

Texas Department of State Health Services

Zoonotic Disease Scenarios: Malaria, Arboviruses, Chagas Disease, Lyme Disease, and Rickettsial Diseases

ELC Meeting – September 2019 Zoonosis Control Branch

Malaria Case Scenario

A new ELR appears in the DRR queue for a blood smear, with a positive result for malaria.



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Health Services

Resulted Tests and Results

Resulted Test: MICROSCOPIC OBSERVATION:PRID:PT:BLD:NOM:MALARIA SMEAR(Malaria Smear)

Result(s): Positive(SNOMED)

Reference Range: Negative

Interpretation: Normal

Result Method:

Date/Time: 2019-02-09 12:09:00.0

Performing Facility: University Med Ctr

Facility ID: 45D0660741

(FI)

Status: Final

Test Code(s): 32700-7 (LN LOINC) /278 (L LOCAL)

Result Code(s): 10828004 (SNM SNOMED) /

Result Comments:



Malaria Case Scenario (continued)

The species has not been determined yet. Upon reviewing the medical record, you learn that the patient is a 62-year-old female who is a resident of Nigeria and returning home next month.

Q: Is this a reportable Texas malaria case? **YES!**

Malaria Reporting Guidelines

Texas Residents

For malaria cases who reside in Texas, but are diagnosed in another Texas jurisdiction, please report by the case patient's residence.

Out of Country Residents

For malaria cases who reside in another country, but are diagnosed in Texas, please report by the location where the patient was diagnosed.

Out of State Residents

For malaria cases who reside in another state, but are diagnosed in Texas, please communicate with the Regional Zoonosis Control (ZC) office so we can work with the other state to determine which state will count it as a case to prevent dual reporting.





Follow-up for Indeterminate/Discrepant Labs

- During the investigation, you obtain the hospital lab report for the blood smear and discover that the result did not identify the infecting *Plasmodium* species for this patient's sample
- What would be the next steps?
 - Inquire whether any further testing is pending (microscopy or PCR test)
 - ➤ If no pending tests and the hospital lab is willing to forward samples, DSHS welcomes slides and/or EDTA blood submissions to identify infecting *Plasmodium* species
 - Coordination between LHD, Regional ZC, and Zoonosis Control Branch (ZCB)



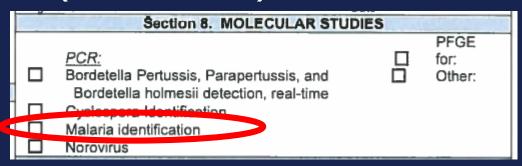
Malaria studies at DSHS (G-2B Form)

Microscopy (Prepared slides or EDTA tube blood)

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Section 4. PARASITOLOGY					
	Cryptosporidium/Cyclospora Exam		Microfilaria Exam @		
	Fecal Ova and Parasite Exam		Microsporidia Exam		
41	Malaria/Blood Parasite Exam @		Worm Identification @		
	Schistosoma/Urine Parasite Exam @		Other:	Ī	
	Water State Control of the Control o			\neg	

Note: "@" symbol indicates brief clinical/travel history is needed with submission

PCR (EDTA tube blood)





Lab Confirmation Tests

- 1) Blood Smear Microscopy
 - Typically the infecting *Plasmodium* species will be identified or at least favored (*P. falciparum, P. vivax, P. ovale, P. malariae*)
 - Record peak parasitemia
- 2) Nucleic Acid Testing by PCR typically ordered to identify infecting species when microscopy alone cannot

DSHS Austin lab offers both types of specimen analysis and can coordinate with CDC as needed



Chemoprophylaxis vs. Therapy

Chemoprophylaxis

Was malaria chemoprophylaxis taken? Yes	□ No □ Unknown	
f yes, which drugs were taken? Chloroquine	☐ Mefloquine ☐ Doxycycline ☐ Primaquine	☐ Atovaquone/proguanil
Other:	Unknown	

- ➤ Typically prescribed to person traveling from non-malaria endemic country to a malaria endemic country
- > Preventative

Therapy

Therapy for this attack (check					
Chloroquine Tetracycline	☐ Doxycycline ☐ Mefle	quine Exchange transfusio	n Artesunate	Artemether/lumefantrine	Unknown
☐ Primaquine ☐ Quinine	Quinidine Clind	amycin Atovaquone/proguan	il 🔲 Other (spec	eify):	

➤ If patient took chemoprophylactic antimalarial medicine during travel, the treatment drug(s) will be different.



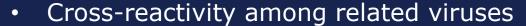
Malaria Resources

- General information
 https://www.cdc.gov/parasites/malaria/index.html
- Malaria travel information and prophylaxis
 https://www.cdc.gov/malaria/travelers/country_table/a.html

Country	Areas with Malaria	Drug Resistance ²	Malaria Species³	Recommended Chemoprophylaxis ⁴	Key Information Needed and Helpful Links to Assess Need for Prophylaxis for Select Countries
Afghanistan	April–December in all areas at altitudes below 2,500 m (8,202 ft).	Chloroquine	<i>P. vivax</i> 95%, <i>P. falciparum</i> 5%	Atovaquone-proguanil, doxycycline, mefloquine, or tafenoquine [©]	1) Month(s) of travel 2) City(ies) of travel 3) Altitude of city(ies) of travel Altitude information ☑ for Afghanistan

Guidelines for treatment in United States
 https://www.cdc.gov/malaria/diagnosis_treatment/treatment.html

Arboviruses: Things to Consider

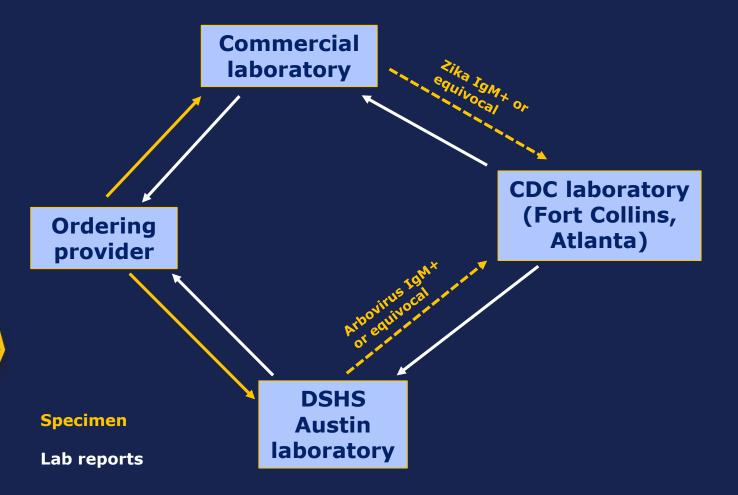


- Overlap of risk areas globally and common clinical manifestations of infection
- Previous history of infection with the same or a related arbovirus can affect immune response in recent infection
- For DSHS disease reporting, multiple case definitions: arbovirus, dengue (three types),
 Zika (four types), yellow fever



Zika & PRNT: Tracking Testing Progress





Arbo Scenario #1: Traveler

 The following test result appears in the DRR queue for a 35-year-old female resident of Bexar county

Reporting Facility: /iraCor	11/09/2018	Dengue virus antibody, IgG: positive - (Final) =7.91 ISR Reference Range: (-<1.65) - (Final)	
		Dengue virus antibody, IgM: positive - (Final) =4.52 ISR Reference Range: (-<1.65) - (Final)	

- After requesting more information from the ordering provider, you discover the patient:
 - Traveled to Thailand for two weeks, returning 11/4/18, and spent a lot of time outdoors while there
 - She has visited Thailand multiples times previously
 - No other infectious disease testing was ordered besides dengue IgM and IgG





Arbo Scenario #1 (continued)

- Clinical information: Onset of illness was 11/5/18 (one day after returning from Thailand) with fever, headache, retro-orbital pain, rash, and myalgia
- →How would this case be classified?
 - → **Probable dengue**, based on the IgM result, travel history, and symptoms.
- →What additional arbovirus testing should the physician have considered ordering?
 - →Given the date of collection of 4 days after onset, PCR should have been used as well as IgM and IgG for dengue. Additionally, Zika, chikungunya at minimum should have been considered as other arboviral diseases endemic to Thailand.



Arbo Scenario #1 (continued)

→ If the dengue IgM had been negative, how would this be classified? Any other action you might have taken in this case?

DENGUE VIRUS AB.IGG:
POSITIVE
Reference Range: (NEGATIVE) - (Final)

DENGUE VIRUS AB.IGM:
NEGATIVE
Reference Range: (NEGATIVE) - (Final)

- → Suspect dengue, based on the clinical symptoms and exposure alone. The positive IgG does *not* make this a probable case.
- → With a previous history of travel to a dengue-endemic area and a day 4 sample, it is possible she may be a secondary dengue case with viremia but a hard-tocatch window of low IgM detectability.
 - → Consider forwarding the sample to DSHS for Trioplex PCR testing; if positive, she could be a confirmed dengue case.

West Nile Virus Case Scenario

A new West Nile Virus IgM positive (in CSF) ELR appears in the DRR queue, with a collection date of 6/25/18:



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Ordered Test: WEST NILE VIRUS AB.IGM

Resulted Tests and Results

Resulted Test: WEST NILE VIRUS AB.IGM

Result(s): positive CSF

Reference Range:

Status:

Result Comments:



WNV Case Scenario (continued)

Information obtained after investigation:

- 62-year-old female from Dallas County
- No recent travel history
- Illness onset date: 6/20/2018
- · Reported symptoms: fever, chills, arthralgia, and myalgia

Is this a case, either of WNF or WNND? **NO!**





Neuroinvasive:

Confirmed: A clinically compatible case (meets neuroinvasive clinical evidence criteria) with laboratory confirmation

Probable: A clinically compatible case (meets neuroinvasive clinical evidence criteria) with virus-specific IgM antibodies in CSF of serum but no other testing OR with lower levels of neutralizing antibodies for potentially cross-reactive* arboviruses endemic to the region where exposure occurred*.

Non-neuroinvasive:

Confirmed: A clinically compatible case (meets non-neuroinvasive clinical evidence criteria) with laboratory confirmation

Probable: A clinically compatible case (meets non-neuroinvasive clinical evidence criteria) with virus-specific IgM antibodies in serum but no other testing OR with lower levels of neutralizing antibodies for potentially cross reactive* arboviruses endemic to the region where exposure occurred



WNV Case Scenario (continued)

What can be done next?

- Check with provider to see if there are any additional test results that were not reported
- Check with provider to see if there are additional tests pending
- If no tests pending, check with provider for possibility of additional testing (serum)
- Review medical records for other potential neurological symptoms (CSF pleocytosis)
- If patient was still hospitalized during initial investigation, obtain updated medical records



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DSHS Chagas Disease Webpage

Chagas Disease

Data Guidance Information Medical Providers Submission and Testing Resources

Chagas disease, also called American trypanosomiasis, is caused by infection with *Trypanosoma cruzi*, a single-celled parasite naturally transmitted by several species of triatomine bugs ("kissing bugs," "cone-nose bug," "vinchuca"). Humans, dogs, and many other species of domestic and wild animals are susceptible to infection. The insect vectors of Chagas disease and the *T. cruzi* parasite are found in all regions of Texas.

- · General Information about Chagas Disease
 - o Chagas Disease Data and Map of Geographic Distribution for Texas
- Chagas Disease Information for Medical Providers
 - · Laboratory Diagnosis of Chagas Disease in Humans
- <u>Triatomine Bug/Kissing Bug/Cone-Nose Bug/Vinchuca Submission and Testing</u>
 Instructions and form for submitting bugs for identification and testing for *T. cruzi*
- Downloadable Information Guide "Kissing Bugs and Chagas Disease: What You Need to Know"
 - o English (PDF, 2.3 MB)
 - Spanish (PDF, 1.7 MB)
- Additional Resources



https://www.dshs.texas.gov/IDCU/disease/Chagas-Disease.aspx

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Chagas Disease in Humans Testing Guidance for Providers

Serologic screening tests for chronic Chagas disease are available at several commercial laboratories. Confirmatory serologic testing for chronic Chagas disease and molecular testing (PCR) for acute Chagas disease are available at the CDC. If you wish to test a patient for Chagas disease, please note the following:

- 1. CDC will not accept serologic specimens for initial screening for chronic Chagas disease. Serologic screening should first be performed at a commercial laboratory. Patients testing positive are eligible for confirmatory testing at CDC.
- 2. All specimens to be tested at CDC must be submitted to the DSHS laboratory and not directly to CDC. The DSHS laboratory will forward all specimens to CDC.
- 3. Providers wishing to submit samples to CDC <u>must</u> consult with the DSHS Regional Zoonosis Control (ZC) program prior to sample submission.



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DSHS Chagas Disease (Trypanosoma cruzi) Exposure Assessment and Testing Guidance

Rev. 7-19

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1

3

Person exposed or potentially exposed to a triatomine bug and the bug or photo of the bug is available for identification Person tests positive at a blood bank OR

Person exposed or potentially exposed to a T. cruzi positive triatomine bug >8 weeks prior

Person with onset of cardiac disease compatible with chronic Chagas disease

Person with Chagas-positive mother or sibling

Person potentially exposed to blood or tissue from an infected person or animal >8 weeks prior (e.g. needlestick injury, tissue transplant) Person exposed or potentially exposed to a T. cruzi positive triatomine bug ≤8 weeks prior

OR

Person traveled to a Chagas-endemic area and has acute symptoms

Person potentially exposed to blood or tissue from an infected person or animal ≤8 weeks prior (e.g. needlestick injury, tissue transplant)

- Email the digital photo(s) to DSHS at bonny.mayes@dshs.texas.gov, whitney.qualls@dshs.texas.gov and the.vet@dshs.texas.gov
- If bug appears to be a triatomine or no photo is available, send the bug to DSHS for identification and testing (instructions and submission form are available on the DSHS Chagas page).
- If the bug is not a triatomine, the person is NOT at risk for Chagas disease
- If the bug tests positive for T. cruzi, go to process 2 or 3, depending on timeframe
- If the bug tests negative for T. cruzi, the person is NOT at risk for Chagas disease
- If the bug appears to be a triatomine, but is not available for testing and you wish to pursue clinical testing, go to process 2

Perform serology at a commercial lab

Negative serology – person does NOT have Chagas disease Positive serology—
request that any
remaining sample be
forwarded to the DSHS
lab or collect a new
sample and send to DSHS
lab for routing to CDC
(select "Chagas Disease"
in Section 9: CDC
Reference Tests on the
G2A submission form)

- Prior to sample submission, consult with Regional DSHS Zoonosis Control staff to 1) determine if PCR testing is warranted, and 2) to discuss other testing options
- If CDC agrees to test by PCR, submit the appropriate sample to the DSHS Lab for routing to CDC (select "Chagas Disease" in Section 9: CDC Reference Tests on the G-2A submission form)
- If CDC recommends serologic testing instead of PCR testing, the sample should be sent to a commercial lab (follow process 2)

 If the person is confirmed positive at the CDC, consult with CDC staff regarding clinical evaluation, management, and treatment* of Chagas disease

- If the person tests negative at CDC, the person does NOT have Chagas disease
- * Benznidazole approved by FDA for use in children 2-12 years of age; Nifurtimox is available as an investigational drug through CDC

https://www.dshs.texas.gov/IDCU/disease/chagas/Chagas Disease Testing Guidance for Healthcare Providers.aspx

09/26/2019 DSHS ELC Conference

Commercial Laboratory Testing

- Mayo Medical Lab
 - ELISA for T. cruzi IgG
- ARUP
 - ELISA for T. cruzi IgG
 - IFA for T. cruzi IgM
 - ONLY appropriate if current or recent infection suspected
 - Should be used in conjunction with a blood parasite screen
 - o False positives are very common with this test
- Quest/Focus Diagnostics
 - Trypanosoma cruzi Antibody, IgG

Disclaimer of Endorsement: Reference herein to any specific commercial laboratory or test does not necessarily constitute or imply its endorsement, recommendation, or favoring by the Texas Department of State Health Services.



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Chagas Disease Scenario 1

- A healthy 45-year-old male that resides in Dallas County donates blood
- The blood collection agency faxed abnormal T.
 cruzi screening test results to ZCB and sent a
 letter to the donor Lab Results:
 - reactive for *T. cruzi* screen at blood collection agency
 - positive for supplemental (confirmatory) *T. cruzi* test at blood collection agency
- The DSHS lab receives a serum sample from the donor's physician – the form indicates that the physician is requesting Chagas Disease Serology at CDC.
- What actions should be taken at ZCB, Region 2/3 ZC, Dallas County, and the DSHS laboratory?

Chagas Disease Scenario 1 (continued)

- The lab notifies ZCB for approval after <u>any</u>
 Chagas specimen is received
 - if unfamiliar with the patient, ZCB checks to see if the patient is in NBS (has a positive *T. cruzi* IgG ELISA)
- Only *T. cruzi* blood donor screening tests were performed
 - the supplemental or confirmatory test is not a diagnostic test
- The physician needs to order a *T. cruzi* IgG
 ELISA test
 - see list of labs/tests on DSHS Chagas page
 The IgM IFA is <u>not</u> appropriate for this!



Chagas Disease Scenario 2

- A 24-year-old female wakes up to find an engorged kissing bug in bed with her
- The following day, she mails (priority mail express) the bug to DSHS for testing at CDC — ZCB forwards the bug to CDC immediately after receipt
- Two days after mailing the bug, submitter contacts the Regional ZC office to find out how long testing will take and is told it may take a month or more

 submitter is concerned and states that she wants to be tested for Chagas disease
- How would you handle this?



Chagas Disease Scenario 2 (continued)



- bug may <u>not</u> be *T. cruzi* positive
- even if it is, bug may not have defecated on submitter
- even if bug defecated on submitter, infected feces may not have been rubbed into a break in the skin, mucus membrane, etc.
- even if exposed to parasite, not enough time has passed for there to be a measurable antibody response!
- Provide information on testing options
 - if nonspecific acute symptoms develop, T. cruzi
 IgM IFA and/or blood smears (PCR an option if acute Chagas suspected by HCP)
 - *T. cruzi* IgG testing at commercial lab if bug tests positive <u>and</u> ~8 weeks has passed since exposed



Chagas Disease Case Investigation



- T. cruzi IgG testing for positive blood donors,
 CDC serology for those with positive T.cruzi IgG testing, etc.
- Get detailed information regarding where patient and mother were born, where patient resided, complete travel history, exposure to triatomines, etc.
- Make sure all lab reports, including blood donor screening, are in NEDSS
 - include hard copy labs if no ELR
- Follow up on testing
 - case status will change based upon commercial lab and/or CDC test results (NAC if negative, confirmed if positive at CDC)



Lyme Disease Testing Issues



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- Sensitivity low during first two weeks of infection (<50%)
- False positive screens are common several possible causes:
 - syphilis, periodontal disease, acute EBV, lupus, RA, tickborne relapsing fever (TBRF)
- IgM Immunoblots (IB) (Western Blot WB)
 - irrelevant if no screen performed first (or if screen/screens negative)
 - only need two of three bands to be "detected"
 - interpretation subjective
 - only relevant up to 30 days after symptom onset
- When pretest probability of Lyme disease is low, a positive test is more likely to be falsely positive
 - i.e. exposure in low incidence area and no symptoms or only nonspecific symptoms

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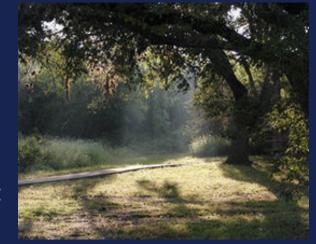
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Lyme Disease Scenario 1

- Patient is a 39-year-old male that resides in Travis
 County
- Exposure History traveled to Indiana for a wedding June 6-12; no tick attachment or outdoor activities noted
- Clinical Information symptom onset July 1; fever/sweats/chills, arthralgias, myalgias, neck pain, fatigue, adenopathy, confusion, Bell's palsy, radiculoneuropathy
- Lab Results
 - Lyme EIA screen positive / IgM WB positive
 DOC 19 days after symptom onset
 - WNV IgM positive at CPL (6.85 acute, 1.95 conval)
 - Dengue IgM negative
- Physician Diagnosis subacute disseminated Lyme disease
- Any follow-up questions or testing recommendations? How would you classify this case?

Lyme Disease Scenario 1 (continued)

- ZCB requested follow up testing at CDC
 - PRNT at CDC negative for DEN, SLE, WNV, ZIKV
 - Tick-borne Relapsing Fever -EIA & WB **Positive**!
- Classified as "Not a Case" for Lyme Disease & Confirmed for TBRF
- Follow up interview patient mentioned that he went to a local park with his wife and new dog ~one week prior to symptom onset







Lyme Disease Scenario 2

- Patient is a 12-year-old male that resides in South Texas
- **Exposure History** 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 WB negative)
 - DOC in March (onset in late fall of prior year)
- **Physician Diagnosis -** early disseminated Lyme disease (med records state "previously negative for Lyme disease and is IgG and IgM positive and confirmed by reflex testing")
- Any follow-up questions or testing recommendations? How would you classify this case?



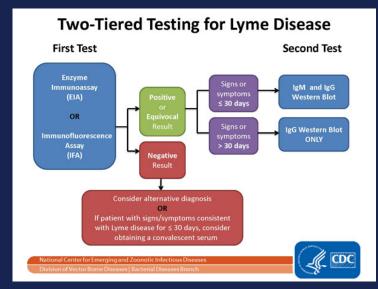
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Lyme Disease Scenario 2 (continued)

- Classified as Not a
 Case
- The IgM WB is not relevant if onset is more than 30 days prior to DOC!
- How would this be classified if the patient had an IgG positive WB but no screen?
- What if the patient had a negative screen and IgG positive WB?

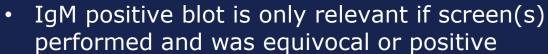




https://www.cdc.gov/lyme/healthcare/clinician_twotier.html



Lyme Disease Case Investigation



- If screen(s) negative, blot should not be run therefore, positive WB(s) preceded by negative screen(s) should be ruled out
- Onset date important!
 - IgM positive blot only relevant if specimen collected ≤30 days after symptom onset
- Make sure all lab reports are in NEDSS
 - Include hard copy labs if no ELR
- Physician does not have to <u>definitively</u> diagnose patient with Lyme ("will not be considered cases if the medical provider specifically states this is not a case of Lyme disease")
- Inquire about travel history!
- Provide records for cases where there is a physician diagnosed EM or late manifestation
- Consider "alternate explanation": Rickettsial illness, rheumatoid arthritis, lupus, etc.



Rickettsial Testing Issues



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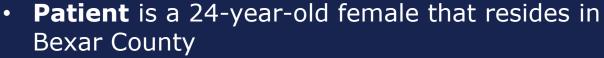
- An antibody response is not expected until ~7 days after symptom onset
 - many HCPs collect too early and fail to collect a convalescent sample
- Following infection, rickettsial IgM titers persist for months and IgG titers persist for years!
 - does titer reflect current infection or past?
- Rickettsial IgM titers are not reliable need IgG!
 - IgM rises at approximately the same time as IgG
- Seroprevalence studies on healthy blood donors indicate that up to 6% of US residents have IgG antibodies reactive with R. rickettsii when tested by IFA
 - <u>really</u> need that convalescent sample, especially if acute titer is very low

Rickettsial Testing Issues (continued)

- Due to antibody cross-reactivity, need to perform rickettsial panel testing
 - often tested for only typhus or only SF
- Due to antibody cross-reactivity, a single acute specimen cannot be used to differentiate between SFGR and flea-borne typhus with confidence (need to see rise in IgG titer)
 - very few HCPs collect a convalescent sample
 - HCPs need to collect <u>both</u> acute and convalescent serum specimens, ideally drawn at least 2 weeks apart
- PCR testing at CDC can differentiate between *R. rickettsii* and *R. typhi*
 - blood or serum sample must be collected during the acute phase of illness no more than two days after doxycycline treatment begins
 - o blood higher sensitivity!
 - sample must be routed through state lab, clinical info must be provided
 - turnaround time is ~6 weeks



Rickettsial Disease Scenario 1



- Exposure History no known tick or flea exposure, no exposure to wild animals, dogs are present at residence
- Clinical Information symptom onset mid-September; fever/chills, headache, anorexia, photophobia, malaise, myalgia, thrombocytopenia, elevated liver function tests, rash (spread from arms/legs to trunk)
- Lab Results
 - RMSF IgG 1:128 / RMSF IgM 1:256
 - DOC October 1
- Classified as probable SFGR
- Any follow-up questions or testing recommendations? How would you classify this case?



Rickettsial Disease Scenario 1 (continued)

- 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
- Ideal if request to forward is initiated ASAP before sample is discarded



Rickettsial Disease Scenario 2

- Patient is a 35-year-old male that resides in Dallas
 County and did not travel within last 30 days
- Exposure History does not report exposure to fleas or ticks but recently took in a feral kitten and has had issues with opossums in his back yard; has one dog
- Clinical Information onset date May 15; fever, headache, nausea/vomiting, malaise, thrombocytopenia
- Lab Results
 - Typhus group IgM 1:128 / Typhus group IgG 1:128
 - SFGR IgM 1:256 / SFGR IgG 1:128
 - DOC May 24
- Classified as probable SFGR
- Any follow-up questions or testing recommendations? How would you classify this case?



Rickettsial Disease Scenario 2 (continued)

- Exposure history and recent increase in flea-borne typhus cases in North Texas points to typhus as the more likely etiologic agent
- Request a convalescent sample if unable to get convalescent testing, classify as "Rickettsiosis, unspecified"
- Update to 2019 Case definition removed requirement that titers be equal:
 - Clinically compatible case (meets clinical evidence criteria) with serological evidence of elevated IgG and/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 and does not have a more likely clinical explanation.



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Rickettsial Case Investigation

- Is further testing warranted? If so:
 - forward to DSHS for rickettsial panel testing
 - request convalescent testing
- Is there an alternate explanation?
 - need to further investigate some cases to ensure that incident cases are being reported rather than patients with past infections
 - early symptoms of both typhus and SFGR (fever, headache) are non-specific
 - "Not a Case" the investigation if rickettsial disease seems unlikely and there is an alternate explanation for the signs/symptoms
- Do NOT report cases that have previously been reported
 - long duration of immunity against re-infection
 - some cross-immunity within groups

https://www.dshs.texas.gov/idcu/health/zoonosis/contact/



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Thank you!

Questions?

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Zoonosis Control Branch