Tickborne Diseases in Wisconsin

Diep (Zip) Hoang Johnson
Wisconsin Division of Public Health
608-267-0249
08/01/11
Overview

• Reporting in WI

• Disease characteristics

• Laboratory testing, results, and interpretations

• Epidemiology and Statistics
Why Are Tickborne Infections Reportable?

**Surveillance**-

- Define demographic, geographic, and seasonal distribution
- Monitor disease trends in a more consistent and unified manner with the same case definition for reporting
- Identify areas where tickborne diseases may be emerging and risk exposures to WI residents
- Evaluate where to target education, prevention, and control measures
- Define disease characteristics and sequelae
- Determine if the current diagnosis/treatment process is effective
- Data available for future funding and research
Reporting in WI

- WI Reporting- hard copy or electronic reporting (ELR)
- WI Electronic Disease Surveillance System (WEDSS)
- All positive laboratory results should be reported
- Tickborne diseases- require lab results and compatible signs/symptoms to determine case status (confirmed, probable, suspect, not a case)
- All patient with EM rash (with or without lab results) should be reported because this is a confirmed Lyme disease case in WI
- All clinical information should be reported by providers using specific disease case report form or entered directly into WEDSS as all the fields requesting information have been programmed into WEDSS
### Surveillance in WI, 2002-2010

#### Tickborne Infections

<table>
<thead>
<tr>
<th>Infection</th>
<th>2010</th>
<th>2002-2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powassan virus</td>
<td>4 (0.1)</td>
<td>7 (0.04)</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>3,499 (85)</td>
<td>14,876 (88)</td>
</tr>
<tr>
<td>Anaplasmosis/Ehrlichiosis</td>
<td>546 (13)</td>
<td>1,968 (12)</td>
</tr>
<tr>
<td>Babesiosis</td>
<td>28 (0.7)</td>
<td>125 (0.7)</td>
</tr>
<tr>
<td>Spotted Fever Rickettsiosis (SPF)*</td>
<td>7 (0.2)</td>
<td>20 (0.1)</td>
</tr>
</tbody>
</table>

* Travel related infections
The 5-step method for providers:

- Request WI user ID and password through the WI Access Management System (WAMS)
  [https://on.wisconsin.gov/WAMS/SelfRegController](https://on.wisconsin.gov/WAMS/SelfRegController)
- Reply to email received
- Register in the HAN (Health Alert Network) using WAMS ID/password
- Contact WEDSS help desk by email to notify
dhswedss@wisconsin.gov
- Follow WEDSS instructions email- include WEDSS access, account, temporary password
  [https://wedss.wisconsin.gov/webvcmr](https://wedss.wisconsin.gov/webvcmr)
## WEDSS-Search Screen in Provider’s Portal

![Search Screen](image)

### Incident Search

**Create a new WEDSS Reporter record:**

**Search for Incidents by:**
- Name (last, first):
- Disease:
- Date Range: From: [ ] To: [ ]

**Select a WEDSS Reporter record from below:**

<table>
<thead>
<tr>
<th>Date</th>
<th>Case ID</th>
<th>Disease</th>
<th>Jurisdiction</th>
<th>Patient</th>
<th>DOB</th>
<th>Submitted By</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/17/2010</td>
<td>452303</td>
<td>UNKNOWN DISEASE</td>
<td>Dane County</td>
<td>TEST,TESTCASE</td>
<td></td>
<td>Provider, Tanya</td>
</tr>
<tr>
<td>9/8/2010</td>
<td>425637</td>
<td>UNKNOWN DISEASE</td>
<td></td>
<td>TEST,TEST</td>
<td></td>
<td>Provider, Tanya</td>
</tr>
<tr>
<td>9/2/2010</td>
<td>423785</td>
<td>CHLAMYDIA TRACHOMATIS INFECTION</td>
<td>unknown</td>
<td>TEST,TESTTESTTEST</td>
<td></td>
<td>Provider, Tanya</td>
</tr>
</tbody>
</table>
Provider’s Web Report
This information is on the Case Investigation tab of the LHD’s view.
**Provider’s Web Report**

### Lyme - Clinical signs and symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Onset date</th>
</tr>
</thead>
<tbody>
<tr>
<td>EM rash (&gt; 5 cm in diameter, physician diagnosed)</td>
<td></td>
</tr>
<tr>
<td>Bells palsy or other cranial neuropathy</td>
<td>Yes</td>
</tr>
<tr>
<td>Lymphocytic meningitis</td>
<td>Yes</td>
</tr>
<tr>
<td>2nd or 3rd degree atrioventricular block</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*If encephalomyelitis is checked "Yes", CSF stir must be higher than serum stir.

### Clinical information

<table>
<thead>
<tr>
<th>Field</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician/medical provider name</td>
<td></td>
</tr>
<tr>
<td>Clinic name</td>
<td></td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>Phone number</td>
<td></td>
</tr>
</tbody>
</table>

### CDC LYME DATA - STATE USE ONLY

[Form fields for data entry]
The submit button is always on the last tab of the providers view.
Supplemental Tab in WEDSS’ Report (left) 
Showing in LHD’s View (right)
Ticks

- Ticks are found in woods, bushes, high grass, and leaf litter
- Active outdoors in warm weather and need moisture to survive
- They can detect heat and carbon dioxide from nearby host
- Attach to host when there is physical contact
- In US, there are 80 species (850 species worldwide)
- 12 species are of public health or veterinary concerns, only one is of concern in WI
- *Ixodes* sp. commonly known as the “blacklegged” or “deer” tick, an important vector for most of the tickborne diseases in WI
*Ixodes scapularis* (Blacklegged or Deer Tick)

Adult female deer tick

Adult male deer tick

Nymph

Larva

Smaller than a American dog/wood tick, adult female and nymph can transmit infection through a bite for a blood meal

Dermacentor variabilis (American dog or wood tick)
Life Cycle of Blacklegged Tick

Based on EM case onsets, nymphs account for most transmission.

Larva do not transmit bacteria.

During the 2-year life cycle, total 3 blood meals.

Courtesy of CDC.
Stages of blood engorgement in female adult *Ixodes* ticks depicted by the durations of attachment (borrowed from IDSA, Dr. Richard Falco-Fordham University)
Dark color of the pie = % deer infested with *Ixodes* ticks
Tickborne Diseases

*Ixodes scapularis* transmit:

– Powassan virus infection (tickborne arbovirus)
– Anaplasmosis (*A. phagocytophilum*)
– Ehrlichiosis (*E. chaffeensis?*, *E. muris*-like)
– Lyme disease
Powassan Virus Infection
Powassan Virus (POWV) Infection

- Rare tickborne arbovirus infection
- Initially isolated in 1958, in Northern Ontario
- First case in US - New Jersey in 1970
- Cases have been reported in northern regions of United States (Maine, Michigan, Minnesota, New York, Vermont, and Wisconsin)
- Reservoir - small mammals
- Vector - *Ixodes scapularis*
Powassan- Clinical Diagnosis

- Incubation period is usually $\geq 1$ week (range from 8-34 days)

- Acute onset of fever, muscle weakness, confusion, headache, nausea, vomiting, and stiff neck

- Severe signs and symptoms- respiratory distress, tremors, seizures, gait unbalance, confusion, paralysis, and coma

- Neuroinvasive disease- most of the cases reported menigoencephalitis leading to long-term neurologic sequelae

- 10%-15% cases are fatal

- Supportive treatment only and no vaccine available
Powassan virus (POWV) Testing

- There is no commercial test available for Powassan virus

- CDC will perform testing for Powassan upon state’s request if symptoms are consistent with an arbovirus-like illness

- All commercial positive results for arbovirus agents need to be confirmed at WI State Laboratory of Hygiene (WSLH) and CDC

- POWV IgM and IgG testing can be performed on serum or CSF using MAC-ELISA and plaque-reduction neutralization test (PRNT) at CDC

- Physician should consider requesting POW testing if commercial tests resulted in non-specific reactivity to an arbovirus agent or a negative result and patient continues to exhibit signs and symptoms consistent with an arbovirus infection
County of Residence and Potential Exposure for Powassan Cases, WI, 2003-2010

Powassan Cases by Year
- 2003
- 2006
- 2007
- 2008
- 2010

Red: Potential county of exposure in addition to county of residence

Revised 3/4/11
Anaplasmosis/Ehrlichiosis

• Prior to 2008, anaplasmosis and ehrlichiosis infections were referred to as human granulocytic ehrlichiosis (HGE) and human monocytic ehrlichiosis (HME), respectively

• As of April 2008, human anaplasmosis and ehrlichiosis are now classified as:
  – Anaplasmosis caused by the *A. phagocytophilum* bacteria
  – Ehrlichiosis caused by *E. chaffeensis*, *E. ewingii*, and new species *E. muris*-like (EML)
  – Anaplasmosis/Ehrlichiosis undetermined (species unknown)

• *A. phagocytophilum* is the second most common tickborne pathogen in WI
• Increase in probable cases of *E. chaffeensis* (*Amblyoma* tick vector not traditionally seen in WI)
• In 2009, identified a cluster of novel *E. muris*-like cases
Anaplasmosis/Ehrlichiosis Clinical Manifestation

- Fever, headache, fatigue, muscle aches, and shaking chills

- Less common symptoms: nausea, vomiting, diarrhea, cough, joint pain, confusion, and occasional rash (maculopapular, petechial, erythroderma)

- Symptoms usually appear 5-10 days after a tick bite

- Treatment is effective with tetracycline antibiotics

- If suspected, treatment should be initiated as soon as possible and not delayed because of pending test results
Anaplasmosis/Ehrlichiosis Testing

• Laboratory findings: anemia, leukopenia, thrombocytopenia, and elevated liver enzymes

• Diagnostic testing- important to test for both agents
  – serology for IgM/IgG antibodies (IFA, ELISA)
  – smear for morulae
  – Isolation
  – PCR (test of choice)

*Anaplasma phagocytophilum* granulocyte morulae

*Ehrlichia chaffeensis* monocyte morulae from Medscape
Serology Testing

IFA test for IgG and IgM to specific Ehrlichia or Anaplasma species

- Most commonly used among commercial labs
- Serology test can have cross-reactivity between agents
- IFA result is reported in titers (positive >=1:64) IgM or IgG antibody
- IgM is not used independently because of false positive and titer can last a long time; IgG is more dependable antibody
- Single sample (serum collected within first week of illness) is considered as probable, a second sample collected 2-4 weeks later to confirm
- Confirmed lab results- 4-fold change in titers between acute/convalescent sample
PCR Testing

PCR is the test of choice

• Result is considered as confirmed (more specific, no cross-reactivity)
• Sample should be collected before treatment (EDTA blood sample)
• PCR multiplex is the only test that can identify the new *E. muris-like* species and can also detect *A. phagocytophilum, E. chaffeensis*, and *E. ewingii* at the same time by identifying melting point curves
• A negative result is not as meaningful, follow-up with serology if patient is ill with tickborne symptoms

$ NNDSS 2000-2007, Incidence per million per year, courtesy of CDC
Total Cases of Ehrlichiosis/Anaplasmosis Infections
Wisconsin, 2001-2010

*In 2008, cases were classified using the new CDC case definition

Revised 5/31/2011
Ehrlichia/Anaplasma Disease Incidence, WI 2009
Cases per 100,000 population

WI incidence = 6.1 cases/100,000

Ehrlichia/Anaplasma Disease Incidence, WI 2010
Cases per 100,000 population

WI incidence = 9.7 cases/100,000
Investigation of Novel *E. muris*-like (EML) Cluster, 2009

- **Index case:** June 12, 2009
- **Male,** 51 years
- **Clinical presentation:** fever, headache, myalgia
- **Laboratory findings:** lymphopenia, throbocytopenia, and elevated liver enzymes
- **Testing performed by Mayo labs:** multiplex PCR, differentiated different agents by melting point curves
- **CDC confirmation:** PCR and sequencing confirmed novel *Ehrlichia* species similar to *E. muris*, referred to as *E. muris*-like
- **From 2009-2010,** WI have identified 8 confirmed EML cases
Melting Point Curve - PCR (Courtesy of Mayo Labs)

- E. muris-like
- Index Case
- E. ewingii
- E. chaffeensis
- A. phagocytophilum
Investigation of *E. muris*-like Cluster (cont.)

- Obtained all acute and convalescent samples of all reported *Ehrlichia* cases for testing at CDC
- Obtained and reviewed medical records
- Standardized investigation questionnaire to interview patients regarding potential exposures

- All EML patients had exposure to ticks at home and/or in another county in WI
- Many reported seeing deer and wild animals in their backyard
• It is uncertain how widely spread the EML infections are in WI because of the limited testing available
• DPH is currently working with Marshfield labs and WSLH to bring the multiplex PCR testing on board
Lyme disease

Borrelia burgdorferi
Lyme Disease High Risk Areas

- Upper Midwest & Northeast

Map indicating risk levels:
- High
- Moderate
- Low
- Minimal or None
### Top 10 Notifiable Diseases in WI, 2009

<table>
<thead>
<tr>
<th>Disease</th>
<th>Confirmed case</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chlamydia</td>
<td>20,946</td>
</tr>
<tr>
<td>2. Gonorrhea</td>
<td>5,212</td>
</tr>
<tr>
<td>3. Lyme disease</td>
<td>2,119</td>
</tr>
<tr>
<td>4. Hepatitis C</td>
<td>1,823</td>
</tr>
<tr>
<td>5. Campylobacteriosis</td>
<td>1,219</td>
</tr>
<tr>
<td>6. Mycobacterial (non-tuberculosis)</td>
<td>1,167</td>
</tr>
<tr>
<td>7. Salmonellosis</td>
<td>688</td>
</tr>
<tr>
<td>8. Cryptosporidiosis</td>
<td>614</td>
</tr>
<tr>
<td>9. Streptococcus pneumoniae</td>
<td>590</td>
</tr>
<tr>
<td>10. Giardiasis</td>
<td>521</td>
</tr>
</tbody>
</table>
Reported Lyme Disease, WI, 1990-2010

(n=21,704)

* Previous to 2008 only confirmed cases were reported. Beginning 2008, the total number of cases includes confirmed and probable cases.
Lyme disease average annual incidence
Wisconsin, 1990-2007, by county
Lyme Disease Average Annual Incidence
Wisconsin, 2008-2010

Statewide average incidence = 35.1/100,000

This map is based on the county of residence of confirmed cases. Some infections may have been acquired during travel to other areas.
Lyme Disease

- Typical symptoms include…
  - Fever
  - Headache
  - Fatigue
  - Characteristic skin rash, erythema migrans, seen in approximately 80% of cases
- If left untreated, infection can spread to joints, the heart, and the nervous system
Signs and symptoms of Lyme disease in humans

- within one month:
  - tick bite transmission
  - erythema migrans (rash)
  - systemic reaction
    - fatigue, chills, fever, headaches, muscle and joint aches and swollen lymph nodes
  - facial (Bell’s) palsy
- three to many months:
  - arthritis
  - meningitis
  - heart block
- one to three months:
  - multiple erythema migrans (rash)

Courtesy of CDC
Clinical features of Lyme disease cases reported to CDC, United States, 1992-2006

- Heart block
- Radiculopathy
- Bells palsy
- Arthritis
- EM

Percent of Cases

N = 150,829
Early Localized Stage - Erythema Migrans (EM)

- Ticks must be attached for at least 24-48 hours to transmit bacteria.

- The EM rash expands in size over time.

- Occurs within 30 days of tick bite (70% people).

- Since Lyme disease is endemic in WI, EM rash (>=5cm) is considered as a confirmed case with or without lab testing and should be reported to health departments.
Confirmed Lyme Disease Cases by Month, 2007-2009, WI (n=5,302)

Month of Illness Onset

No. of Confirmed Cases

Date revised: 01/04/2011
Lyme Disease by Age, 2007-2009, WI (n=5,302)
Age-Specific Incidence of Reported Anaplasmosis, Wisconsin, 2009 (confirmed cases per 100,000 population)
Lyme Disease- Testing Methods

Most common serologic assays to detect antibodies include:

- Enzyme immunoassay (EIA) tests
- Immunofluorescent assays (IFA)
- Western Blot test

- Culture- detects growth of organism to confirm active infection
- PCR- molecular method of detecting DNA of organism (synovial fluid)
Lyme Disease- Antibody Response

Both IgM and IgG can persist for years (10-20yrs)

Specific IgM response
- Produce earlier than IgG
- Peaks within the first several weeks
- IgM is less specific than IgG
- Generally highest among patients with early infection
Lyme Disease - Antibody IgG Response

Specific IgG response (more reliable than IgM for Lyme and rickettsial infections)

- Produce a few weeks after IgM
- Peaks months to years
- Generally highest in later stages of infection
- Most active infections should have a positive IgG test result in one month
Lyme Disease- Treatment

- CDC uses the guidelines by the Infectious Diseases Society of America (IDSA)
- Antibiotics- very effective if treated early
  - children>=8yrs and adult= doxycycline 100mg 2x/day for 14days
  - children <8yrs= amoxicillin 50mg/kg/day in 3 divided doses
- Usually oral but may be given intravenously in more severe cases
- Recurrent symptoms may require a second course of antibiotic
- Long-term intravenous courses (months to years) have not been shown to be beneficial but may cause more complications (gallstones, catheter associated bloodstream infections,...)
Prevention

• Prophylaxis (follow the IDSA guidelines)
  - 1 single dose of doxycycline (200mg) for adults and children >/=8yrs
  - within 72 hrs after tick removal and tick was attached for at least 36hrs
  - at least 20% tick infectivity
  - WI average nymphal tick infectivity rate is about 22% (range from 20-24%)

• No lasting immunity, can get infected more than once

• No current available vaccine for humans since 2002, on-going research
Recurrent Episodes of Lyme Disease

Study of EM patients

• Uncertain if having one episode provides short-lived immunity

• Repeated episodes of Lyme disease may reflect relapse of a persistent infection or reinfection

• Most recurrent episodes are due to reinfection

• Reinfection may be due to at least 17 different sub-types of *B. burgdorferi* strains in the US

• More difficult to differentiate between reinfection and relapse if no EM is present
Lyme Disease Reinfection

• EM rash at a different site from the original episode of infection; recent tick bite within 30 days from the site of lesion

• EM rash usually has a raised or indented red point within the center of the rash at the site where the tick was removed from the skin

• Usually seasonal during spring or summer in places where nymphs are abundant

• Symptoms appears to be less severe with each episode of reinfection

• Reinfection may occur (>= 1 year after initial episode)
Lyme Disease Relapse

- Relapses can occur if patient with Lyme disease is left untreated or treatment failure
- Patient with EM rash that has been treated usually does not have relapses
- Relapse rash can reappear anytime usually within a year of the first EM (untreated) episode
- EM rash can appear at the same site as the original episode of infection
- EM rash does not have a raised or indented red point within the center of the rash
Don’t get “Tick-ed”

- Avoid areas that could have ticks (wooded areas)
- Wear protective clothing, long pants and sleeves
- Tuck pants into socks or boots to prevent ticks from crawling under clothing
- Tuck shirts into pants
- Use repellants per label instructions (adults-20-30% DEET, children-10%)
- Permethrin spray for clothing
- Check for ticks after being outdoors
- Tick control- environmental landscape to create tick safe areas, spraying acaricides
References

2. CDC Lyme disease case definition
3. CDC. Recommendation for test performance and interpretation from the second national conference on serologic diagnosis of Lyme disease. MMWR 1995;44:590-591
5. CDC. Notice to readers: caution regarding testing of Lyme disease. MMWR 2005;54:125-126
Additional Questions

Feel free to contact DPH:

Diep (Zip) Hoang Johnson, Epidemiologist
Phone: (608) 267-0249
E-mail: diep.hoangjohnson@wi.gov