of infection, but no clinical information available

Note: Lyme disease reports will not be considered cases if the medical provider specifically states this is not a case of Lyme disease, or the only symptom listed is "tick bite" or "insect bite"

Lyme Disease Laboratory Confirmation Tests

Positive culture for *Borrelia burgdorferi*

OR

IgG immunoblot seropositivity using established criteria*

OR

IgM immunoblot seropositivity using established criteria*
with positive/equivocal EIA or IFA test
AND specimen collected ≤30 days after symptom onset

Notes:

- *CDC Immunoblot interpretation criteria
- While a single IgG WB is adequate for surveillance purposes, a two tier test is still recommended for patient diagnosis.

Lyme Disease
Immunoblot (Western Blot)
CDC Interpretation Criteria

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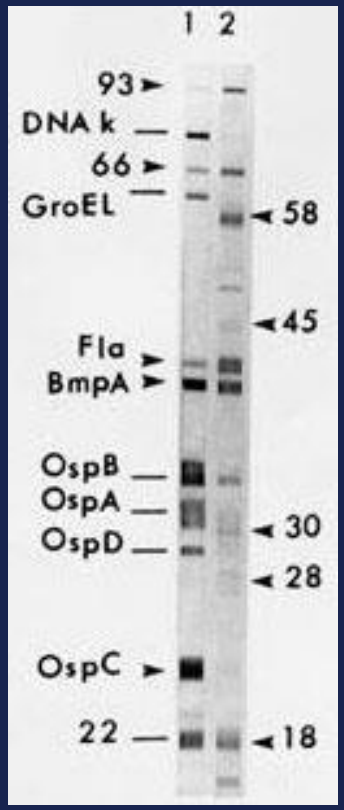
IgM immunoblot

- Considered positive if 2 of the following 3 bands are present: 24 kDa (*OspC), 39 kDa (BmpA), and 41 kDa (Fla)

IgG immunoblot

- Considered positive if 5 of the following 10 bands are present: 18 kDa, 24 kDa (*OspC), 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa (Fla), 45 kDa, 58 kDa, 66 kDa, and 93 kDa



wwwn.cdc.gov/nndss/conditions/lyme disease/case definition/2017/
*Depending upon the assay, OspC could be indicated by a band of 21, 22, 23, 24 or 25 kDA

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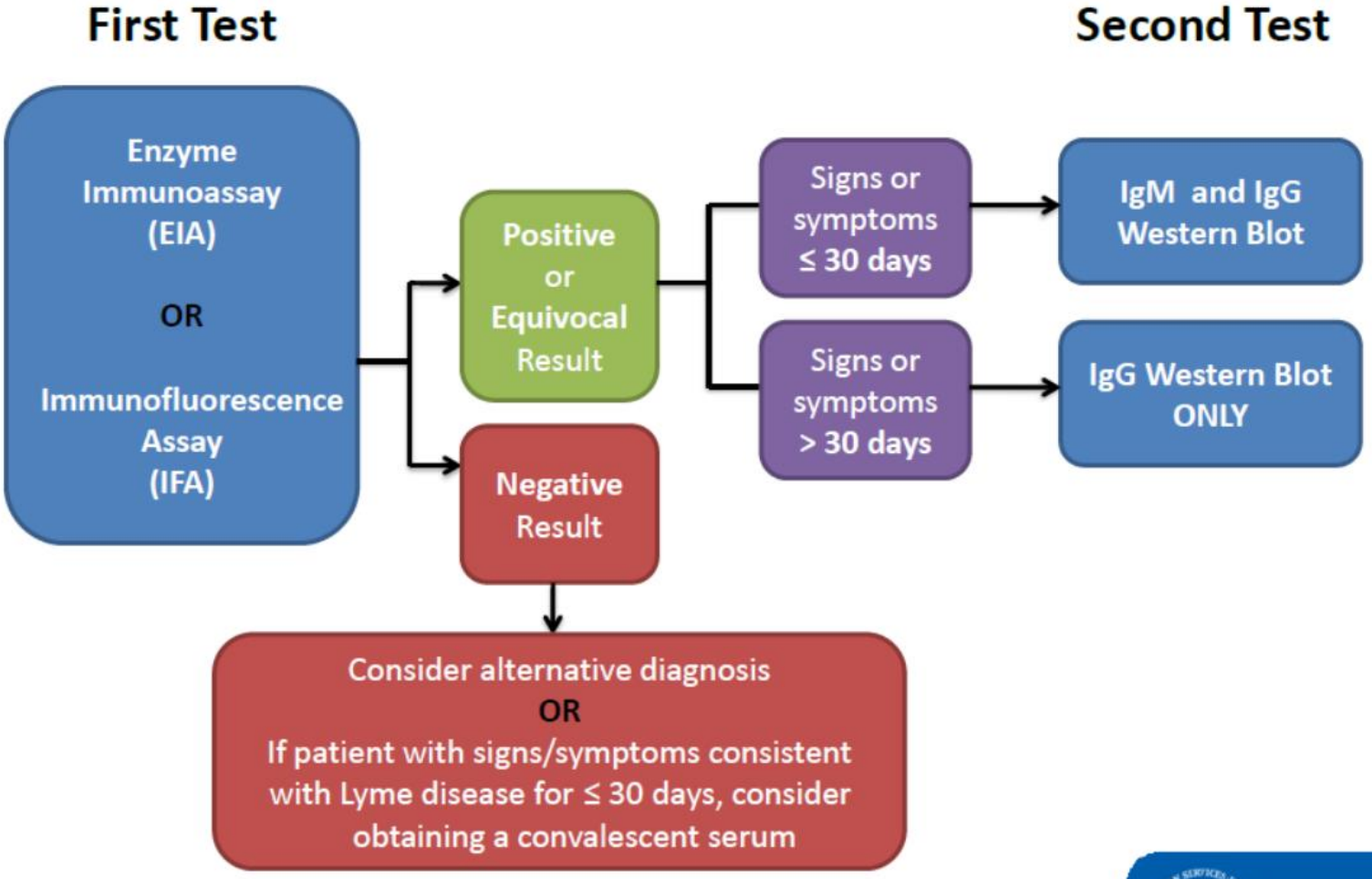
Two-Tiered Testing for Lyme Disease



National Center for Emerging and Zoonotic Infectious Diseases
Division of Vector Borne Diseases | Bacterial Diseases Branch

CDC

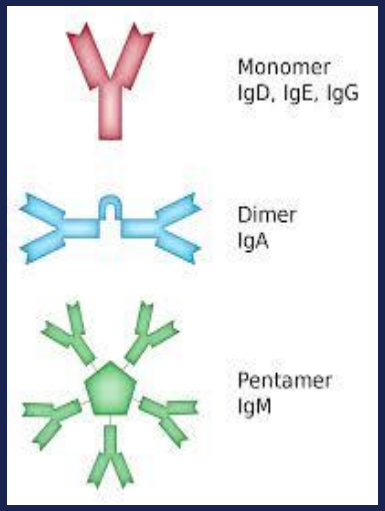
https://www.cdc.gov/lyme/diagnosistesting/labtest/twostep/index.html

Lyme Disease
ELISA or EIA (Screen)

- **False-negative results common if tested too early**
  - Only 50% sensitivity if test taken within first two weeks of infection
  - Patients with EM typically seronegative
- **Sensitivity of screen is very good AFTER the EM stage of illness**
  - Antibody levels may remain elevated for months to years after treatment!
- **False positive results are an issue also - some possible causes of false-positive screening tests include:**
  - Tick-borne relapsing fever
  - Syphilis (*Treponema pallidum*)
  - Periodontal disease (*Treponema denticola*)
  - Systemic lupus erythematosus
  - Acute Epstein-Barr virus infection
  - *Helicobacter pylori*
  - Subacute bacterial endocarditis
  - Rheumatoid arthritis

Lyme Disease
IgM Immunoblot Issues

- Omitting the screen and using immunoblot only decreases specificity of serological testing!
  - Immunoblot will NOT be done if screen is negative
  - With NO screen, more immunoblots will be run – some will be false positives
  - Erroneous scoring of a faint band is a common reason for false-positive readings
  - IgM results more affected by this problem:
    - IgM Abs are more non-specifically "sticky" than IgG Abs
    - Only 2 of 3 bands are required for an IgM to be reported as positive (as opposed to 5 of 10 for IgG)
    - "A single erroneously scored faint band will affect IgM results more readily than it will affect IgG results."

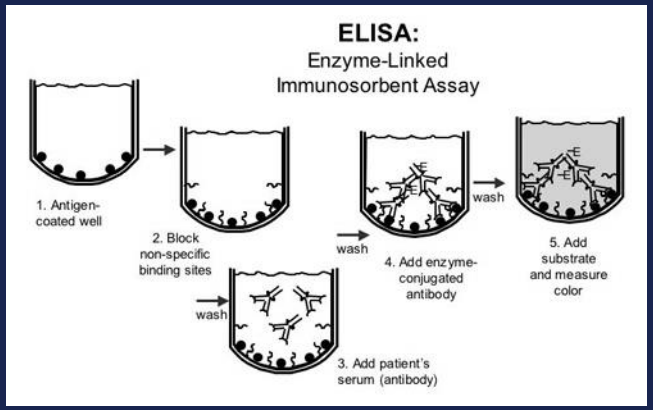


Johnson, B.J. "Chapter 4: Laboratory diagnostic testing for *Borrelia burgdorferi* infection" in Lyme disease: An Evidence-based Approach, J.J. Halperin, Ed. (CAB International, 2011). Complete Article Reproduced with Permission

Examples of Lyme Screens and Immunoblots

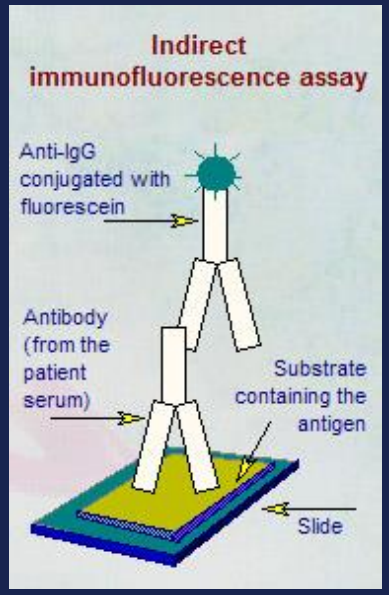
Lyme Screens (EIA/ELISA/IFA):

- **Lyme disease (Borrelia burgdorferi) Antibody Screen:**
  1.22 (Final)
- **Borrelia burgdorferi Ab.IgG+IgM:**
  1.47 index
- **Borrelia burgdorferi Ab.IgM:**
  0.94 index
- **BORRELIA BURGDORFERI AB**:
  Positive
  80
  Lyme IFA Screen



Immunoblots (Western Blots)

- **Borrelia burgdorferi Ab.IgM band pattern:**
  Positive
- **B BURGDOR IGG SER QL IB:**
  Positive
- **Borrelia burgdorferi antibody band pattern:**
  Lyme IgG Western Blot bands 30, 39, 41, 45, and 58 present
  positive
- **Borrelia burgdorferi 28kD Ab.IgG:** Present or Absent (*Labcorp there will be a separate ELR for all 10 bands*)



Lyme Disease
Laboratory Tests That Are NOT Recommended

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Some laboratories offer Lyme disease testing using assays for which the accuracy and clinical usefulness have NOT been adequately established.

Examples of unvalidated tests include:

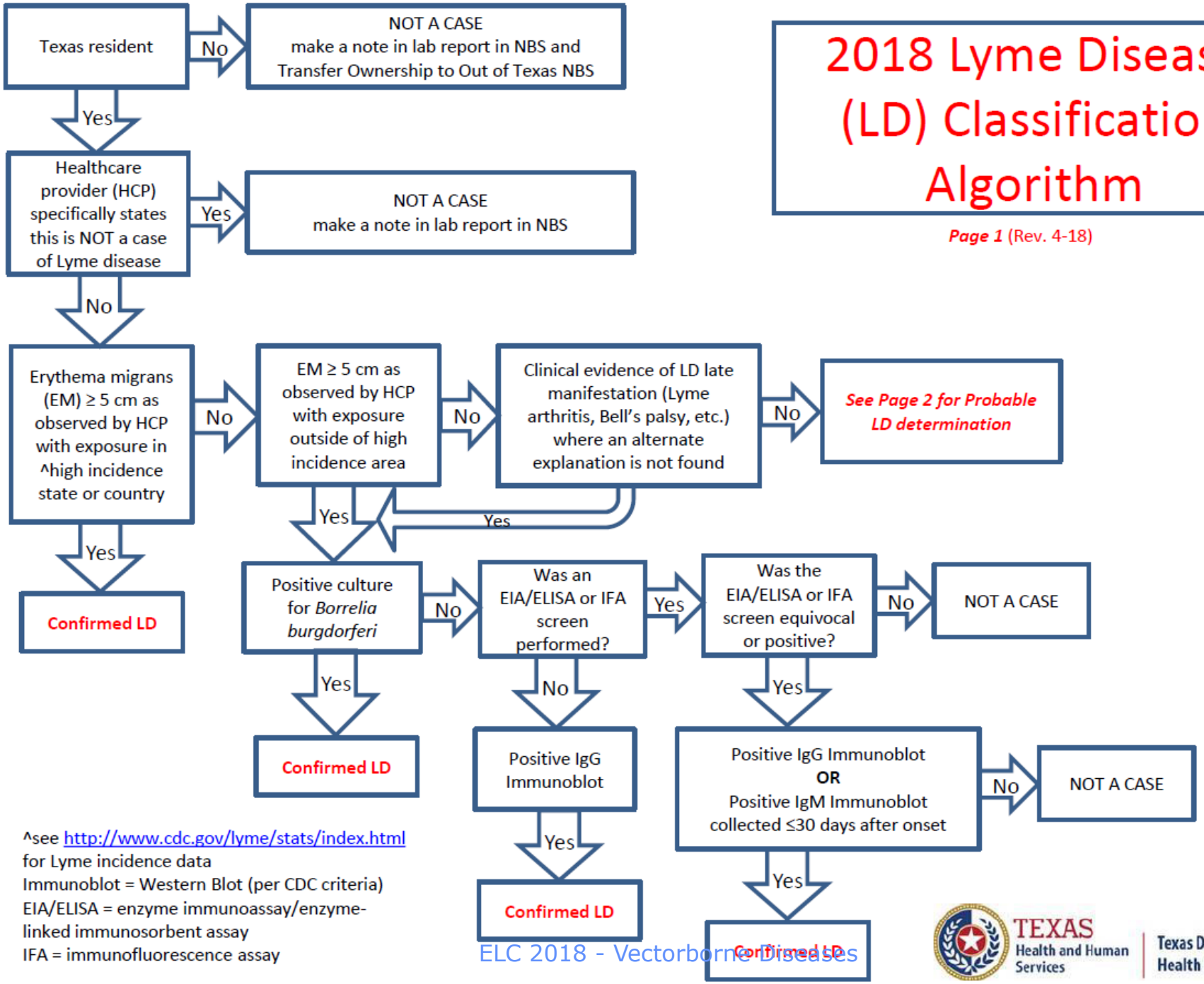
- Capture assays for antigens in urine
- Culture, immunofluorescence staining, or cell sorting of cell wall deficient or cystic forms of *B. burgdorferi*
- Lymphocyte transformation tests
- Quantitative CD57 lymphocyte assays
- "Reverse Western blots"
- In house criteria for interpretation of immunoblots
- Measurements of antibodies in joint fluid (synovial fluid)
- IgM immunoblot tests without a previous ELISA/EIA/IFA
- Lyme CSF Ab tests

www.cdc.gov/lyme/diagnosistesting/labtest/otherlab/index.html

www.medscape.com/viewarticle/764501?src=par_cdc_stm_mscpedt&faf=1
PCR testing has limitations…DNA testing does not distinguish between living and dead organisms, and laboratory contamination with amplified DNA poses a risk for false-positive results…Is PCR useful for the diagnosis of Lyme disease? In general, the answer is no.

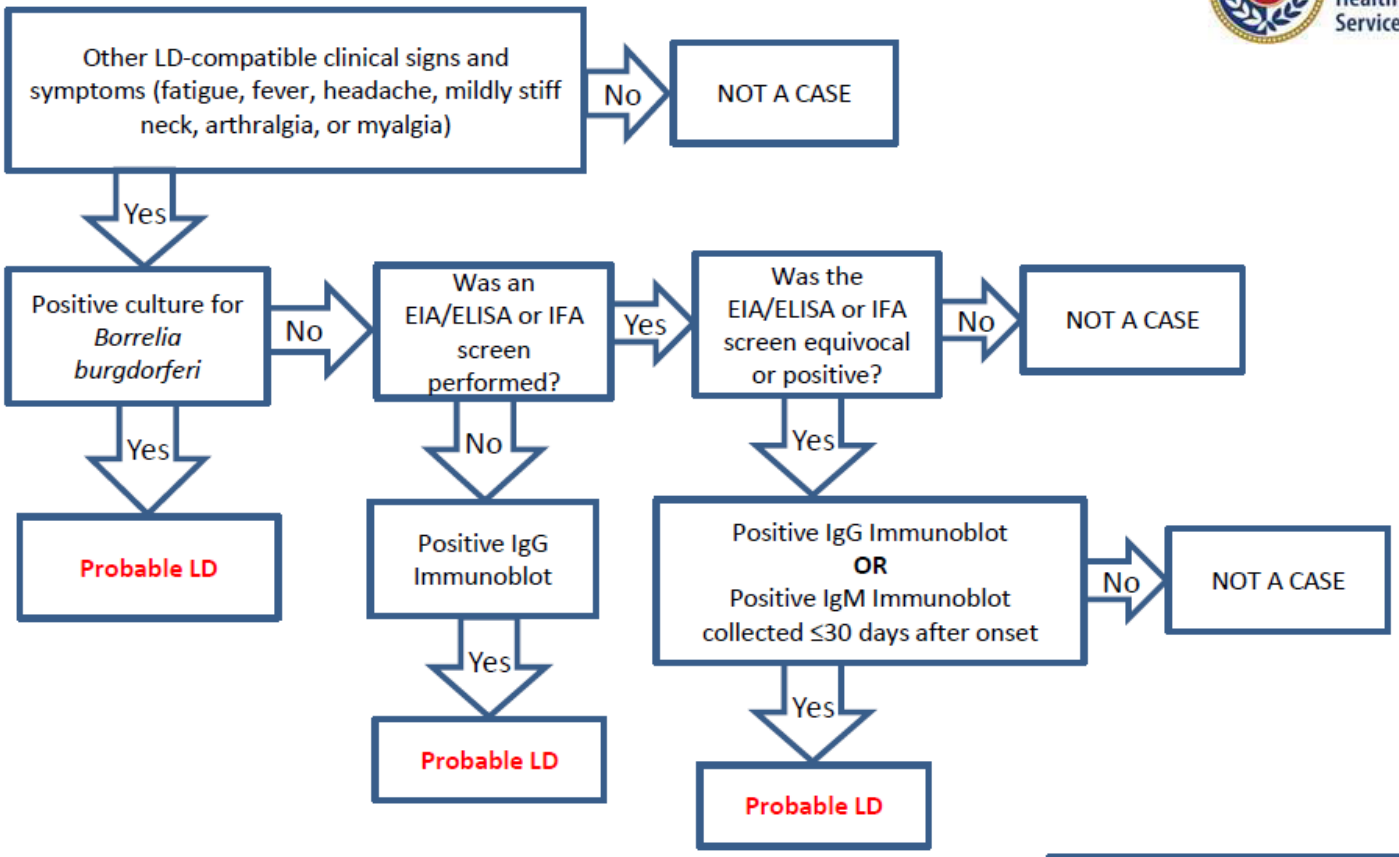
2018 Lyme Disease (LD) Classification Algorithm

Page 1 (Rev. 4-18)



^see http://www.cdc.gov/lyme/stats/index.html for Lyme incidence data
Immunoblot = Western Blot (per CDC criteria)
EIA/ELISA = enzyme immunoassay/enzyme-linked immunosorbent assay
IFA = immunofluorescence assay

(Continued from page 1)



2018 Lyme Disease (LD) Case Classification Algorithm

^see http://www.cdc.gov/lyme/stats/index.html for Lyme incidence data
Immunoblot = Western Blot (per CDC criteria)
EIA/ELISA = enzyme immunoassay/enzyme-linked immunosorbent assay
IFA = immunofluorescence assay

Lyme Disease Case Investigation

- IgM positive blot is only relevant if screen performed and was equivocal or positive
- Onset date important!
  - IgM positive blot only relevant if specimen collected ≤30 days after symptom onset
- Make sure all lab reports are in NEDSS
- Physician does not have to definitively diagnose patient with Lyme disease ("will not be considered cases if the medical provider specifically states this is *not* a case of Lyme disease")
- Inquire about travel history!
- Consider "alternate explanation"
  - Rheumatoid arthritis, lupus, etc.
- Make sure all required fields are completed in NEDSS (*refer to Data Entry Guidelines – Quick Reference section for patient demographics/lab report*)

Useful Resources

- DePietropaolo DL, Powers JH, Gill JM. **Diagnosis of Lyme Disease.** Am Fam Physician. 2006 Mar 1;73(5):776.
  - clinical recommendations, how to determine pre-test probability, interpretation of serologic testing
- Lantos PM, et al. **Poor Positive Predictive Value of Lyme Disease Serologic Testing in an Area of Low Disease Incidence.** Clin Infect Dis. 2015 Nov 1;61(9):1374-80. doi: 10.1093/cid/civ584. Epub 2015 Jul 20.
  - study on positive predictive value of two-tiered testing
- www.cdc.gov/lyme/
  - signs and symptoms, treatment, diagnosis and testing, data and statistics, transmission, post-treatment Lyme disease syndrome, info for healthcare providers, educational materials, tick bite/removal/testing info
- www.dshs.state.tx.us/idcu/disease/lyme/
  - overview, data, resources

Scenario 1

- **Patient**
  - 39 yo male that resides in Central Texas; denies outdoor activity, other than sitting in back yard with dog at night (backyard faces woods); did travel to Indiana for a wedding 3 weeks prior but spent no time outdoors
- **Clinical Information**
  - Fever/sweats/chills, arthralgias, myalgias, neck pain, fatigue, adenopathy, confusion, Bell's palsy, radiculoneuropathy
- **Lab results**
  - Lyme EIA screen positive/IgM WB positive
  - WNV IgM positive at CPL (6.85 acute, 1.95 conval)
  - Dengue IgM negative
- **Diagnosis**
  - Subacute disseminated Lyme disease

Scenario 1 (cont.)

- Requested follow up testing at CDC
- PRNT at CDC:
  - Negative for DEN, SLE, WNV, ZIKV
- Tick-borne Relapsing Fever
  - TBRF EIA & WB **Positive**!
- Classified as "Not a Case" for Lyme Disease

Scenario 2

- **Patient**
  - 12 yo male that resides in South Texas – no recent travel outside of county of residence
- **Clinical Information**
  - Arthralgias, fatigue, muscle weakness, myalgia, shortness of breath
  - Symptom onset gradual, followed tick bite months prior
- **Lab results**
  - Lyme EIA screen equivocal/IgM WB positive (IgG negative)
  - DOC in March (onset in prior year)
- **Diagnosis**
  - Early disseminated Lyme disease (med records state "previously negative for Lyme disease and is IgG and IgM positive and confirmed by reflex testing")

Scenario 2

- Classified as **Not a Case**

- Lab results
  - Lyme EIA screen equivocal/IgM WB positive (IgG negative)
  - DOC in March (onset in prior year)
  - IgM blot is not relevant if onset is more than 30 days prior to DOC!

Scenario 3

- **Patient**
  - 45 yo female that resides in East Texas
  - No travel outside of Texas
  - Frequently walks in park
- **Clinical information**
  - Fever, headache, arthralgias, fatigue, myalgias
- **Lab results**
  - IgG WB positive
  - DOC in July (onset mid-February)
- **Diagnosis**
  - Not stated in med records, but patient was treated with doxycycline for 2 weeks

Scenario 3

- Classified as **Probable** Lyme Disease case
  - No EM or late manifestation
- Lab results
  - IgG WB positive
- Confirmatory: IgG immunoblot seropositivity using established criteria
- While a single IgG WB is adequate for surveillance purposes, a two-tier test is still recommended for patient diagnosis

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Rickettsial Disease Diagnostics and Epidemiology

Bonny Mayes, MA, RYT
Zoonosis Control Branch
Department of State Health Services
Austin, Texas

Rickettsial Infections
Spotted Fever & Typhus Groups

Typhus Group

- *Rickettsia prowazekii* (louse-borne, epidemic, sylvatic typhus)
- ***R. typhi* (flea-borne, endemic, murine typhus)**

Spotted Fever Group (tick borne)

- *R. aeschlimannii* (Rickettsiosis)
- *R. africae* (African tick-bite fever)
- *R. australis* (Queensland tick typhus)
- *R. conorii* (Mediterranean spotted fever, Boutonneuse fever)
- *R. heilongjiangensis* (Far Eastern spotted fever)
- *R. Helvetica* (Aneruptive fever)
- *R. honei* (Flinders Island spotted fever, Thai tick typhus)
- *R. japonica* (Japanese spotted fever)
- *R. marmionii* subspecies (Australian spotted fever)
- *R. massiliae* (Mediterranean spotted fever-like disease)
- ***R. parkeri* (Maculatum infection)**
- ***R. rickettsii* (Rocky Mountain Spotted Fever)**
- *R. sibirica* (North Asian tick typhus, Siberian tick typhus)
- *R. sibirica mongolotimonae* (Lymphangitis-associated rickettsiosis)
- *R. slovaca* (Tickborne lymphadenopathy)
- ***Rickettsia* species 364D**

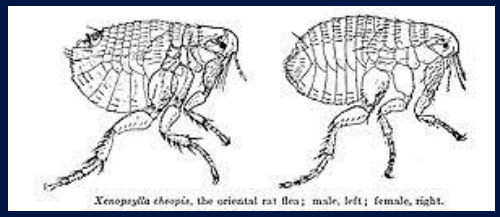
http://www.microbeworld.org/index.php?option com_jlibrary&view article&id 3343

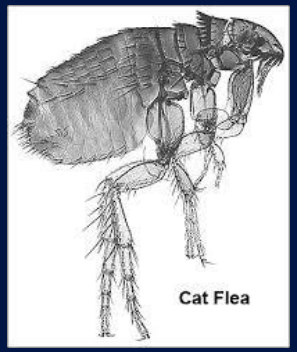
http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious diseases related to travel/rickettsial spotted typhus fevers related infections anaplasmosis ehrlichiosis

http://www.cdc.gov/otherspottedfever/

Flea-borne Typhus

- **Etiologic Agent**:
  - bacterium *Rickettsia typhi* (and possibly *R. felis*)
- **Vectors:**
  - primarily rat fleas (*Xenopsylla cheopis*) and cat fleas (*Ctenocephalides felis*)
- **Reservoirs:**
  - rats, opossums, domestic cats, and other small mammals
- **Modes of transmission:**
  - transmission to humans can occur when flea feces*, containing the bacteria, are scratched into the bite site or other abrasion in the skin, or are rubbed into the conjunctiva
  - another possible mode of transmission is inhalation of dried rat or cat flea feces*





*Infection by *R. felis* has been attributed to flea saliva rather than feces
http://www.ehtjournal.net/index.php/ehtj/article/view/7168/9204#CIT0013

Flea-borne Typhus History

- Also known as murine or endemic typhus
- Worldwide distribution
- First identified in the United States in 1913
- Over 5,000 cases were reported annually through the mid-1940's mainly in SE states and California
- 1945 US Public Health Service initiated campaign to control rats and their fleas – by late 1980's, case counts reduced to less than 100 cases/yr
- Most states discontinued reporting flea-borne typhus after the drastic reduction of cases
- Not nationally reportable, so reliable case counts are not known
- Still reportable in some states, including Texas, California and Hawaii, where the majority of cases are thought to occur

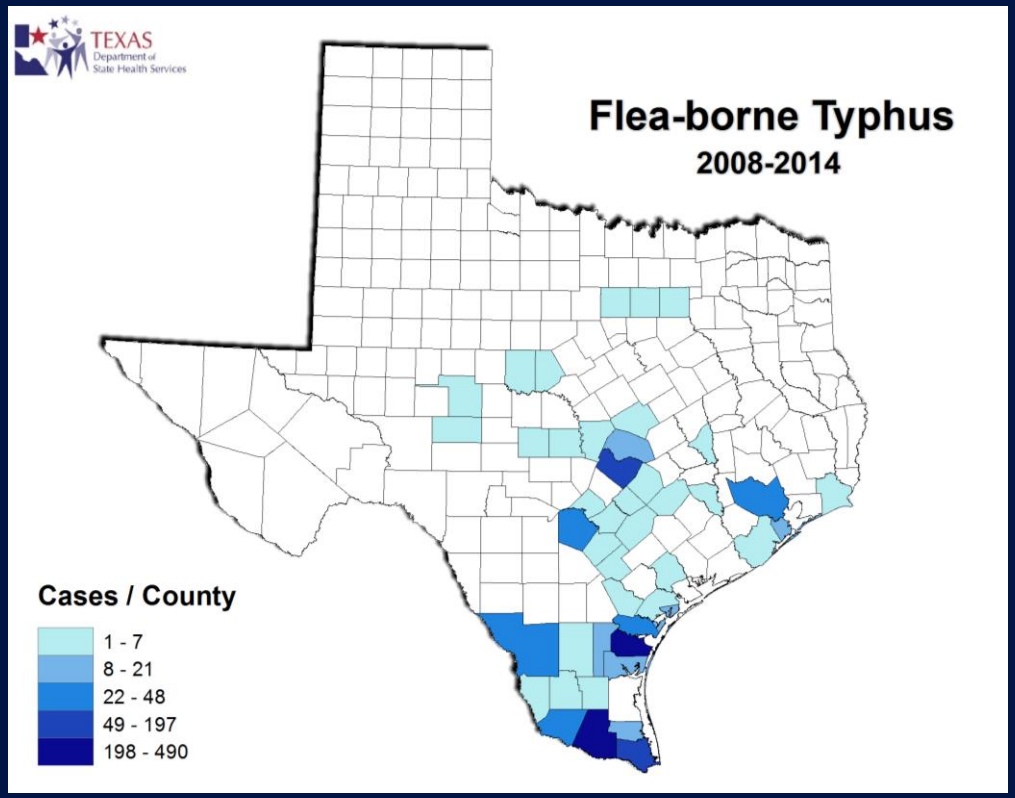
Flea-borne Typhus Disease in Humans

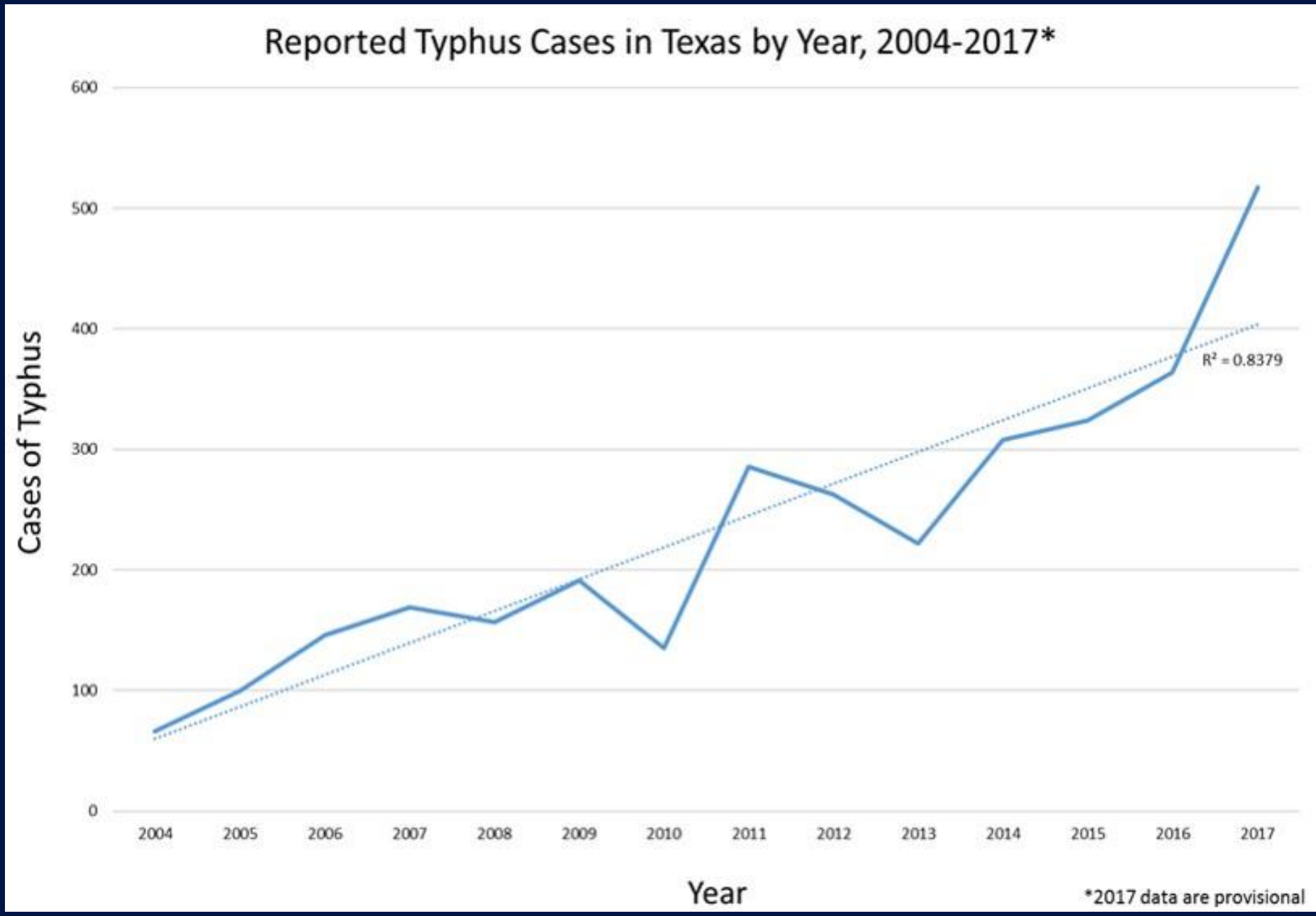
- Symptoms occur from 6 to 14 days after exposure
- Most common symptoms include:
  - Fever
  - Headache
  - Malaise
  - Anorexia
  - Myalgia
  - Nausea and/or vomiting
  - Rash – occurs in ~50% of those infected
    - Generally starts on trunk and spreads to the arms and legs but usually does not occur on the face, palms or soles
  - Thrombocytopenia*
  - Elevated liver enzymes**
- Typhus-associated deaths are rare but may occur in 5% of those infected

**reported in 16% of cases in Texas, 2003 2013*
*** reported in 27% of cases in Texas, 2003 2013*

Flea-borne Typhus Epidemiology in Texas

- Flea-borne typhus has been included in the Annual Summary of Notifiable Diseases in Texas since 1946
- From 1946 to 2014, there were 6,729 cases reported (mean=97.5); highest number of cases reported in 1946 (n=1147) and lowest in 1994 (n=9)
- Typhus cases occur year round, but majority of cases occur from May to July
- Most cases occur in the southern portion of the state, from Nueces County southward to the Rio Grande Valley




Reported Typhus Cases in Texas by Year, 2004-2017*
Cases of Typhus
600
500
400
300
200
100
0
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Year
R² = 0.8379
*2017 data are provisional

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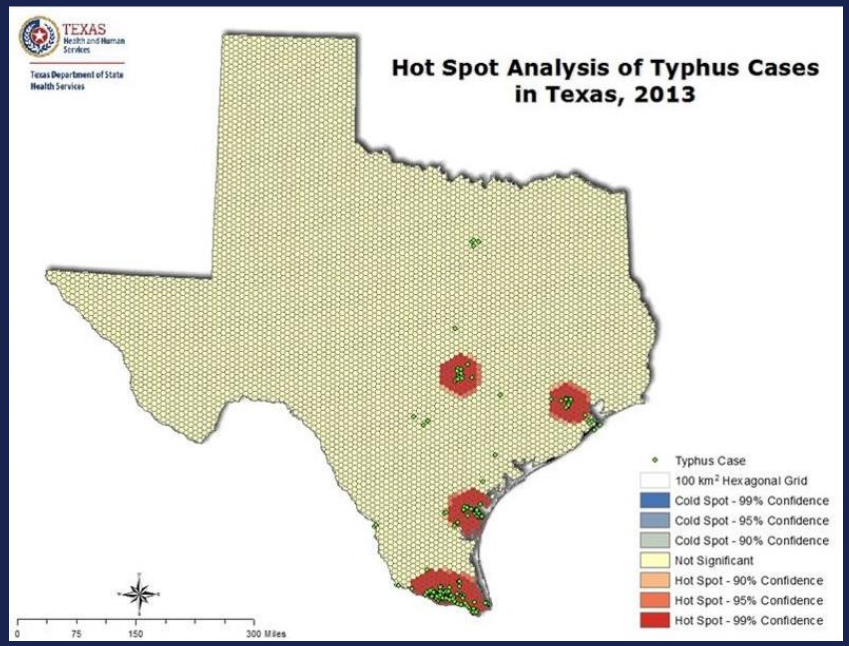
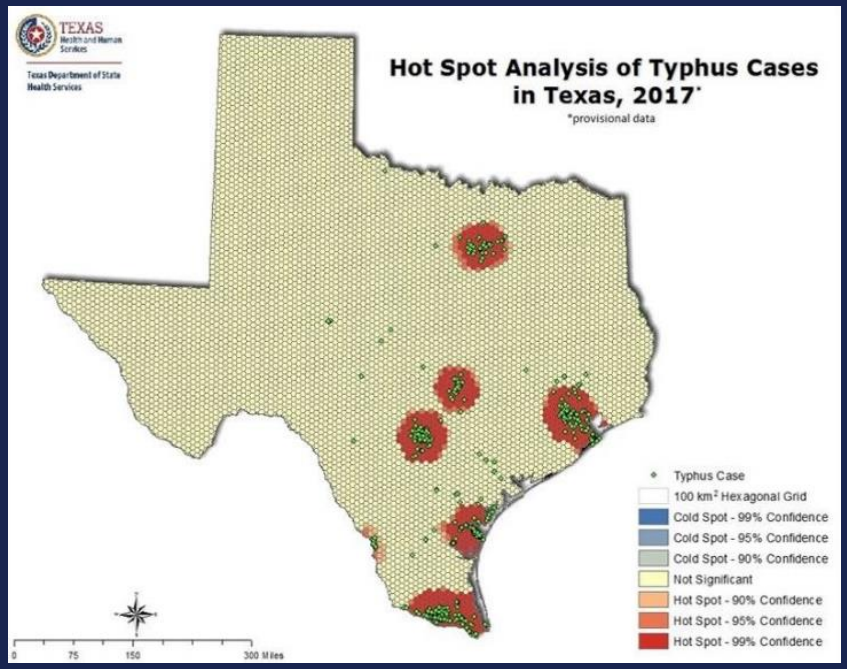


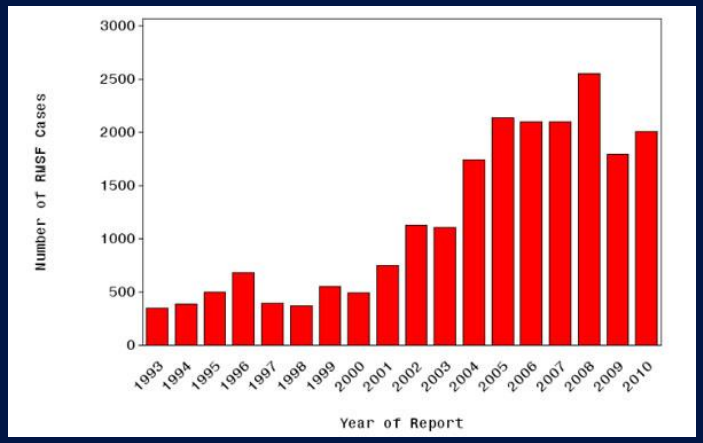


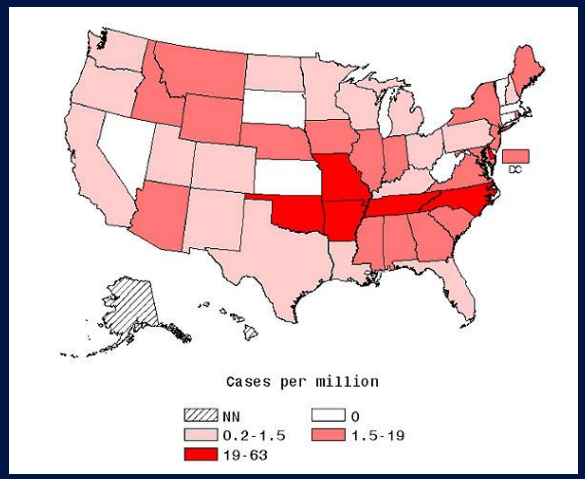
Tick-borne Spotted Fever Group Rickettsia (SFGR)

- **Etiologic Agents (in the U.S.)**:
  - *Rickettsia* sp. Bacteria
    - *Rickettsia rickettsii* (Rocky Mountain Spotted Fever)
    - *Rickettsia parkeri* (Maculatum infection)
    - *Rickettsia* species 364D (Eschar-associated illness)
    - *Rickettsia amblyommii?? (detected in many ticks; pathogenicity has not been determined)*
- **Vectors:**
  - *Rickettsia rickettsii* - mainly:
    - The American dog tick (*Dermacentor variabilis*), Rocky Mountain dog tick (*Dermacentor andersoni*), brown dog tick (*Rhipicephalus sanguineus*), cayenne tick (*Amblyomma cajennense*)
  - *Rickettsia parkeri*:
    - Gulf Coast tick (*Amblyomma maculatum*)
  - *Rickettsia* species 364D
    - Pacific Coast tick (*Dermacentor occidentalis*)
- **Reservoirs:**
  - ticks; dogs and rodents
- **Modes of transmission:**
  - transmitted to a vertebrate host via the bite of an infected tick
  - generally, the tick must be attached and feeding for about 24 hours before the bacteria can be transmitted to the host

SFGR History

- **Rocky Mountain spotted fever (RMSF)**, the protypic disease of the spotted fever group, has been a reportable disease in the US since the 1920's
- This disease was first described in the Rocky Mountain region of the US, but has been reported throughout most of the contiguous US
- The majority of cases (>60%) are reported from only five states (North Carolina, Oklahoma, Arkansas, Tennessee and Missouri)





www.cdc.gov/rmsf/stats/

- As of 2010, RMSF has been included in a broader category called Spotted Fever Group Rickettsiosis (SFGR) many of the cases being reported as RMSF were not actually identified as being specifically *Rickettsia rickettsii*

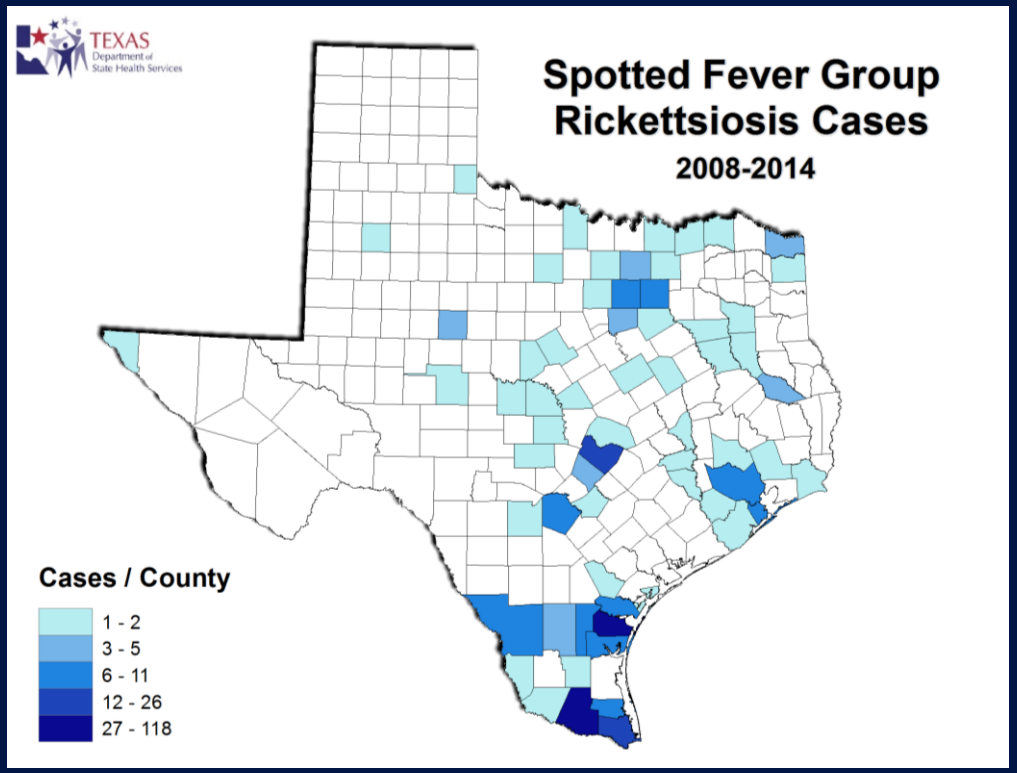
SFGR
Disease in Humans

- Disease onset averages one week following the bite of an infected tick (*for RMSF, first symptoms typically begin 2-14 days after tick bite*)
- Most common symptoms include:
  - Fever
  - Headache
  - Myalgia
  - Anemia
  - Myalgia
  - Nausea and/or vomiting
  - Rash – occurs in >80% of those infected with RMSF
    - generally starts on ankles and wrist and spreads to the torso; often present on the palms and soles
  - Thrombocytopenia
  - Elevated liver enzymes
- RMSF can be fatal in as many as 20% of untreated cases

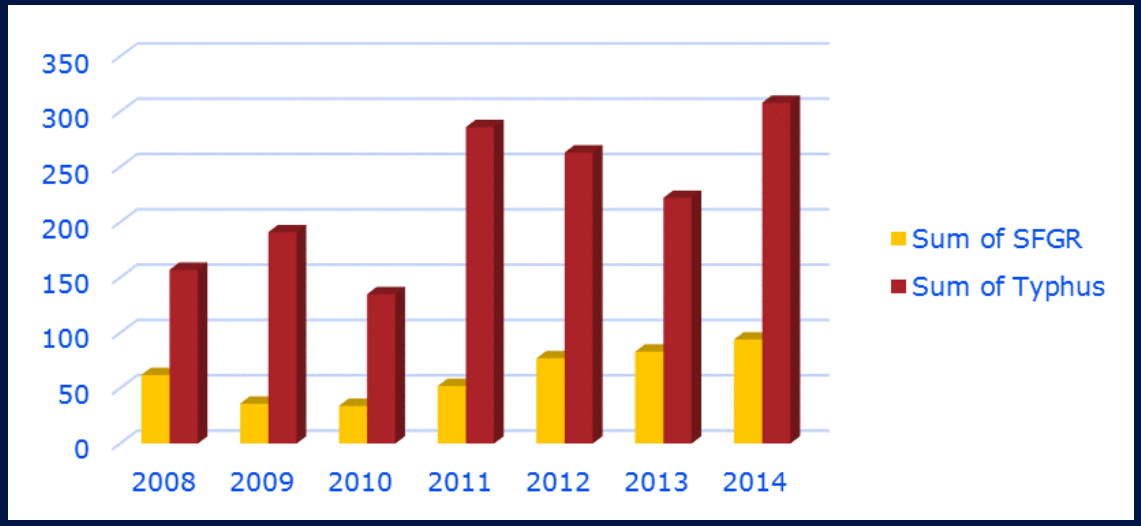
Spotted Fever Epidemiology in Texas

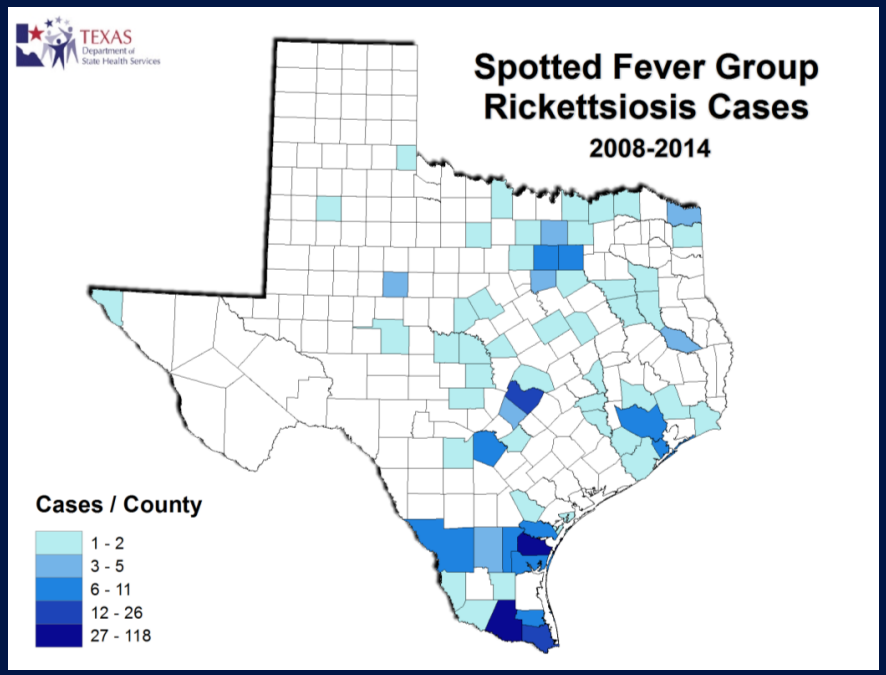
- Rocky Mountain Spotted Fever/Spotted Fever Group Rickettsiosis has been included in the Annual Summary of Notifiable Diseases in Texas since 1951

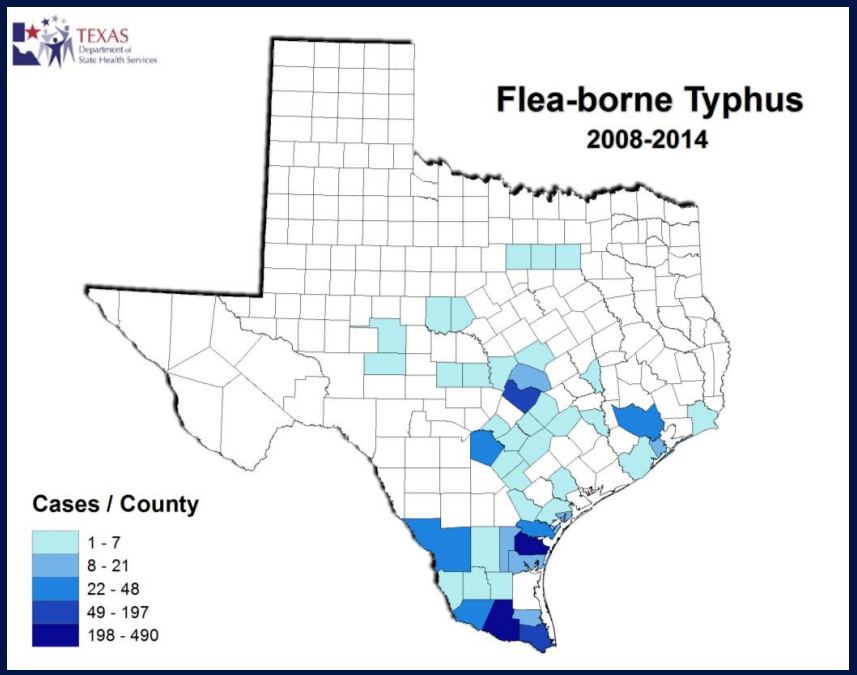
- From 1951 to 2014, there were 1,353 cases reported (mean=21); highest number of cases reported in 1983 (n=108) and lowest in 1958, 1962, 1965 and 2001 (n=0)



Flea-borne Typhus and SFGR in Texas, 2008-2014







Flea-borne Typhus Epi Case Criteria 2018 Case Definition/Case Classification

Flea-borne typhus is a rickettsial disease whose course resembles that of louse-borne typhus, but is generally milder. The onset is variable, often sudden and marked by headache, chills, fatigue, fever and general pains. A macular rash may appear on the 5th or 6th day, initially on the upper trunk, followed by spread to the entire body, but usually not to the face, palms or soles. Absence of louse infestation, geographic and seasonal distribution, and sporadic occurrence of the disease help to differentiate it from louse-borne typhus.

Flea-borne Typhus Epi Case Criteria 2018 Case Definition/Case Classification (cont.)

Clinical evidence: Any reported acute onset of fever and one or more of the following: headache, myalgia, anorexia, rash, nausea/vomiting, thrombocytopenia, or any hepatic transaminase elevation.

Confirmed: Clinically compatible case that is laboratory confirmed

Probable: Clinically compatible case with supportive laboratory results:

- IFA serologic titer of ≥1:128, **OR**
- A single CF of >16, **OR**
- Other supportive serology (single titer ≥1:128 by an LA, IHA, or MA test)

Note: Because serologies for rickettsial diseases can be cross-reactive, specimens should be tested against a panel* of *Rickettsia* antigens, including, at a minimum, *R. rickettsia* and *R. typhi*, to differentiate between SFGR and non-SFGR *Rickettsia* spp. In addition, according to CDC, Rickettsial IgM tests lack specificity (resulting in false positives); thus, IgG titers are considered to be much more reliable.

** Specimens can be forwarded to the DSHS Serology lab for Rickettsial panel testing.*

Flea-borne Typhus Epi Case Criteria 2018
Laboratory Confirmation Tests

Serological evidence of an elevation (four-fold change) in immunoglobulin G (IgG)-specific antibody titer reactive with *R. typhi* or *R. felis* by IFA, complement fixation (CF), latex agglutination (LA), microagglutination (MA), or indirect hemagglutination antibody (IHA) test in acute – and convalescent – phase specimens ideally taken at least 3 **weeks apart,**

OR

Positive PCR assay to *R. typhi* or *R. felis,*

OR

Demonstration of positive *R. typhi* or *R. felis* IF of skin lesion (biopsy) or organ tissue (autopsy),

OR

Isolation of *R. typhi* or *R. felis* from clinical specimen

SFGR Epi Case Criteria 2018
Case Definition/Case Classification

Spotted fever group rickettsioses (SFGR) are a group of tick borne infections caused by some members of the genus *Rickettsia*. The most well known SFGR is Rocky Mountain spotted fever (RMSF), an illness caused by *Rickettsia rickettsii*. Disease onset for RMSF averages one week following a tick bite. Illness is characterized by acute onset of fever and can be accompanied by headache, malaise, myalgia, nausea/vomiting, or neurologic signs; a macular or maculopapular rash may appear 4 7 days following onset in many (~80%) patients, often present on the palms and soles. RMSF can be fatal in as many as 20% of untreated cases, and severe fulminant disease can occur. In addition to RMSF, human illness associated with other spotted fever group *Rickettsia* species, including infection with *Rickettsia parkeri*, has also been reported. In these patients, clinical presentation appears similar to, but can be milder than, RMSF; the presence of an eschar at the site of tick attachment has been reported for some other SFGR.

SFGR Epi Case Criteria 2018
Case Definition/Case Classification (cont.)

Clinical evidence: Any reported acute onset of fever and one or more of the following: rash, eschar, headache, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

Confirmed: Clinically compatible case (meets clinical evidence criteria) that is laboratory confirmed

Probable: Clinically compatible case (meets clinical evidence criteria) with serological evidence of elevated IgG or IgM antibody reactive with *R. rickettsii* or other spotted fever group antigen* by IFA (serologic titer of ≥1:128)

Note: Because serologies for rickettsial diseases can be cross-reactive, specimens should be tested against a panel* of *Rickettsia* antigens, including, at a minimum, *R. rickettsia* and *R. typhi*, to differentiate between SFG and non-SFG *Rickettsia* spp. In addition, according to CDC, Rickettsial IgM tests lack specificity (resulting in false positives); thus, IgG titers are considered to be much more reliable.

** Specimens can be forwarded to the DSHS Serology lab for Rickettsial panel testing.*

SFGR Epi Case Criteria 2018
Laboratory Confirmation Tests

Serological evidence of an elevation (four fold change) in immunoglobulin G (IgG) specific antibody titer reactive with *Rickettsia rickettsii* or other spotted fever group antigen* between paired serum specimens (one taken in the first week of illness and a second 2 4 weeks later), as measured by a standardized indirect immunofluorescence assay (IFA),

OR

Detection of *R. rickettsii* or other spotted fever group DNA* in a clinical specimen by polymerase chain reaction (PCR) assay,

OR

Demonstration of spotted fever group antigen* in a biopsy/autopsy specimen by IHC,

OR

Isolation of *R. rickettsii* or other spotted fever group rickettsia* from a clinical specimen in cell culture

* Note: Spotted fever group species included are: *R. aeschlimannii, R. africae, R. australis, R. conorii, R. heilongjiangensis, R. helvetica, R. honei, R. japonica, R. marmionii, R. massiliae, R. parkeri, R. rickettsii, R. sibirica, R. sibirica mongolotimonae, R. slovaca*.
Spotted fever group species **excluded** from this condition are: *R. felis* and *R. akari*

Typhus & SFGR - Clinical Evidence

Flea-borne Typhus	Spotted Fever Group Rickettsiosis
Must have **Fever**	Must have **Fever**
Headache	Headache
Myalgia	Myalgia
	Anemia
Anorexia (**reported in 52% of cases in Texas, 2003-2013*)	
Rash, if present, typically starts on upper trunk and spreads, but generally not to palms/soles (**reported in <50% of cases in Texas, 2003-2013*)	Rash occurs in ~80% of patients with RMSF; typically begins on ankles and wrists and spreads to trunk – may be on palms/soles
Nausea/vomiting (**reported in 51% of cases in Texas, 2003-2013*)	Nausea/vomiting
Thrombocytopenia (**reported in 16% of cases in Texas, 2003-2013*)	Thrombocytopenia
Elevated liver enzymes (**reported in 27% of cases in Texas, 2003-2013*)	Elevated liver enzymes

Serologic Testing for Rickettsial Diseases

- IFA is considered the gold standard of serologic testing for Rickettsial diseases (*94-100% sensitive after 14 days – may lack titers in first 7 days of illness*)
- HOWEVER, "serological testing is limited by **antibody cross-reactivity** with RMSF and typhus antigens, leading to false positives by both ELISA and IFA" which can contribute to misdiagnosis and misreporting of both diseases
- **IgM titers are not reliable** (*CDC: "We do not recommend IgM testing for Rickettsial diseases, especially in the absence of IgG testing, as false positives and false negatives are common."*)
- If cost restrictions limit testing, **IgG is preferred over IgM**!
- Physicians need to collect **both** acute and convalescent serum specimens and order IFA tests
- Should test for both (order **Rickettsial panel**)

2014 Probable Typhus Cases - Titers

Onset, Date Blood Collected	*R. typhi* IgM	*R. typhi* IgG	*R. rickettsia* IgM	*R. rickettsia* IgG
12/8, 12/15	1:512	1:256	1:512	<1:64
3/25, 4/1	1:128	1:64	1:128	<1:64
1/22, 2/3	1:512	1:512	1:64	1:128
4/11, 4/22	1:128	1:512	1:128	1:128
4/29, 5/2	1:128	1:128	1:64	1:128
12/31, 1/7	1:512	1:256	1:256	1:64

Of the first 45 case investigation forms reviewed, ~25% had positive RMSF titers (and not all had RMSF testing done!)

Laboratory Criteria

Flea borne typhus	Spotted Fever Group Rickettsiosis
Fourfold or greater increase in IgG Ab titer in acute and convalescent sera* (C)	Fourfold or greater increase in IgG Ab titer in acute and convalescent sera* (C)
IFA* – IgM or IgG Titer of ≥1:128 (P)	IFA* – IgM or IgG Titer of ≥1:128 (P)
	ELISA (EIA) only good for screening purposes – values do not reflect accurate quantification of Ab titers
PCR can detect *Rickettsia* sp. and differentiate from *R. rickettsii* (CDC)	PCR** on punch skin biopsy, swab of rash, serum or blood is best test for RMSF! (CDC)
Immunohistochemistry or culture (CDC)	Immunohistochemistry or culture (CDC)

* *A single specimen cannot be used to differentiate between SFGR and flea-borne typhus with confidence*

** *Must collect during acute phase of illness no more than two days after doxycycline treatment begins*

Rickettsial Disease
Case Investigation Example

- Patient with fever/chills, headache, anorexia, photophobia, malaise, myalgia, thrombocytopenia, elevated liver function tests, rash (spread from arms/legs to trunk)
- Doctor orders RMSF IgG and IgM
  - IgG 1:128
  - IgM 1:256
- No convalescent testing
- No known tick or flea exposure, no exposure to wild animals, dogs are present at residence
- Classified as probable SFGR

Rickettsial Disease
Case Investigation Example (cont.)

- No typhus testing done
- ZCB requested that the serum be forwarded from commercial lab to DSHS for Rickettsial panel testing
- Results:
  - *R. rickettsii* IgG 1:128
  - ***R. typhi* IgG 1:1024**
- Changed condition to probable flea-borne typhus!

How would you classify this case?

Onset, Date Blood Collected	*R. typhi* IgM	*R. typhi* IgG	*R. rickettsia* IgM	*R. rickettsia* IgG
1/8, 1/16	1:256	1:128	1:256	1:128

- Patient has fever, headache, nausea/ vomiting, malaise, thrombocytopenia
- Patient does not report exposure to fleas or ticks
- Patient does not have rash
- Patient from area with both typhus & spotted fever occur
- Patient did not travel
- Physician unable to get convalescent sample for testing

"Rickettsia, unspecified" Epi Case Criteria 2018 Case Definition/Case Classification

Flea-borne typhus and spotted fever group rickettsioses (SFGR) are a group of vector-borne infections caused by some members of the genus *Rickettsia*. These infections can be difficult to differentiate clinically and serologically (due to antibody cross-reactivity). Illness is characterized by acute onset of fever that may be accompanied by: headache, malaise, myalgia, nausea and/or vomiting, anorexia, and rash.

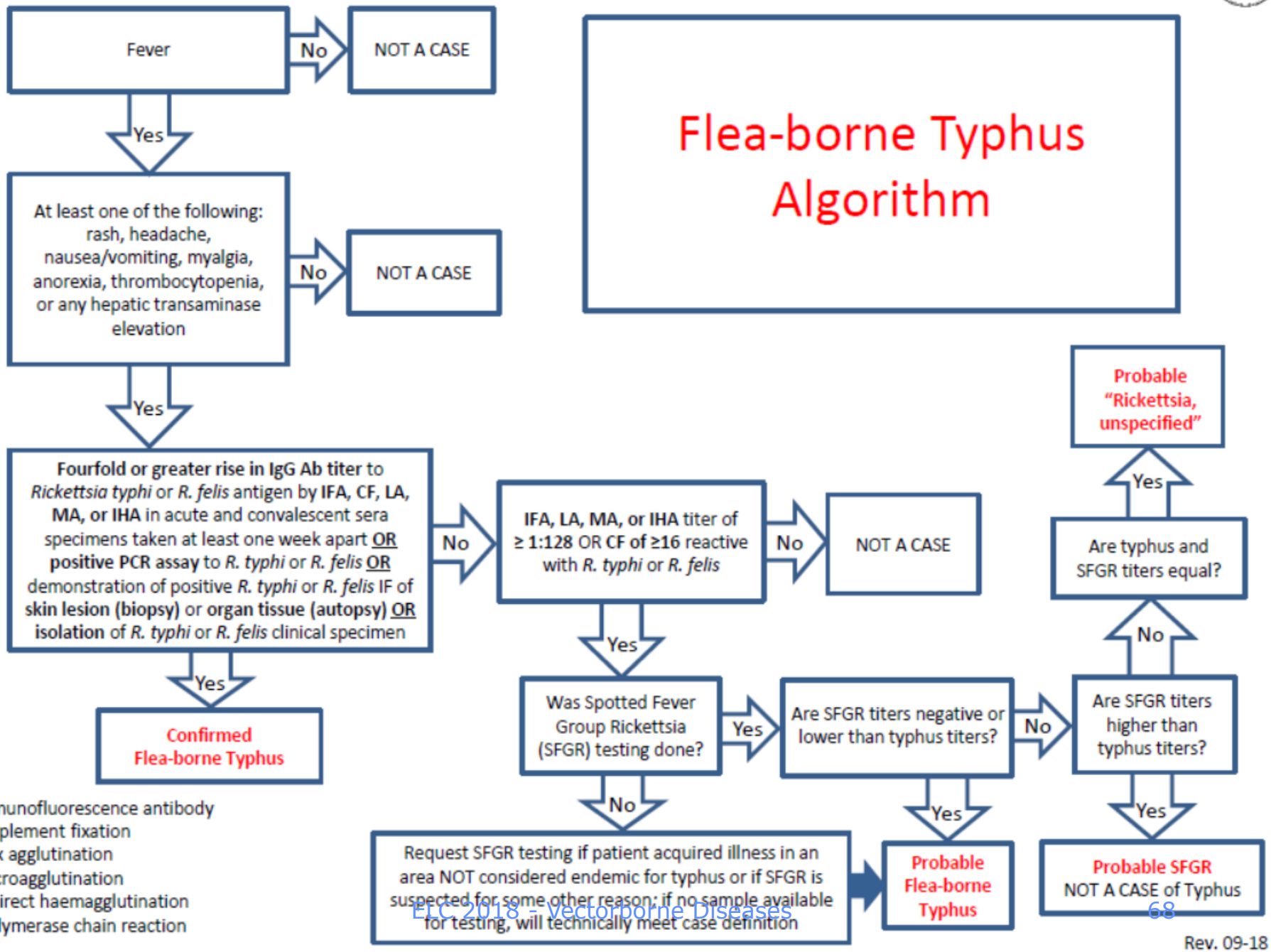
Clinical evidence: Acute onset of fever and one or more of the following: rash, headache, nausea/vomiting, anorexia, myalgia, anemia, thrombocytopenia, or any hepatic transaminase elevation.

"Rickettsia, unspecified" Epi Case Criteria 2018 Case Definition/Case Classification (cont.)

Probable: Clinically compatible case (meets clinical evidence criteria) with serological evidence of elevated IgG or IgM antibody reactive with spotted fever AND typhus group antigens by IFA (serologic titers of ≥1:128) that cannot be classified as either flea-borne typhus or SFGR.

Note: For "Rickettsia, unspecified," an undetermined case can only be classified as probable. This occurs when a case has compatible clinical criteria with laboratory evidence to support infection, but spotted fever and typhus fever group titers are equal.

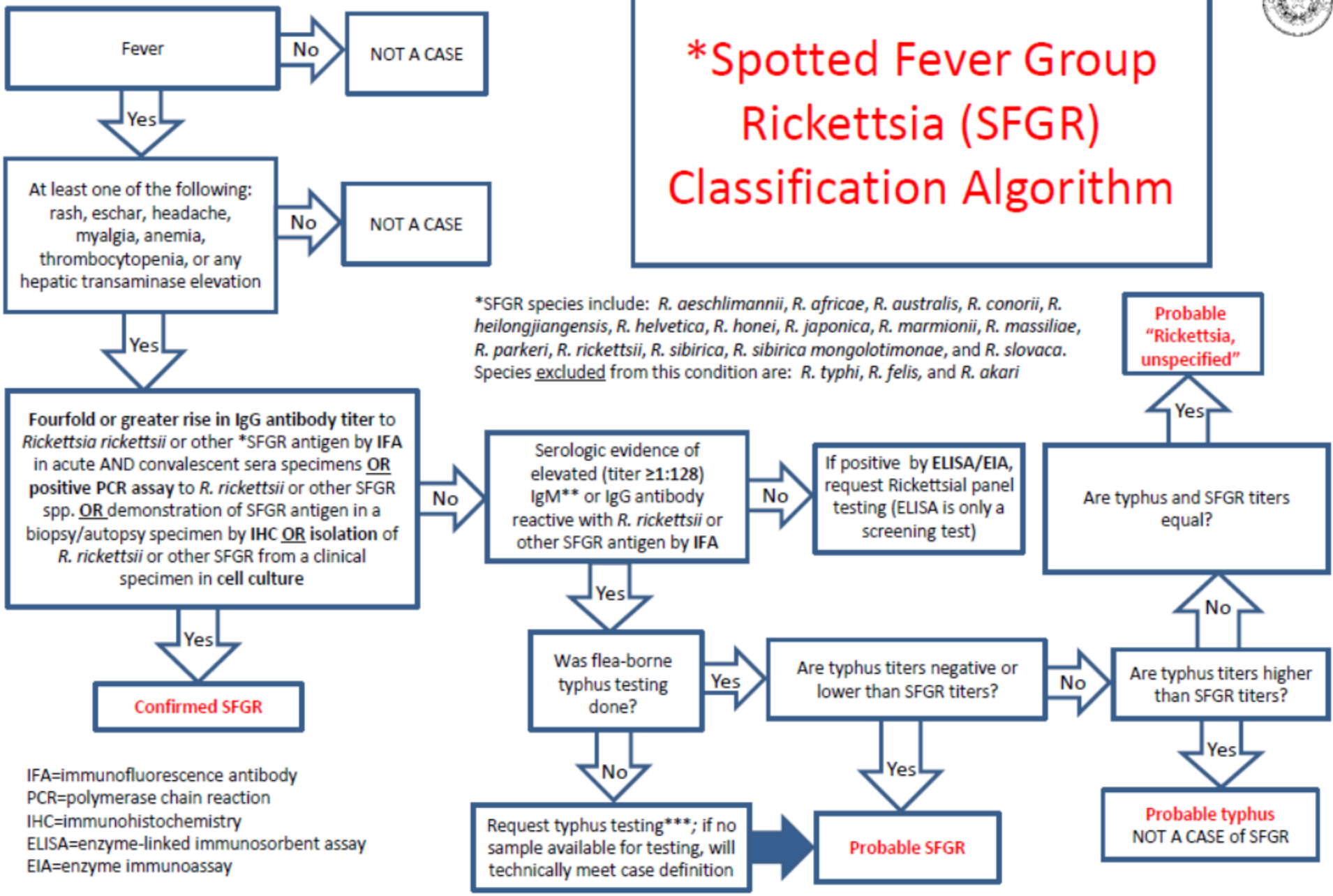
Flea-borne Typhus Algorithm



IFA=immunofluorescence antibody
CF=complement fixation
LA=latex agglutination
MA=microagglutination
IHA=indirect haemagglutination
PCR=polymerase chain reaction

Rev. 09-18

*Spotted Fever Group Rickettsia (SFGR) Classification Algorithm



*SFGR species include: *R. aeschlimannii*, *R. africae*, *R. australis*, *R. conorii*, *R. heilongjiangensis*, *R. helvetica*, *R. honei*, *R. japonica*, *R. marmionii*, *R. massiliae*, *R. parkeri*, *R. rickettsii*, *R. sibirica*, *R. sibirica mongolotimonae*, and *R. slovaca*. Species excluded from this condition are: *R. typhi*, *R. felis*, and *R. akari*

IFA=immunofluorescence antibody
PCR=polymerase chain reaction
IHC=immunohistochemistry
ELISA=enzyme-linked immunosorbent assay
EIA=enzyme immunoassay

**IgM titers are not reliable: false negatives and false positives are common; if only a low IgM titer, look for alternate explanation for illness*
**** Cannot rule out flea-borne typhus without testing because antibodies cross react*

Rickettsial Disease Case Investigation

- Make sure ALL Rickettsial lab reports are in NEDSS
- If only spotted fever testing done, see if sample can be forwarded to DSHS Rickettsial panel testing
- Need to contact patient
  - Information about exposure to vectors
  - Travel history
- Treatment information, including dates
- Make sure all required fields are completed in NEDSS (*refer to Data Entry Guidelines – Quick Reference section for patient demographics/lab report*)

References

- Centers for Disease Control and Prevention website: www.cdc.gov/rmsf/
- Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever, Ehrlichioses, and Anaplasmosis --- United States. A practical Guide for Physicians and Other Health-Care and Public Health Professionals: www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm
- Byork, A. Trip Report: Assessment of human spotted fever in the Lower Rio Grande Valley of Texas (Epi-Aid 2010-101).

Arboviruses

Testing options & interpretation

- Test availability & requesting special testing for uncommon arboviruses
- Blood donor screening for arboviruses (West Nile virus and Zika virus): how does it work?
- Suspected false positive result at a commercial lab? What next?
- Scenarios

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Arboviral Diagnostic Assays

Test Type	Availability	Specimen Types	Caveats
IgM antibody detection	Widespread - commercial and public health labs	Serum, CSF	False positives and cross-reactivity common, unclear duration of IgM
Plaque Reduction Neutralization Test (PRNT)	Limited – public health labs only (certain states, CDC)	Serum, CSF	Time consuming, cannot distinguish timing of infection
PCR	Widespread - commercial and public health labs	Serum, urine*, CSF, whole blood, amniotic fluid*	Limited window of detection, false positives possible
Tissue pathology (*Zika only)	Very limited – CDC only (requires pre-approval)	Placenta, umbilical cord, products of conception, fetal losses	Very time consuming, cannot distinguish between maternal and fetal infection

Plaque-Reduction Neutralization Test (PRNT)

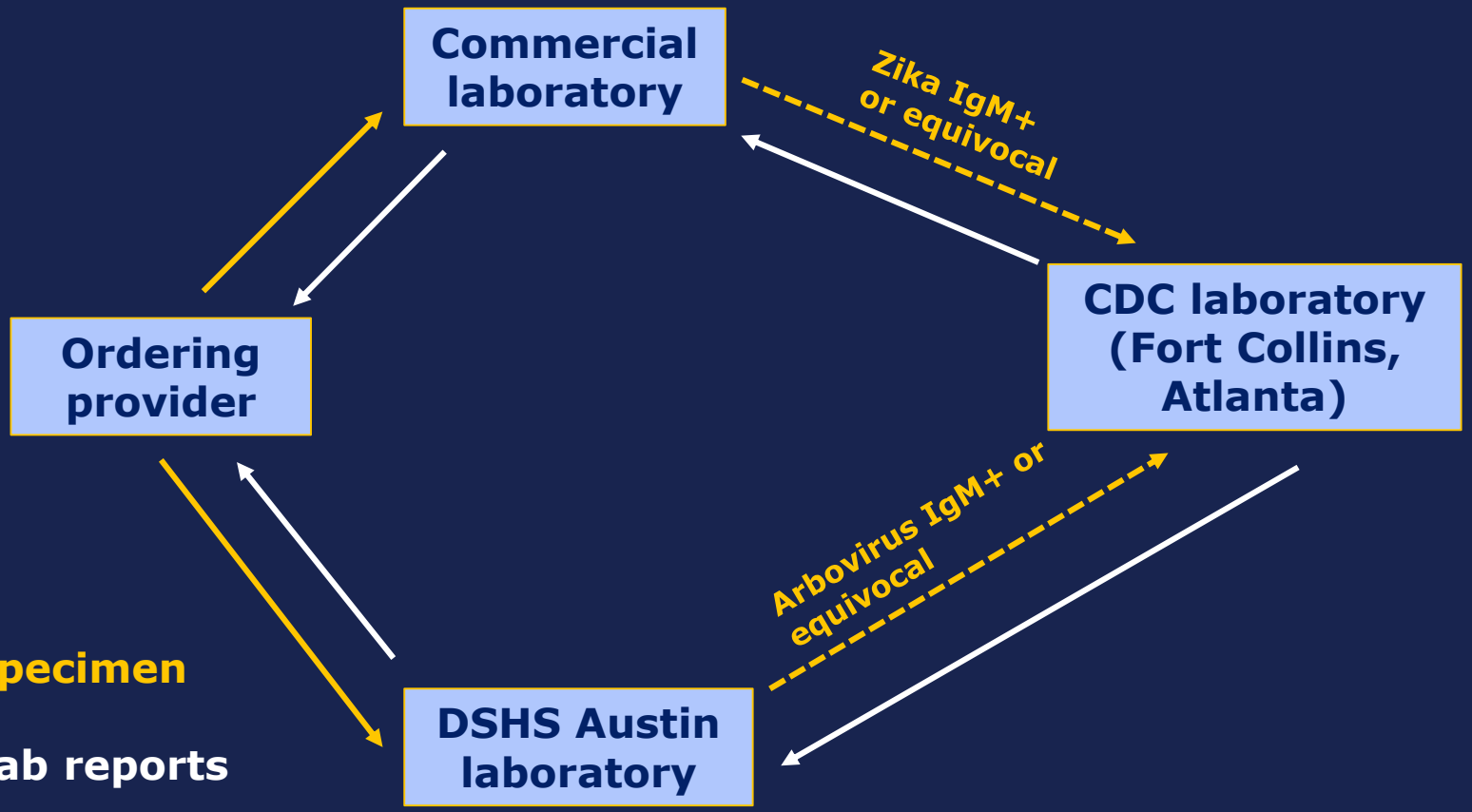
TEXAS Health and Human Services

Texas Department of State Health Services

- Requires mixing the patient's serum with live virus to determine how effective it is at neutralizing the virus
- Measures total neutralizing antibody rather than IgM specifically
- Cross-reactivity issues with similar viruses
  - Zika, dengue, WNV

Source: http://www1.paho.org/hq/dmdocuments/2010/p4.lanciotti CHIK%20PAHO%20mtg%20Peru%202010_1_1.pdf

Tracking Testing Progress



Uncommon Arboviral Diseases

TEXAS Health and Human Services

Texas Department of State Health Services

- **Tick borne Encephalitis**: endemic to parts of Europe
- **Japanese Encephalitis**: endemic to Asia, vaccination available (diagnostic cross-reactivity with flaviviruses)
- **Yellow Fever**: central Africa, South America (Brazil outbreak) at risk, vaccination available (diagnostic cross-reactivity with flaviviruses)
- **Powassan**: rare, highest risk in Northeast US (flavivirus)
- **St. Louis Encephalitis**: rare but endemic to Texas and US, cross-reactivity with West Nile as a flavivirus (panel test recommended)
- **Cache Valley**: rare but some activity in North & Central America (Bunyamwera serogroup)
- **California serogroup**, including California encephalitis, Jamestown Canyon, Keystone, La Crosse, Snowshoe hare, Keystone, and Trivittatus viruses: isolated cases
- **Eastern & Western Equine Encephalitis**: rare, but picked up in animal surveillance in Texas
- **Heartland**: emerging, <50 cases nationwide, likely spread by Lone Star Tick
- **Colorado Tick Fever**: *Dermacenter andersoni* ticks (high elevation), uncommon

Arbovirus Testing Options and Locations (as of September 2018)				
Arbovirus	**DSHS**	**CDC Fort Collins[1]**	**CDC Dengue Branch[1]**	**Commercial Lab**
Chikungunya				
PCR[2]	Yes[3]	Yes	Yes (last resort)	Yes, Mayo Medical lab, CPL[4], Focus Diagnostics (Quest), and ARUP
IgM/IgG	Yes[3]	Yes	Yes (last resort)	Yes, Mayo Medical lab, CPL[4], Focus Diagnostics (Quest), and ARUP
PRNT	No	Yes	Yes (last resort)	No
Dengue				
PCR[2]	Yes[3]	No	Yes	Yes, Focus Diagnostics (Quest), ARUP
NS1	No	No	Yes	Yes, Mayo Medical Lab and Focus Diagnostics (Quest)
IgM/IgG	Yes[3]	Yes	Yes (last resort)	Yes, CPL[4], Viracor, Focus Diagnostics (Quest), Mayo Medical lab and ARUP
PRNT	No	Yes	Yes (last resort)	No
Eastern/Western Equine Encephalitis				
PCR	No	Yes	No	No
IgM/IgG	No	Yes	No	Yes[5], Mayo Medical lab and most commercial labs
PRNT	No	Yes	No	No
Japanese Encephalitis				
PCR	No	Yes	No	No
IgM/IgG	No	Yes	No	Yes, ARUP
PRNT	No	Yes	No	No
St. Louis Encephalitis				
PCR	No	Yes	No	No
IgM/IgG	Yes[3]	Yes	No	Yes[5], Mayo Medical Lab and most commercial labs
PRNT	No	Yes	No	No
West Nile				
PCR	No	Yes	No	Yes[5], ARUP, CPL, Mayo Medical Lab, LabCorp, and Focus Diagnostics (Quest)
IgM/IgG	Yes[3]	Yes	No	Yes[5], ARUP, CPL, Mayo Medical Lab, LabCorp, and Focus Diagnostics (Quest)
PRNT	No	Yes	No	No
Yellow Fever				
PCR	No	Yes	No	No
IgM/IgG	No	Yes	No	No
PRNT	No	Yes	No	No
Zika				
PCR[2]	Yes[3]	Yes	Yes (last resort)	Yes, ARUP, CPL[4], Focus Diagnostics (Quest), Mayo Medical lab, LabCorp, Viracor and BioReference
IgM[2]/IgG	Yes[3]	Yes	Yes (last resort)	Yes, ARUP, CPL[4], Focus Diagnostics (Quest), Mayo Medical lab, LabCorp, Viracor and BioReference
PRNT	No	Yes	Yes (last resort)	No
California serogroup, Cache Valley, Powassan, Tick-borne Encephalitis, and other rare arboviruses				
PCR, IgM, and/or PRNT	No	Yes	No	Uncommon; California serogroup serology available through ARUP, Focus Diagnostics (Quest), and Mayo Medical lab

[1] Samples that require CDC testing should be sent through DSHS after prior coordination with Zoonosis Control. Please indicate which CDC test is being requested under section 9 (CDC reference test) on the G-2A form.

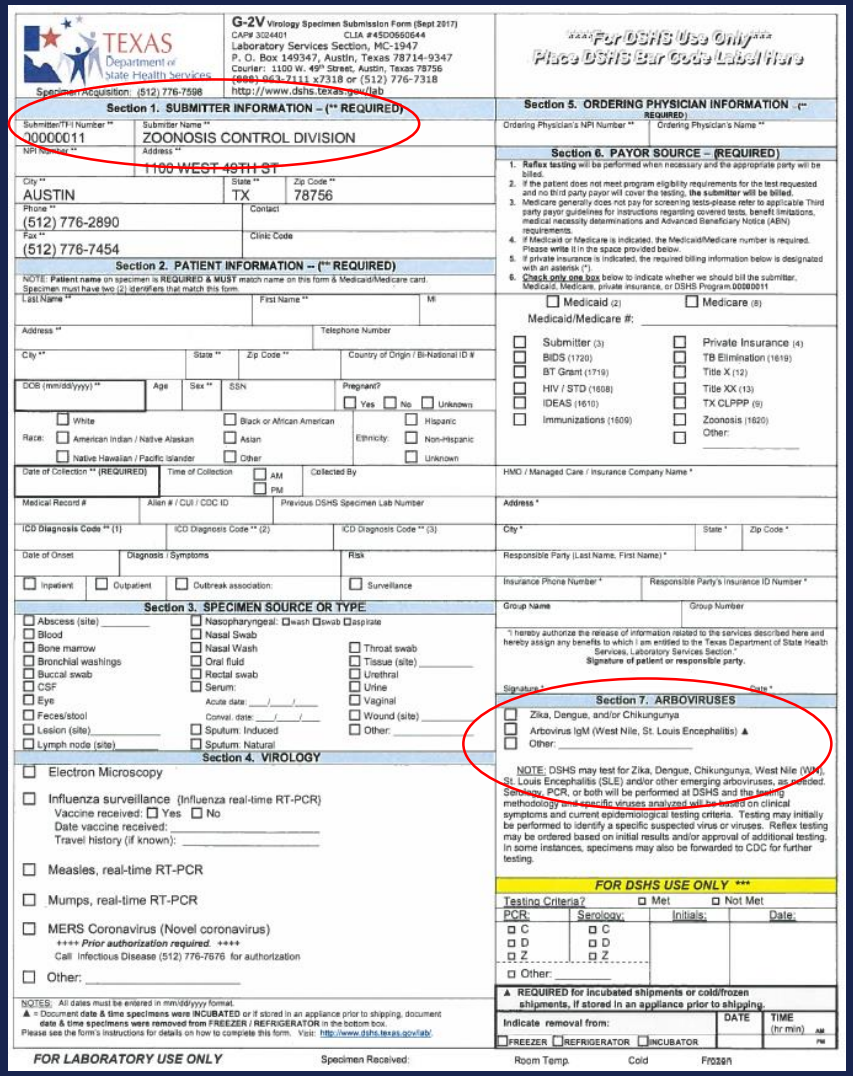
[2] May also be performed at select LRNs, military bases and hospitals (contact your local LRN, military base or hospital for information on which tests are being performed).

[3] Use G-2V form request IgM or PCR for CHIK, ZIKA, DEN and/or IgM for WNV and SLE; no IgG available. DSHS will forward to CDC, as needed.

[4] CPL (9200 Wall St.) is known by the following aliases: Sonic reference lab and Sonic Healthcare USA.

[5] Testing for SLE and Western/Eastern equine encephalitis included in a panel at Focus Diagnostics (Quest), Mayo Medical Lab, ARUP, and CPL (includes West Nile plus previous arboviruses mentioned on their panel).

DSHS Specimen Submission: G-2V



G-2V Virology Specimen Submission Form (Sept 2017)
CA# 3024401 CLIA #4500660644
Laboratory Services Section, MC-1947
P. O. Box 149347, Austin, Texas 78714-9347
Courier: 1100 W. 49th Street, Austin, Texas 78756
(866) 963-7111 x7318 or (512) 776-7318
http://www.dshs.texas.gov/lab
Specimen Acquisition: (512) 776-7598

*** For DSHS Use Only ***
Place DSHS Bar Code Label Here

Section 1. SUBMITTER INFORMATION – (** REQUIRED)
Submitter/TFI Number **: 00000011
Submitter Name **: ZOONOSIS CONTROL DIVISION
Address **: 1100 WEST 49TH ST
City **: AUSTIN
State **: TX
Zip Code **: 78756
Phone **: (512) 776-2890
Contact:
Fax **: (512) 776-7454
Clinic Code:

Section 2. PATIENT INFORMATION – (** REQUIRED)
NOTE: Patient name on specimen is REQUIRED & MUST match name on this form & Medicaid/Medicare card. Specimen must have two (2) identifiers that match this form.
Last Name **, First Name **, MI
Address **, Telephone Number
City **, State **, Zip Code **, Country of Origin / Bi-National ID #
DOB (mm/dd/yyyy) **, Age, Sex **, SSN, Pregnant? Yes No Unknown
Race: White, Black or African American, American Indian / Native Alaskan, Asian, Native Hawaiian / Pacific Islander, Other
Ethnicity: Hispanic, Non-Hispanic, Unknown
Date of Collection ** (REQUIRED), Time of Collection AM PM, Collected By
Medical Record #, Alien # / CUI / CDC ID, Previous DSHS Specimen Lab Number
ICD Diagnosis Code ** (1), ICD Diagnosis Code ** (2), ICD Diagnosis Code ** (3)
Date of Onset, Diagnosis / Symptoms, Risk
Inpatient, Outpatient, Outbreak association, Surveillance

Section 3. SPECIMEN SOURCE OR TYPE
Abscess (site), Blood, Bone marrow, Bronchial washings, Buccal swab, CSF, Eye, Feces/stool, Lesion (site), Lymph node (site)
Nasopharyngeal: wash swab aspirate, Nasal Swab, Nasal Wash, Oral fluid, Rectal swab, Serum: Acute date: Conval. date:, Sputum: Induced, Sputum: Natural
Throat swab, Tissue (site), Urethral, Urine, Vaginal, Wound (site), Other:

Section 4. VIROLOGY
Electron Microscopy
Influenza surveillance (Influenza real-time RT-PCR)
Vaccine received: Yes No
Date vaccine received:
Travel history (if known):
Measles, real-time RT-PCR
Mumps, real-time RT-PCR
MERS Coronavirus (Novel coronavirus)
++++ Prior authorization required. ++++
Call Infectious Disease (512) 776-7676 for authorization
Other:

NOTES: All dates must be entered in mm/dd/yyyy format.
▲ = Document date & time specimens were INCUBATED or if stored in an appliance prior to shipping, document date & time specimens were removed from FREEZER / REFRIGERATOR in the bottom box.
Please see the form's instructions for details on how to complete this form. Visit: http://www.dshs.texas.gov/lab/

FOR LABORATORY USE ONLY
Specimen Received: Room Temp. Cold Frozen

Section 5. ORDERING PHYSICIAN INFORMATION – (** REQUIRED)
Ordering Physician's NPI Number **, Ordering Physician's Name **

Section 6. PAYOR SOURCE – (REQUIRED)
1. Reflex testing will be performed when necessary and the appropriate party will be billed.
2. If the patient does not meet program eligibility requirements for the test requested and no third party payor will cover the testing, the submitter will be billed.
3. Medicare generally does not pay for screening tests-please refer to applicable Third party payor guidelines for instructions regarding covered tests, benefit limitations, medical necessity determinations and Advanced Beneficiary Notice (ABN) requirements.
4. If Medicaid or Medicare is indicated, the Medicaid/Medicare number is required. Please write it in the space provided below.
5. If private insurance is indicated, the required billing information below is designated with an asterisk (*).
6. Check only one box below to indicate whether we should bill the submitter, Medicaid, Medicare, private insurance, or DSHS Program 00000011

Medicaid (2), Medicare (8)
Medicaid/Medicare #:
Submitter (3), BIDS (1720), BT Grant (1719), HIV / STD (1608), IDEAS (1610), Immunizations (1609)
Private Insurance (4), TB Elimination (1619), Title X (12), Title XX (13), TX CLPPP (9), Zoonosis (1620), Other:

HMO / Managed Care / Insurance Company Name *
Address *, City *, State *, Zip Code *
Responsible Party (Last Name, First Name) *
Insurance Phone Number *, Responsible Party's Insurance ID Number *
Group Name, Group Number

"I hereby authorize the release of information related to the services described here and hereby assign any benefits to which I am entitled to the Texas Department of State Health Services, Laboratory Services Section."
Signature of patient or responsible party.
Signature *, Date *

Section 7. ARBOVIRUSES
Zika, Dengue, and/or Chikungunya
Arbovirus IgM (West Nile, St. Louis Encephalitis) ▲
Other:
NOTE: DSHS may test for Zika, Dengue, Chikungunya, West Nile (WN), St. Louis Encephalitis (SLE) and/or other emerging arboviruses, as needed. Serology, PCR, or both will be performed at DSHS and the testing methodology and specific viruses analyzed will be based on clinical symptoms and current epidemiological testing criteria. Testing may initially be performed to identify a specific suspected virus or viruses. Reflex testing may be ordered based on initial results and/or approval of additional testing. In some instances, specimens may also be forwarded to CDC for further testing.

FOR DSHS USE ONLY ***
Testing Criteria? Met Not Met

PCR:	Serology:	Initials:	Date:
C	C		
D	D		
Z	Z		
Other:			

▲ REQUIRED for incubated shipments or cold/frozen shipments, if stored in an appliance prior to shipping.
Indicate removal from: FREEZER REFRIGERATOR INCUBATOR
DATE, TIME (hr:min) AM PM

→ Do not use sample forms from DSHS Lab website! Must contact the lab to create an account or request forms.

Section 7. ARBOVIRUSES
Zika, Dengue, and/or Chikungunya
Arbovirus IgM (West Nile, St. Louis Encephalitis) ▲
Other:

NOTE: DSHS may test for Zika, Dengue, Chikungunya, West Nile (WN), St. Louis Encephalitis (SLE) and/or other emerging arboviruses, as needed. Serology, PCR, or both will be performed at DSHS and the testing methodology and specific viruses analyzed will be based on clinical symptoms and current epidemiological testing criteria. Testing may initially be performed to identify a specific suspected virus or viruses. Reflex testing may be ordered based on initial results and/or approval of additional testing. In some instances, specimens may also be forwarded to CDC for further testing.

FOR DSHS USE ONLY ***
Testing Criteria? Met Not Met

PCR:	Serology:	Initials:	Date:
C	C		
D	D		
Z	Z		
Other:			

DSHS Specimen Submission: G-2A

TEXAS
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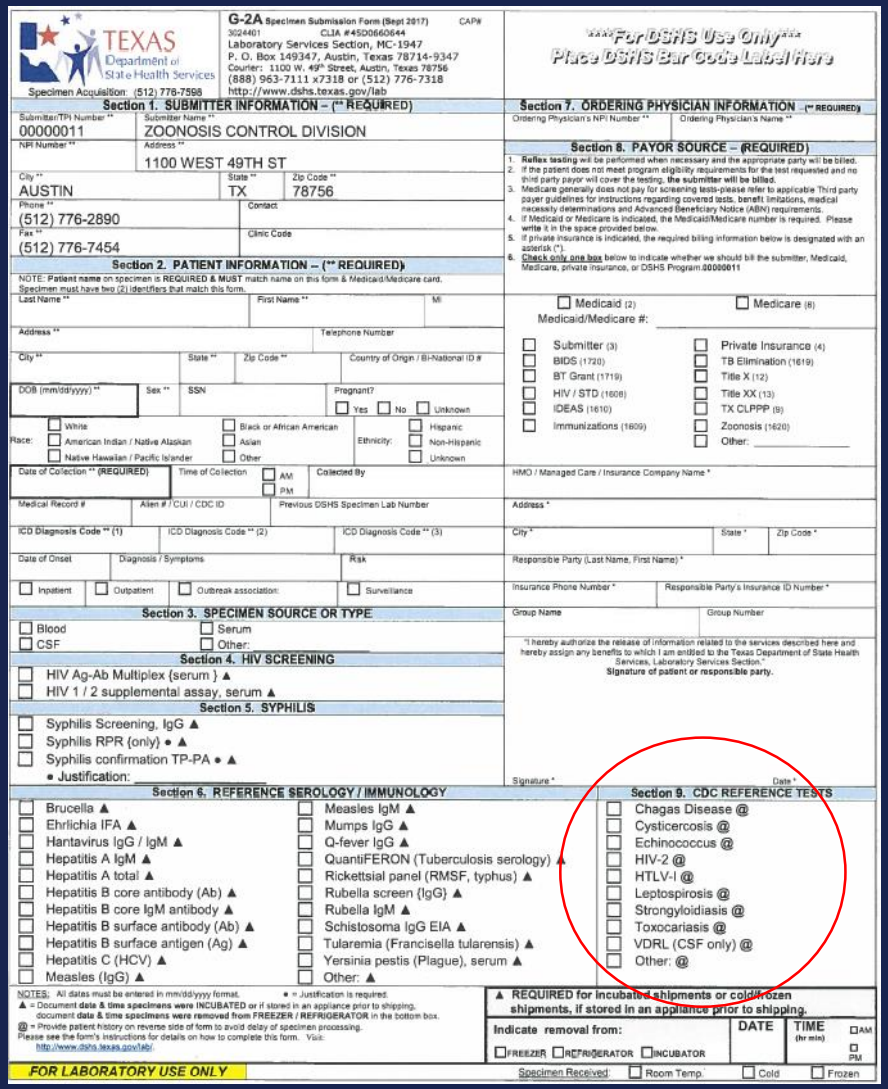
Texas Department of State Health Services



TEXAS Department of State Health Services
Specimen Acquisition (512) 776-7598

G-2A Specimen Submission Form (Sept 2017) CAP#
3024401 CLIA #45D0660644
Laboratory Services Section, MC-1947
P. O. Box 149347, Austin, Texas 78714-9347
Courier: 1100 W. 49th Street, Austin, Texas 78756
(888) 963-7111 x7318 or (512) 776-7318
http://www.dshs.texas.gov/lab

For DSHS Use Only
Place DSHS Bar Code Label Here

Section 1. SUBMITTER INFORMATION – (REQUIRED)**
Submitter/TPI Number **: 00000011
Submitter Name **: ZOONOSIS CONTROL DIVISION
NPI Number **:
Address **: 1100 WEST 49TH ST
City **: AUSTIN
State **: TX
Zip Code **: 78756
Phone **: (512) 776-2890
Contact:
Fax **: (512) 776-7454
Clinic Code:

Section 2. PATIENT INFORMATION – (REQUIRED)**
NOTE: Patient name on specimen is REQUIRED & MUST match name on this form & Medicaid/Medicare card. Specimen must have two (2) identifiers that match this form.
Last Name **: First Name **: MI:
Address **: Telephone Number:
City **: State **: Zip Code **: Country of Origin / Bi-National ID #:
DOB (mm/dd/yyyy) **: Sex **: SSN: Pregnant? ☐ Yes ☐ No ☐ Unknown
Race: ☐ White ☐ Black or African American ☐ Hispanic ☐ American Indian / Native Alaskan ☐ Asian ☐ Non-Hispanic ☐ Native Hawaiian / Pacific Islander ☐ Other ☐ Unknown
Ethnicity:
Date of Collection ** (REQUIRED): Time of Collection ☐ AM ☐ PM: Collected By:
Medical Record #: Alien # / CUI / CDC ID: Previous DSHS Specimen Lab Number:
ICD Diagnosis Code ** (1): ICD Diagnosis Code ** (2): ICD Diagnosis Code ** (3):
Date of Onset: Diagnosis / Symptoms: Risk:
☐ Inpatient ☐ Outpatient ☐ Outbreak association: ☐ Surveillance

Section 3. SPECIMEN SOURCE OR TYPE
☐ Blood ☐ Serum
☐ CSF ☐ Other:

Section 4. HIV SCREENING
☐ HIV Ag-Ab Multiplex (serum) ▲
☐ HIV 1 / 2 supplemental assay, serum ▲

Section 5. SYPHILIS
☐ Syphilis Screening, IgG ▲
☐ Syphilis RPR (only) • ▲
☐ Syphilis confirmation TP-PA • ▲
• Justification:

Section 6. REFERENCE SEROLOGY / IMMUNOLOGY

☐ Brucella ▲	☐ Measles IgM ▲
☐ Ehrlichia IFA ▲	☐ Mumps IgG ▲
☐ Hantavirus IgG / IgM ▲	☐ Q-fever IgG ▲
☐ Hepatitis A IgM ▲	☐ QuantiFERON (Tuberculosis serology) ▲
☐ Hepatitis A total ▲	☐ Rickettsial panel (RMSF, typhus) ▲
☐ Hepatitis B core antibody (Ab) ▲	☐ Rubella screen (IgG) ▲
☐ Hepatitis B core IgM antibody ▲	☐ Rubella IgM ▲
☐ Hepatitis B surface antibody (Ab) ▲	☐ Schistosoma IgG EIA ▲
☐ Hepatitis B surface antigen (Ag) ▲	☐ Tularemia (Francisella tularensis) ▲
☐ Hepatitis C (HCV) ▲	☐ Yersinia pestis (Plague), serum ▲
☐ Measles (IgG) ▲	☐ Other: ▲

Section 7. ORDERING PHYSICIAN INFORMATION – (REQUIRED)**
Ordering Physician's NPI Number **:
Ordering Physician's Name **:

Section 8. PAYOR SOURCE – (REQUIRED)
1. Reflex testing will be performed when necessary and the appropriate party will be billed.
2. If the patient does not meet program eligibility requirements for the test requested and no third party payor will cover the testing, the submitter will be billed.
3. Medicare generally does not pay for screening tests-please refer to applicable Third party payer guidelines for instructions regarding covered tests, benefit limitations, medical necessity determinations and Advanced Beneficiary Notice (ABN) requirements.
4. If Medicaid or Medicare is indicated, the Medicaid/Medicare number is required. Please write it in the space provided below.
5. If private insurance is indicated, the required billing information below is designated with an asterisk (*).
6. Check only one box below to indicate whether we should bill the submitter, Medicaid, Medicare, private insurance, or DSHS Program.00000011

☐ Medicaid (2) ☐ Medicare (8)
Medicaid/Medicare #:

☐ Submitter (3)	☐ Private Insurance (4)
☐ BIDS (1720)	☐ TB Elimination (1619)
☐ BT Grant (1719)	☐ Title X (12)
☐ HIV / STD (1608)	☐ Title XX (13)
☐ IDEAS (1610)	☐ TX CLPPP (9)
☐ Immunizations (1609)	☐ Zoonosis (1620)
	☐ Other:

HMO / Managed Care / Insurance Company Name *:
Address *:
City *: State *: Zip Code *:
Responsible Party (Last Name, First Name) *:
Insurance Phone Number *: Responsible Party's Insurance ID Number *:
Group Name: Group Number:

"I hereby authorize the release of information related to the services described here and hereby assign any benefits to which I am entitled to the Texas Department of State Health Services, Laboratory Services Section."
Signature of patient or responsible party.
Signature *: Date *:

Section 9. CDC REFERENCE TESTS

☐ Chagas Disease @	☐ Toxocariasis @
☐ Cysticercosis @	☐ VDRL (CSF only) @
☐ Echinococcus @	☐ Other: @
☐ HIV-2 @	
☐ HTLV-I @	
☐ Leptospirosis @	
☐ Strongyloidiasis @	

NOTES: All dates must be entered in mm/dd/yyyy format. • = Justification is required.
▲ = Document **date & time specimens were INCUBATED** or if stored in an appliance prior to shipping, document **date & time specimens were removed from FREEZER / REFRIGERATOR** in the bottom box.
@ = Provide patient history on reverse side of form to avoid delay of specimen processing.
Please see the form's instructions for details on how to complete this form. Visit: http://www.dshs.texas.gov/lab/.

▲ REQUIRED for incubated shipments or cold/frozen shipments, if stored in an appliance prior to shipping.
Indicate removal from: ☐ FREEZER ☐ REFRIGERATOR ☐ INCUBATOR
DATE:
TIME (hr min): ☐ AM ☐ PM

FOR LABORATORY USE ONLY
Specimen Received: ☐ Room Temp. ☐ Cold ☐ Frozen

Section 9. CDC REFERENCE TESTS

- ☐ Chagas Disease @
- ☐ Cysticercosis @
- ☐ Echinococcus @
- ☐ HIV-2 @
- ☐ HTLV-I @
- ☐ Leptospirosis @
- ☐ Strongyloidiasis @
- ☐ Toxocariasis @
- ☐ VDRL (CSF only) @
- ☐ Other: @

Laboratory Response Network

- All LRNs have Trioplex PCR (Zika, chikungunya, and dengue)
- Select LRNs have West Nile and/or Zika IgM capability → consult with your LRN for confirmation on options

Blood Donor Screening

- Blood collection agencies screen year-round for many infectious diseases using Nucleic Acid Amplification Tests (NAATs)*
  - **West Nile**: pooled donations
  - **Zika**: individual donations & pools
- Reactive donors should be reported by blood collectors to wnv@dshs.texas.gov
  - **West Nile**: report as a Presumptive Viremic Donor (PVD) in NBS/ArboNet
  - **Zika**: further testing and/or investigation needed before any reporting in NBS

*NOT considered equivalent to diagnostic PCR assays in terms of case reporting

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Health and Human Services
Texas Department of State Health Services

TEXAS
Health and Human Services
Texas Department of State Health Services

TEXAS DEPARTMENT OF STATE HEALTH SERVICES

P.O. Box 149347
Austin, Texas 78714-9347
1-888-963-7111
TTY: 1-800-735-2989
www.dshs.state.tx.us

JOHN HELLERSTEDT, M.D.
COMMISSIONER

March 6, 2018

Dear Colleague,

The Texas Department of State Health Services (DSHS) Zoonosis Control Branch (ZCB) utilizes multiple forms of statewide surveillance to detect the presence of arboviruses, such as West Nile virus (WNV), and other zoonotic pathogens in Texas. The DSHS-ZCB relies on reports from blood collection agencies to detect WNV, Zika virus (ZIKV), and Chagas disease.

I write to ask that all blood collection centers appropriately report all donors with reactive tests for WNV, ZIKV, and Chagas disease. If your center uses a screening assay under an IND protocol, please include results of follow-up testing.

Communicable disease reporting is required under the Texas Health and Safety Code Section 81.042 and Texas Administrative Code Section 97.2. To report, simply send a secure email to WNV@dshs.texas.gov or fax the report to **512-776-7454**. Providing the following data points will suffice:

Collection Agency; Unique BUI #; Test Name, Collection Date; Last Name, First Name, Donor Phone Number, Donor Address, Date of Birth, Age, Sex, Race, and Hispanic Ethnicity (Y/N).

If your location has a city or county health department, we recommend that you also share this same information with them. Contact information for the health department(s) serving the county where you are located can be found at www.dshs.texas.gov/idcu/investigation/conditions/contacts/.

Thank you in advance for your partnership in this important public health activity. If you have questions, you may contact me at tom.sidwa@dshs.texas.gov.

Sincerely,

Tom J. Sidwa, D.V.M., M.P.H.
Manager, Zoonosis Control Branch

Two types of Zika screening NAAT:

- **Procleix** – under IND protocol, follow up PCR, IgM, IgG required
- **Cobas** – FDA approved, no longer IND protocol

Basel, 06 October 2017

FDA approves Roche cobas Zika as first commercially-available donor screening test for Zika virus

Blood Donor Screening

Expectations	ZIKA		WNV
	Procleix NAAT	Cobas NAAT	
Follow up testing by blood collector expected?	Yes, repeats, Trioplex PCR ("alternative NAT"), Zika IgM & Zika IgG	No (only 2 repeats of initial test)	No (only repeats of initial test, sometimes WNV IgM and IgG)
Public health testing needed?	No, unless concern of local transmission	Case-by-case, but unlikely	Yes, if symptoms develop post-donation
Report as a confirmed or probable case with only initial reactive result?	No	No	No (only as a "not a case" WNV PVD)

Commercial Lab Issues

False positive results

- ARUP chikungunya IgM assay has been causing concern in recent months; CDC and ARUP working on a solution
  - IgM positive results in individuals who meet clinical criteria (at least fever) should be verified at DSHS

- All commercial Zika IgM assays have specificity and sensitivity issues, and still require repeat and follow up testing at a public health lab (an **automatic process**!)
  - Interpret non-negative Zika IgMs with a grain of salt!

→ Coordinate submission of suspected false-positive specimens to DSHS with your Regional Zoonosis Control office

Scenario #1

→ **A physician contacts your office about a patient who recently returned one week ago from a trip to visit family in upstate New York, where they spent time outdoors and removed at least one tick from themselves. They are experiencing fever, headache, weakness, confusion, loss of coordination, and difficulty with speech.**

→ **The provider wants to test CSF and serum for Powassan virus. What next?**

- Exposure and symptoms are plausible for Powassan
- Consult Arbovirus Testing Options cheat-sheet
  - Testing available at CDC Fort Collins
  - Contact Regional Zoonosis Control office about the patient's background and to coordinate submission of specimens

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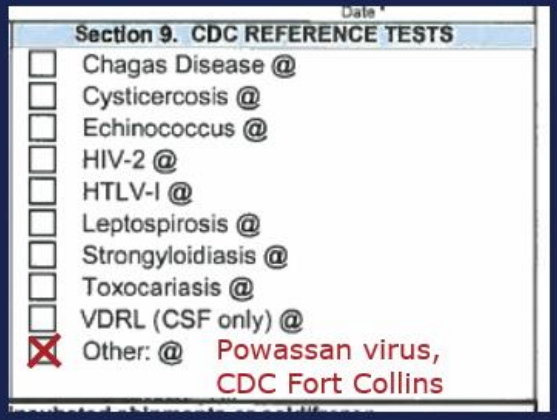
Texas Department of State Health Services

Scenario #1, continued

→ Which DSHS submission form should be filled out and how? Which tests do you want to request?

- G-2A form, either using your public health submitter account or work with the patient's provider to submit one



Can recommend the physician pursue West Nile testing through commercial labs (or possible at DSHS)

→ How should the specimen be shipped and the form be sent? Expected turnaround time for results?

- Ensure the G 2A form is sent **with** the specimens, which should be shipped **frozen** to DSHS Austin.
- At least 2 weeks, up to a month likely for IgM and PRNT; let physician know.

Scenario #2

→ You see this result in NBS for a patient who lives in Houston, with no other arbovirus testing. What next?

Lab Reports (6)

Date Received	Reporting Facility/Provider	Date Collected	Test Results
07/06/2018 9:12 AM E	**Reporting Facility:** ARUP LABORATORIES **Ordering Provider:** Paul Saleeb	06/28/2018	**Chikungunya virus Ab.IgM:** 1.49 IV **Reference Range:** (<=0.79) - (Final)

- You speak with the ordering provider and find out that the patient has not left their residence county in a month.
  - On 6/23/18, they felt feverish with chills and had a headache and myalgia after spending some evenings outside with family

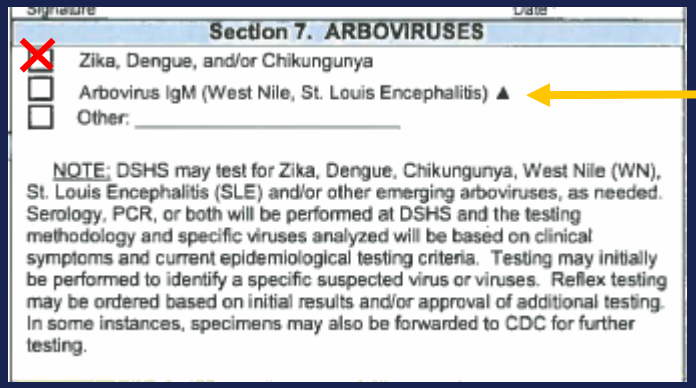
→ Should this result be reported as an arbovirus disease case yet? If yes, how? If no, what next?

- With no exposure, does not make sense despite meeting lab and clinical criteria as probable chikungunya
  - Call ARUP to request the specimen be forwarded to DSHS Austin (ideally, frozen)

Scenario #2, continued

→ Which DSHS submission form should be filled out and how? Which tests do you want to request?

- G-2V form, either using your public health submitter account or work with the patient's provider to submit one



Section 7. ARBOVIRUSES

- [x] Zika, Dengue, and/or Chikungunya
- [ ] Arbovirus IgM (West Nile, St. Louis Encephalitis) ▲
- [ ] Other: _____

NOTE: DSHS may test for Zika, Dengue, Chikungunya, West Nile (WN), St. Louis Encephalitis (SLE) and/or other emerging arboviruses, as needed. Serology, PCR, or both will be performed at DSHS and the testing methodology and specific viruses analyzed will be based on clinical symptoms and current epidemiological testing criteria. Testing may initially be performed to identify a specific suspected virus or viruses. Reflex testing may be ordered based on initial results and/or approval of additional testing. In some instances, specimens may also be forwarded to CDC for further testing.

Can consider West Nile fever as well, but priority is to verify or rule out the chikungunya result

→ Where to send the form? What information does Zoonosis Control need to have?

- Let ZCB know the background info (and ideally a **tracking shipment #** for the specimen from ARUP) and send the form securely to ZCB; we will coordinate with DSHS lab

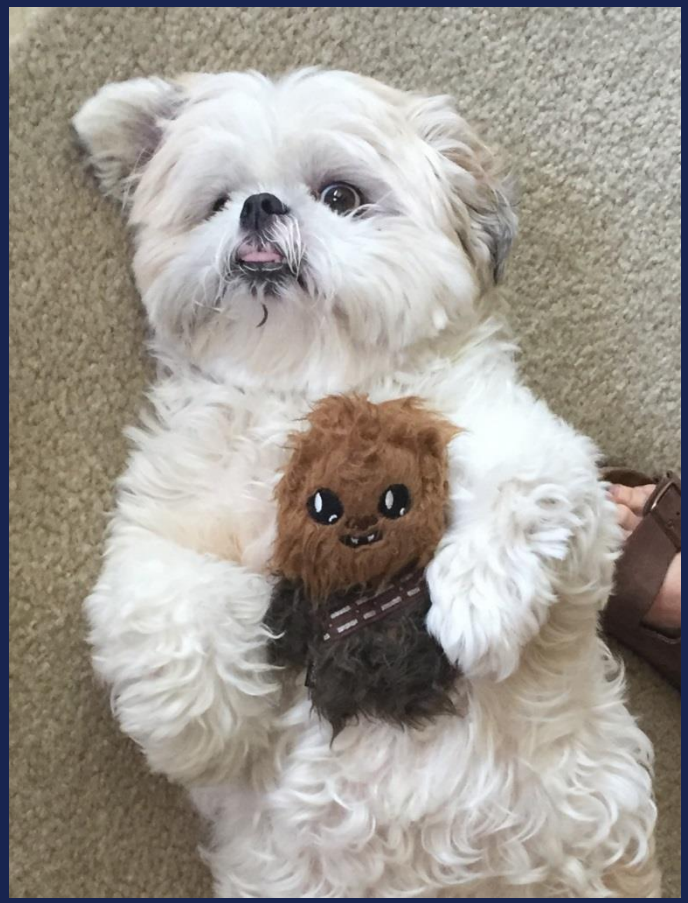
Scenario #2, continued

→ One week after the sample is shipped to DSHS, you see this result in NBS for the patient. What next? Should you report this as an arbovirus disease case?

Date Received	Reporting Facility/Provider	Date Collected	Test Results
09/20/2018 9:38 AM E	**Reporting Facility:** TX.Austin.SPHL	06/28/2018	**Chikungunya virus Ab.IgM:** Negative
09/17/2018 3:52 PM E	**Reporting Facility:** TX.Austin.SPHL	06/28/2018	**Chikungunya virus RNA:** Not Detected
09/17/2018 3:52 PM E	**Reporting Facility:** TX.Austin.SPHL	06/28/2018	**DENGUE VIRUS 1+2+3+4 RNA:** Not Detected
09/17/2018 3:52 PM E	**Reporting Facility:** TX.Austin.SPHL	06/28/2018	**Zika virus RNA:** Not Detected

- The ARUP result has been ruled out as a false positive by the result from DSHS. Note Trioplex PCR ordered as it was a day 5 specimen.
  - Make comments in the ARUP lab to explain why it is "Not A Case", or make a "Not A Case" chikungunya investigation and associate all labs

Questions?



TEXAS
Health and Human Services

Texas Department of State Health Services

Thank you

Kamesha Owens, MPH

Bonny Mayes, MA

Kelly Broussard, MPH

Zoonosis Control Branch Epi Team