Introduction to Tickborne Disease Case Investigations

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Bureau of Infectious Disease and Laboratory Sciences
Division of Epidemiology
June 2022
Learning objectives

- Participants will learn how to conduct tickborne disease case investigations and understand best practices for speaking with Infection Preventionists and providers.

- Participants will understand the importance of data collection completeness from routine case investigations to inform statewide preventative measures.

- Participants will learn about the prevalent ticks in Massachusetts, diseases they carry, and individual prevention measures.
Tickborne Diseases in MA

- Lyme Disease
  - ~6,000 confirmed & probable cases as of 2014
- Babesiosis
  - 580 confirmed & probable cases as of 2021
- Human Granulocytic Anaplasmosis (HGA)/Anaplasmosis
  - 769 confirmed & probable cases as of 2021
- Borrelia *miyamotoi*
  - 32 confirmed & probable cases as of 2019, as of 2021 there are 2 probable cases and 0 confirmed, but this is likely due to poor follow-up and fewer people seeking testing during 2020.

- In MA, but rare: Tularemia, Ehrlichiosis, Rocky Mountain Spotted Fever, Powassan
Incidence Rates (per 100,000 population\(^*\)) for Confirmed and Probable Lyme Disease in Massachusetts 2010-2014\(^*\)

Statewide Totals
Incidence Rate: 68.30
Population: 6,547,629
Unknown City/Town: 2,588

Incidence Rate
- \(\leq 100\)
- 101 - 250
- 251 - 500
- > 500
- Suppressed ~
- No Reported Cases

* Data as of 6/3/2015 and subject to change
~ Case counts less than 5 in populations\(^*\) less than 50,000 are suppressed to maintain patient confidentiality.

\(^*\) Population based on 2010 Census data.
Five-year Babesiosis incidence rates per 100,000

State Population: 6,966,655
Incidence Rate 39.09
Population based on 2019 Census Data
Data are current as of March 17, 2022 and subject to change

Massachusetts Department of Public Health
Bureau of Infectious Disease and Laboratory Sciences
Five-year Anaplasmosis incidence rates per 100,000

State Population: 6,966,655
Incidence Rate 60.62
Population based on 2019 Census Data
Data are current as of March 17, 2022 and subject to change

Massachusetts Department of Public Health
Bureau of Infectious Disease and Laboratory Sciences
Five-year Borrelia *miyamotoi* total cases

Data are current as of March 17, 2022 and subject to change.
Step 1 in All Case Investigations

- Check the lab tab and call the ordering provider or hospital Infection Preventionist.

Investigation Tip

• Always call the provider first to confirm the diagnosis and obtain clinical information BEFORE contacting the patient.

• If you can collect all the information from the provider/IP, the investigation is complete.

• It is NOT REQUIRED, but you may choose to contact the patient directly to provide yourself as a resource to answer questions and provide educational materials.
A Word on HIPAA

- If providers refuse to provide you with the necessary information, remind them that providing information for public health investigations is **necessary and permissible under HIPAA**.

Example Call Script

• “Hi, my name is ___ I am calling from the local health department. I’d like to speak with the doctor or nurse who worked with patient [provide name and DOB].
• [Once transferred to the nurse/doctor] We received a report of a case you treated as being positive for Babesiosis. In order to determine if this is a true case I need to collect clinical information.”
• [allow them to ask questions, navigate to the medical notes]
• “All I need are the symptoms they presented with, and any risk information you collected, particularly if they mentioned tick bites, any travel (if so, where), and any mention of recent blood transfusions.”
Step 2: Collect Pertinent Information

- Lab results are not reliable on their own.
- For all tickborne diseases, collect the **clinical** and **risk** information by completing the MAVEN variables following the wizard.
  - Check the most important symptom information needed for that disease by consulting the **case classification manual**.
Why is this important?

- The goal is to appropriately classify the case (confirmed, probable, revoked). In order to do that, we need data completeness.
  - MDPH Epidemiologists do a final review and classify these cases based upon information collected in your investigations.

- If we don’t have enough information to classify, the case is left as suspect, this negatively impacts our surveillance reporting.

- If we have an underestimate of surveillance reporting we cannot allocate the adequate resources toward tickborne disease prevention efforts.
Lyme Disease

- Lyme disease is the most common tickborne disease in MA. It is spread by deer ticks which also carry our other diseases of concern.
- MA no longer conducts active surveillance of Lyme.
- Why? MA is a high Lyme disease incidence state. DPH utilizes syndromic surveillance rather than laboratory reporting.
Babesiosis

- Classification requires at least one of the clinical symptoms along with lab evidence.

### BABESIOSIS

| Event Name: | BAB |
| Event Time Period: | 1 year |

**Clinical Description (CDC 2011):**

Babesia infection can range from subclinical to life-threatening. Clinical manifestations, if any, can include hemolytic anemia and nonspecific influenza-like signs and symptoms (e.g., fever, chills, sweats, headache, myalgia, arthralgia, malaise, fatigue, generalized weakness). Splenomegaly, hepatomegaly, or jaundice may be evident. In addition to signs of hemolytic anemia, laboratory findings may include thrombocytopenia, proteinuria, hemoglobinuria, and elevated levels of liver enzymes, blood urea nitrogen, and creatinine.

**Clinical criteria for the purposes of surveillance:**

**Objective:** one or more of the following: fever, anemia, or thrombocytopenia

**Subjective:** one or more of the following: chills, sweats, headache, myalgia, or arthralgia

<table>
<thead>
<tr>
<th>CDC Event Classification (2011):</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Confirmed</strong> A case with at least one of the objective or subjective clinical evidence criteria and meets one of the following confirmatory laboratory criteria:</td>
</tr>
<tr>
<td>1. Identification of intraerythrocytic Babesia organisms by light microscopy in a Giemsa, Wright, or Wright-Giemsa-stained blood smear; OR</td>
</tr>
<tr>
<td>2. Detection of Babesia microti DNA in a whole blood specimen by polymerase chain reaction (PCR); OR</td>
</tr>
<tr>
<td>3. Detection of Babesia spp. genomic sequences in a whole blood specimen by nucleic acid amplification; OR</td>
</tr>
<tr>
<td>4. Isolation of Babesia organisms from a whole blood specimen by animal inoculation.</td>
</tr>
</tbody>
</table>

| **Probable** A case with at least one of the objective clinical evidence criteria and meets one of the following supportive laboratory criteria: |
| 1. Demonstration of a Babesia microti Indirect Fluorescent Antibody (IFA) total immunoglobulin (Ig) or IgG antibody titer of greater than or equal to (≥) 1:256 (or ≥1:64 in epidemiologically linked blood donors or recipients); OR |
| 2. Demonstration of a Babesia microti Immunoblot IgG positive result; OR |
| 3. Demonstration of a Babesia divergens IFA total Ig or IgG antibody titer of greater than or equal to (≥) 1:256; OR |
| 4. Demonstration of a Babesia duncanii IFA total Ig or IgG antibody titer of greater than or equal to (≥) 1:512. OR |
| A case that is in a blood donor or recipient epidemiologically linked to a confirmed or probable babesiosis case AND: has confirmatory laboratory evidence but does not meet any objective or subjective clinical evidence criteria; OR has supportive laboratory evidence and may or may not meet any subjective clinical evidence criteria but does not meet any objective clinical evidence criteria. |

| **Suspect** A case that has confirmatory or supportive laboratory results, but insufficient clinical or epidemiologic information available for case classification (e.g., only a laboratory report was provided). |
| Massachusetts Event Classification (2015): | Same as CDC |
Babesiosis
Babesiosis

- The wizard will pull the key questions needed for classification.
Babesiosis

• The wizard will pull the key questions needed for classification and crucial risk questions.

Once these four questions have been completed, the concerns will no longer appear on the dashboard. You must complete all four.
Human Granulocytic Anaplasmosis (HGA)

- HGA classification requires us to know if they had **fever AND one other symptom** along with lab evidence.

<table>
<thead>
<tr>
<th>Event Time Period:</th>
<th>CDC Event Classification (2008):</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td><strong>Confirmed</strong></td>
</tr>
<tr>
<td></td>
<td>Clinically compatible with one of the following laboratory criteria:</td>
</tr>
<tr>
<td></td>
<td>1. Serological evidence of a four-fold change in IgG specific antibody titer to <em>A. phagocytophila</em> antigen by indirect immunofluorescence assay (IFA) in paired serum samples (one taken in first week of illness and a second 2-4 weeks later), <strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>2. Detection of <em>A. phagocytophila</em> DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay, <strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>3. Demonstration of anaplasmal antigen in a biopsy/autopsy sample by immunohistochemical methods, <strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>4. Isolation of <em>A. phagocytophila</em> from a clinical specimen in cell culture.</td>
</tr>
<tr>
<td></td>
<td><strong>Probable</strong></td>
</tr>
<tr>
<td></td>
<td>Clinically compatible with one of the following laboratory criteria:</td>
</tr>
<tr>
<td></td>
<td>1. Serological evidence of elevated IgG or IgM antibody reactive with <em>A. phagocytophila</em> antigen by IFA, ELISA, dot-ELISA, or assays in other formats, <strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>2. Identification of morulae in the cytoplasm of neutrophils or eosinophils by microscopic examination</td>
</tr>
<tr>
<td></td>
<td><strong>Suspect</strong></td>
</tr>
<tr>
<td></td>
<td>A case with laboratory evidence of past or present infection, but no clinical information available</td>
</tr>
</tbody>
</table>

Massachusetts Event Classification (2014):
Follows the CDC event classification except when determining clinical compatibility, any of the following reported symptoms will be considered subjective evidence of hepatic transaminase elevation when liver function test values are not available: anorexia, nausea, vomiting or abdominal pain.
Human Granulocytic Anaplasmosis (HGA)
Human Granulocytic Anaplasmosis (HGA)

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**Key Questions for Case Investigation - Donald Duck - Human Granulocytic Anaplasmosis**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did case have symptoms?</td>
<td>Yes</td>
</tr>
<tr>
<td>Symptom onset date:</td>
<td>02/11/2019</td>
</tr>
<tr>
<td>Anemia:</td>
<td>Yes</td>
</tr>
<tr>
<td>Elevated liver function tests (LFTs):</td>
<td>Unknown</td>
</tr>
<tr>
<td>Fever</td>
<td>Yes</td>
</tr>
<tr>
<td>Highest temperature:</td>
<td>101</td>
</tr>
<tr>
<td>Headache</td>
<td>Yes</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>Unknown</td>
</tr>
<tr>
<td>Muscle aches/pains (myalgia)</td>
<td>Yes</td>
</tr>
<tr>
<td>Thrombocytopenia:</td>
<td>No</td>
</tr>
<tr>
<td>Other symptoms (specify):</td>
<td>Nausea</td>
</tr>
<tr>
<td>Was case hospitalized?</td>
<td>No</td>
</tr>
<tr>
<td>Outcome:</td>
<td>Died</td>
</tr>
<tr>
<td>Date of death</td>
<td>02/13/2019</td>
</tr>
<tr>
<td>Location of death</td>
<td>Emergency Department (ED)</td>
</tr>
</tbody>
</table>

**Once these three questions have been completed, the concern will no longer appear on the dashboard. You must complete all three.**
Borrelia *miyamotoi*

- Classification requires **any** symptom within the list along with the lab evidence.

<table>
<thead>
<tr>
<th>BORRELIA MIYAMOTOI INFECTION</th>
<th>NON-IMMEDIATE NOTIFICATION</th>
<th>EPIDEMIOLOGY PROGRAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Event Name:</td>
<td>Borrelia miyamotoi infection</td>
<td></td>
</tr>
<tr>
<td>Event Time Period:</td>
<td>1 YEAR</td>
<td></td>
</tr>
<tr>
<td>Clinical Description:</td>
<td>A systemic, tickborne disease presenting as fever, chills, malaise, myalgia and arthralgia and which may also include: headache, anorexia, abdominal pain, thrombocytopenia and elevated LFTs.</td>
<td></td>
</tr>
<tr>
<td>CDC Event Classification:</td>
<td>NONE</td>
<td></td>
</tr>
</tbody>
</table>
| Massachusetts Event Classification: | **Confirmed** | Clinically compatible AND the following laboratory evidence:  
  1. Detection of *Borrelia miyamotoi* specific DNA by PCR; OR  
  2. Serologic evidence of a four-fold or greater change in specific antibody titer to *Borrelia miyamotoi*; OR  
  3. Isolation of *Borrelia miyamotoi* from a clinical specimen in culture |
|                              | **Probable** | Clinically compatible AND the following laboratory evidence:  
  1. Serologic evidence of *Borrelia miyamotoi* reactive antibody |
|                              | **Suspect** | A case with laboratory evidence but no clinical information available |
Borrelia *miyamotoi*

- There is not a wizard for this TBD, so just follow along with the question packages keeping in mind the most important variables for classification.

- **BEFORE** you investigate, check to see if there is an attached lab result. Almost ALL Borrelia *miyamotoi* events are from Igenex “TBRF” results.
  - You will need to review the lab attachment to see if the Borrelia *miyamotoi* result is positive, since TBRF encompasses multiple species of Borrelia.
Borrelia miyamotoi

The TBRF result in the lab tab may show as positive, but Borrelia miyamotoi specifically may not be.

Go to the attached lab result, scroll down until you see the “Tickborne Relapsing Fever” (TBRF) results.

Once you find the TBRF result that is positive, there is usually a further breakdown of which Borrelia species is positive.

In this example, this positive TBRF result is actually negative for Borrelia miyamotoi – no investigation required.
In Summary

• Receive tickborne disease (TBD) event in your workflow.
• Check the lab tab and call the provider/IP to collect the clinical and risk information.
• Complete the variables in MAVEN using the wizard.
  • Lab result is not reliable on its own, need compatible symptoms.
  • If you leave a field blank, we will assume it wasn’t asked.
  • Example: if you ask about symptoms in general and the provider says “headache, fever” – ask specifically about each symptom, or select “no” if the doctor clearly states: “they only had headache.”
• Call the case if you have time to provide resources and education
  • Guide people to seek tickborne panel testing, not just Lyme (includes HGA, Babesia, TBRF/Borrelia *miyamotoi*), as there is potential for co-infection.
Tip Sheet Available

- Follow-up Tip Sheet is available to help you with different Tickborne Diseases.


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HELPFUL HINTS:
Follow up for Suspect Cases of Tickborne Disease

This information is intended to help you prioritize the follow up of suspect cases of tickborne disease based on laboratory test results that are reported to you. A “positive” result does not necessarily indicate presence of disease. For this reason, you should ALWAYS call the ordering provider first to confirm a diagnosis before contacting the patient. If you are not able to confirm a diagnosis with the physician and choose to follow up with the patient, be aware that the patient may not have been given a diagnosis of a tickborne disease by the doctor. If the patient has not been given a diagnosis of infection with a tickborne disease, further case investigation is not required.

Is there a positive lab result for Babesia?  
- NO
  - Babesiosis is prevalent throughout the state and can be transmitted by blood transfusion. These suspect cases should be followed up promptly to determine if there is a history of blood transfusion or donation.
  - Lab results indicating a positive serology or positive specific PCR are most likely to represent true cases and should be prioritized for follow up of other suspect cases of babesiosis.
  - Suspect cases with a single- or Babesia-specific IgG antibody titre of ≥128 (≥1:512 for B. duttonii) may or may not represent actual infection and should be investigated. No follow up is required if there is no evidence of prior infection.

Is there a positive lab result for Anaplasma or Ehrlichia?  
- YES
  - Because A. phagocytophilum and E. chaffeensis are often found throughout Massachusetts, suspect A. phagocytophilum or E. chaffeensis cases should be prioritized for follow up.
  - Lab results indicating detection of A. phagocytophilum or E. chaffeensis by PCR are most likely to represent true cases and should be prioritized for follow up over other suspect cases of A. phagocytophilum or E. chaffeensis.
  - Suspect cases with a single- or A. phagocytophilum or E. chaffeensis-specific IgG antibody titre of ≥1:512 may or may not represent actual infection and should be investigated. No follow up is required if there is no evidence of prior infection.

Is there a positive lab result for Borrelia burgdorferi?  
- NO
  - Because there are likely to be few Borrelia burgdorferi cases and lab information is available on patients with this disease, suspect cases should be a priority following Babesia and Anaplasma investigations.
  - Positive lab results may come in by IgM, IgG, or PCR for B. burgdorferi, all of which should be prioritized for follow up. If lab results that come in from a IMB, check the attached lab to see if the Borrelia burgdorferi result is positive. If not, no follow up is required.

Is there a positive lab result for Chlamydia pneumoniae?  
- YES
  - Because Chlamydia pneumoniae is transmitted by the respiratory tract and because the use of antibiotics is less common in Massachusetts, true cases of chlamydial infections are also rare. Suspect Chlamydia pneumoniae cases are therefore not a priority for follow up. In the event that a case is confirmed, follow up of other suspect cases of chlamydial infections is advised.
  - Lab results indicating detection of C. pneumoniae by PCR are most likely to represent true cases and should be prioritized for follow up over other suspect cases of chlamydial infections.
  - Suspect cases with a single- or C. pneumoniae-specific IgG antibody titre of ≥1:128 may or may not represent actual infection and should be investigated. No follow up is required if there is no evidence of prior infection.

Is there a positive lab result for Rocky Mountain spotted fever?  
- NO
  - RMSF is a rare disease in Massachusetts. Since 2000, there have only been five confirmed cases in the state. This means that most suspect cases are not likely true cases and can be prioritized after suspect babesiosis, HGE, A. phagocytophilum, and HME cases.
  - Lab results indicating detection of Rickettsia rickettsii or spotted fever group-specific IgG antibody titre of ≥1:128 may or may not represent actual infection and should be investigated. No follow up is required if there is no evidence of prior infection.

Is there a positive lab result for Mycoplasma pneumoniae?  
- YES
  - Mycoplasma pneumoniae is a rare disease in Massachusetts. Since 2000, there have only been five confirmed cases in the state. This means that most suspect cases are not likely true cases and can be prioritized after suspect babesiosis, HGE, A. phagocytophilum, and HME cases.
  - Lab results indicating detection of M. pneumoniae are most likely to represent true cases and should be prioritized for follow up over other suspect cases of M. pneumoniae.
  - Suspect cases with a single- or M. pneumoniae-specific IgG antibody titre of ≥1:128 may or may not represent actual infection and should be investigated. No follow up is required if there is no evidence of prior infection.

The information above is intended as guidance only and local protocols for follow up may vary.

*LGOHs are not asked to conduct case-based follow up for Lyme disease.*

Updated: June 2022
EDUCATION & PREVENTION
Education

• While there is a seasonality to tick activity (nymphs April-June, adults July-November) ticks are active throughout the year when temperatures are above freezing.

• If you are hiking through the woods in February and it’s 41ºF degrees, you could be at risk!

• Remind people ticks are very susceptible to desiccation and tend to be found in **shady, damp areas that are brushy with lots of leaf litter** such as woodpiles or stonewalls.

• Ticks do not jump or fly! Deer and dog ticks require direct contact in order to catch a host.
What do ticks look like?

- Adult female deer ticks have reddish abdomens and dark legs.
- Adult dog ticks are nearly twice the size of deer ticks, have a white scutum and striations on the abdomen, the legs are banded.
- Lone Star ticks are rare in MA. Note the white spot on the abdomen.

Deer tick aka “Black-legged tick”

American Dog Tick

Lone Star Tick
### Different Tick Species Transmit Different Pathogens

<table>
<thead>
<tr>
<th></th>
<th>Black-Legged Tick</th>
<th>Western Black-Legged Tick</th>
<th>American Dog Tick</th>
<th>Brown Dog Tick</th>
<th>Lone Star Tick</th>
<th>Groundhog Tick</th>
<th>Rocky Mountain Wood Tick</th>
<th>Soft Tick</th>
</tr>
</thead>
<tbody>
<tr>
<td>ixodes scapularis</td>
<td>ixodes pacificus</td>
<td>Dermacentor variabilis</td>
<td>Rhipicephalus sanguineus</td>
<td>Amblyomma americanum</td>
<td>Ixodes cookei</td>
<td>Dermacentor andersoni</td>
<td>Ornithodoros spp.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease</th>
<th>Black-Legged Tick</th>
<th>Western Black-Legged Tick</th>
<th>American Dog Tick</th>
<th>Brown Dog Tick</th>
<th>Lone Star Tick</th>
<th>Groundhog Tick</th>
<th>Rocky Mountain Wood Tick</th>
<th>Soft Tick</th>
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<tbody>
<tr>
<td>Lyme Disease</td>
<td>✓</td>
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<tr>
<td>Rocky Mountain Spotted Fever</td>
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<tr>
<td>Babesiosis</td>
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<td>Tularemia</td>
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<td>Tick-Borne Relapsing Fever</td>
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<td>Erlichiosis</td>
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<tr>
<td>STARI (Southern Tick-Associated Rash Illness)</td>
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<tr>
<td>Colorado Tick Fever</td>
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<tr>
<td>Heartland Virus</td>
<td></td>
<td></td>
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<td></td>
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<td>✓</td>
</tr>
</tbody>
</table>
Individual Prevention Efforts

- Use EPA approved repellents:
  - **DEET** (N,N-diethyl-meta-toluamide)
    - Use products that contain 20% or more for adults
    - No more than 10-15% for children
    - Do not exceed 30% concentrations
  - **Permethrin** kills ticks on contact
    - Can only be used on clothing (Do not apply on the hands or face of young children or on infants or infant clothing)

- Check for ticks daily: Inside and behind the ears, along your hairline, back of your neck, armpits, groin, legs, vehicle.

- Shower soon after being outdoors and throw clothes in dryer to kill off ticks.

- Wear long-sleeved shirts and pants whenever possible.

- Call your doctor if you get a fever or rash.
Proper Tick Removal

- Grab the tick as close to the skin as possible and pull straight out with steady pressure.
Required Tick Attachment for Disease Transmission

- Removing infected ticks within 24 hours reduces the risk of disease transmission.
Resources

- Information on ticks and mosquitoes in MA, as well as links to the risk maps of WNV and EEE
  - [https://www.mass.gov/mosquitoes-and-ticks](https://www.mass.gov/mosquitoes-and-ticks)
- Information about mosquito control programs and aerial spraying FAQs
  - [https://www.mass.gov/service-details/mosquito-control-and-spraying](https://www.mass.gov/service-details/mosquito-control-and-spraying)
- Links to educational materials on tickborne disease, as well as surveillance reports
  - [https://www.mass.gov/tick-borne-diseases](https://www.mass.gov/tick-borne-diseases)
- Other key resources
  - [https://web.uri.edu/tickencounter/fieldguide/ticks-by-species/](https://web.uri.edu/tickencounter/fieldguide/ticks-by-species/) - great website for identifying ticks and prevention tips!
- Places that conduct tick testing:
  - [https://ag.umass.edu/resources/tick-testing-resources](https://ag.umass.edu/resources/tick-testing-resources)
  - [https://www.mass.gov/service-details/tick-identification-and-testing-services](https://www.mass.gov/service-details/tick-identification-and-testing-services)
- the best resource for MA residents is likely ECO Laboratories in Acton, MA: [https://ticktests.com/](https://ticktests.com/)
QUESTIONS?
Questions that came in ahead of time

1. Will babesia smear determine if IgG positive is old and already treated vs. old and untreated?
2. Why is it not standard practice during an H&P to ask the basic questions about possible tick exposure, travel, blood donations?
3. What is "tick-borne recurring [sic relapsing] fever"?
4. What does it mean when event status says "revoked" after investigation? (I had a Babesiosis case recently where this happened.)
5. Please cover understanding the limitations of the most frequently used lab tests.
6. I usually obtain answers to Wizard questions by sending provider a fax and waiting for response. Is that still acceptable?
7. How long does a deer tick need to be on a person to cause Lyme Disease or other co-infections? (HGA vs Babesia etc.)
8. Does the state have an official list for Tick testing labs to refer people to?
9. Discuss babesiosis; what PHN primary goal for tickborne illnesses are?