RECOGNIZING AND TREATING TICK-BORNE DISEASES

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Eastern Shore Community College, Melfa VA
Disclosures

- David Chang, M.D.
  - No Financial Interests or Relationships to Disclose
Objectives

- By the end of this presentation, you will be able to:
  - Understand the complexity and difficulty of identifying and treating tick-borne diseases appropriately
  - Identify the 5 reportable tick-borne diseases
  - Identify 3 tick-borne diseases most likely to affect you and your family on the Eastern Shore
  - Recognize the basic signs and symptoms of the major tick-borne diseases
  - Understand some of the ongoing controversies in the field of tick-borne infections
Geographic Distribution of Ticks

Blacklegged Tick

Lone Star Tick

American Dog Tick

Gulf Coast Tick
Tick-Borne Diseases in US

- Anaplasmosis
- Babesiosis
- Ehrlichiosis
- Lyme Disease
- Rickettsia parkeri Rickettsiosis
- Rocky Mountain Spotted Fever (RMSF)
- Southern Tick-Associated Rash Illness (STARI)
- Tickborne relapsing fever (TBRF)
- Tularemia
- 364D Rickettsiosis - new disease in CA
Tick-Borne Diseases Abroad

- Crimean-Congo hemorrhagic fever
- Other Rickettsial infections
- European Lyme Disease: Eastern Europe + Northern Asia, different species, different symptoms
- Tick-borne Encephalitis
Babesiosis

- Caused by microscopic parasites that infect red blood cells
- Vector: black-legged ticks
- Symptoms: flu-like symptoms, often asymptomatic, but sometimes causes breakdown of blood cells (including red blood cells, platelets, and clotting factors), jaundice, dark urine
- Treatments: Atovaquone + Azithromycin or Clindamycin + Quinine x 7-10 Days
- Distribution: www.cdc.gov
Other Rickettsial Diseases (not RMSF)

**Rickettsia parkeri Rickettsiosis**
- **Vector:** Gulf Coast Tick
- **Distribution:** E/S US along coast
- **Symptoms:** Fever, headache, eschar, rash
- **Treatment:** Doxycycline 100 mg BID x 7-14 d

**364D Rickettsiosis**
- **Vector:** Pacific Coast Tick
- **Distribution:** Northern CA
- **Symptoms:** Fever, Eschar
- **Treatment:** Doxycycline 100 mg BID x 7-14 d
R. Parkerii Eschaar
Southern Tick-Associated Rash Illness (STARI)

- Unknown cause
- Vector: Lone Star Tick
- Symptoms: Similar to Lyme Disease — bulls-eye lesion, flu-like symptoms
- Treatment: Unclear, but most physicians treat as LD
- Distribution: SE and E
Distinctions between STARI & LD

**STARI**
- Patients recall tick bite
- Shorter onset of rash appearance (6 vs 14 d)
- EM more circular and more central clearing
- Faster recovery with antibiotics

**Lyme Disease**
- Accompanying symptoms with erythema migrans (EM)
- More skin lesions, larger skin lesions (6-28 cm vs 6-10 cm)
STARI vs LD

Circular

More Central Clearing

Characteristic Bulls-Eye Rash

Smaller

Multiple Skin Lesions

www.cdc.gov
Tick-Borne Relapsing Fever (TBRF)

- Caused by bacterium Borrelia (several species)
- Vector: Soft Ticks
- Distribution: High altitudes and caves, squirrels, owls, chipmunks
- Symptoms: relapsing fever, flu-like symptoms

www.cdc.gov
TBRF

Treatment: Tetracycline 500 mg QID x 10 D or Ceftriaxone 2 grams daily x 10-14 D
<table>
<thead>
<tr>
<th>Cause:</th>
<th>Anaplasma phagocytophilum</th>
<th>Ehrlichia chaffeensis, E. Ewingii, E. muris-like</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vector:</td>
<td>Black-legged &amp; Deer ticks</td>
<td>Lone star tick</td>
</tr>
<tr>
<td>Geography:</td>
<td>Upper MW and NE</td>
<td>SE and S Central</td>
</tr>
<tr>
<td>Symptoms:</td>
<td>Fever, headache, chills, muscle aches</td>
<td>Fever, headache, fatigue, and muscle aches</td>
</tr>
<tr>
<td>Diagnosis:</td>
<td>PCR, A. phagocytophilum antigen, blood smear</td>
<td>PCR, E. Chaffeensis antigen, blood smear</td>
</tr>
<tr>
<td>Treatment:</td>
<td>Doxycycline 100 mg PO BID x 1-2 W</td>
<td>Doxycycline 100 mg PO BID x 1-2 W</td>
</tr>
</tbody>
</table>
## Anaplasmosis/Ehrlichiosiis

|                  | Anaplasmosis                                                                 | Ehrlichiosiis                                                                 |
|------------------|------------------------------------------------------------------------------|                                                                            |
| Fatality Rate:   | □ < 1%                                                                       | □ 1.8%                                                                     |
| Rash:            | □ None                                                                        | □ 60% children, 30% adults                                                |
| Transfusions:    | □ Risk through infected wbc's                                                | □ Risk through infected wbc's                                             |
| Delay:           | □ 1-2 weeks                                                                  | □ 1-2 weeks                                                                |
| Diagnosis:       | □ Recent tick bites, exposure history, leukopenia and thrombocytopenia, elevated LFTs | □ Recent tick bites, exposure history, leukopenia and thrombocytopenia, elevated LFTs |
| Blood Smear:     | ![Blood Smear Image](image1.png)                                              | ![Blood Smear Image](image2.png)                                           |

www.cdc.gov
Anaplasmosis/Ehrlichiosis: Incidence

- **Anaplasmosis**
  - History: Recognized in 1990s, reportable in 1999
  - Incidence: Rising

- **Ehrlichiosis**
  - History: Recognized in 1980s, reportable in 1999
  - Incidence: Rising, plateaued in 2008

Number of Annual Anaplasmosis Cases, 1994-2010

Number of Annual Ehrlichiosis Cases, 1994-2010

[Charts showing annual cases from 1994 to 2010 for both Anaplasmosis and Ehrlichiosis]

www.cdc.gov
Anaplasmosis/Ehrlichiosis: Fatality

**Anaplasmosis**

**Ehrlichiosis**

*Anaplasmosis Case Fatality Rate, 2000-2010*

*Ehrlichiosis Case Fatality Rate, 2000-2010*
Anaplasmosis/Ehrlichiosis: Geography

Anaplasmosis

Ehrlichiosis

Anaplasmosis Incidence, 2010

Cases per million

0.1-0.7
0.7-3.1
3.1-136

Ehrlichiosis Incidence, 2010

Cases per million

0.03-1.0
1.0-3.3
3.3-26

www.cdc.gov
Anaplasmosis/Ehrlichiosis: Seasonality

Percent of Anaplasmosis Cases Reported each Month, 1994-2010

Percent of Ehrlichiosis Cases Reported each Month, 1994-2010
Anaplasmosis/Ehrlichiosis: Persons at Risk

Anaplasmosis Incidence by Age Group, 2000-2010

Ehrlichiosis Incidence by Age Group, 2000-2010

www.cdc.gov
Anaplasmosis/Ehrlichiosis Incidence on ES and VA

**Eastern Shore Incidence**

**Virginia Incidence**

**Cases in Virginia**

- **Cases Accomack County**
- **Cases Northampton County**

- **Cases in Virginia**
Lyme Disease

- **Cause:** Bacterium Borrelia Burgdorferi
- **Vector:** Black-legged tick on E, NE, MW, & Western black-legged tick on Pacific Coast
- **TRANSMISSION?:**
  - Person-to-person contact
  - Maternal-child; breastmilk
  - Blood transfusion
  - Pets
  - Eating squirrel or venison meat
  - Air
  - Water
  - Bites of mosquitos, flies, fleas, or lice
Lyme Disease: Incidence in US

[Bar chart showing the incidence of Lyme disease from 2002 to 2011, with bars representing confirmed and probable cases.]

www.cdc.gov
# Reportable Diseases: US 2010

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reported Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chlamydia</td>
<td>1,307,893</td>
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<tr>
<td>2. Gonorrhea</td>
<td>309,341</td>
</tr>
<tr>
<td>3. Salmonellosis</td>
<td>54,424</td>
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<tr>
<td>4. Syphilis</td>
<td>45,834</td>
</tr>
<tr>
<td>5. HIV/AIDS</td>
<td>35,741</td>
</tr>
<tr>
<td>6. Lyme Disease</td>
<td>30,158</td>
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<tr>
<td>7. Pertussis</td>
<td>27,550</td>
</tr>
<tr>
<td>8. Giardiasis</td>
<td>19,811</td>
</tr>
<tr>
<td>9. Strep Pneumo</td>
<td>16,569</td>
</tr>
<tr>
<td>10. Varicella</td>
<td>15,427</td>
</tr>
</tbody>
</table>
## Reportable Diseases: Eastern Shore 2012

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reported Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chlamydia</td>
<td>357</td>
</tr>
<tr>
<td>2. Gonorrhea</td>
<td>55</td>
</tr>
<tr>
<td>3. Salmonellosis</td>
<td>27</td>
</tr>
<tr>
<td>4. Campylobacter</td>
<td>11</td>
</tr>
<tr>
<td>5. Lyme Disease</td>
<td>9</td>
</tr>
<tr>
<td>6. Rocky Mountain Spotted Fever</td>
<td>8</td>
</tr>
<tr>
<td>7. HIV/AIDS</td>
<td>4</td>
</tr>
<tr>
<td>8. Elevated Lead Levels in Children</td>
<td>3</td>
</tr>
<tr>
<td>8. Pertussis</td>
<td>3</td>
</tr>
<tr>
<td>10. Tuberculosis</td>
<td>2</td>
</tr>
</tbody>
</table>
Recognizing Lyme Disease

- Early Localized (3-30 days post-tick bite)
  - Flu-like symptoms
  - Red, expanding rash (Erythema Migrans)

- Early Disseminated (days to weeks)
  - Additional EM lesions
  - Facial Bell’s Palsy
  - Meningitis
  - Arthritis
  - A-V Block

www.cdc.gov
Erythema Migrans

Typical, Early, Homegenous

Atypical, Late, Multiple

Dr. Michael Melia, June 2013 VDH Lyme Disease Presentation
Late Disseminated & Post-Treatment Lyme Disease Syndrome

- 60% untreated progress to late disseminated
- Symptoms: intermittent bouts of arthritis, severe joint pain and swelling, chronic neurologic complaints

- Approximately 10-20% have symptoms after treatment
- Symptoms: joint and muscle pain, cognitive deficits, sleep disturbance, fatigue
- No evidence due to ongoing infection with B. burgdorferi (autoimmune)
Diagnosis of Lyme Disease

- EM + Right Epidemiology = Lyme Disease
- NO NEED FOR LAB TESTING! TREAT.

- Typical LD symptoms + Lab Testing + EM History = Lyme Disease

- If uncertain, test during acute stage, and then test 4-6 weeks later (typically negative for first month)

- Atypical Symptoms + Wrong Epidemiology + No EM History + Positive Lyme IgG = Likely other cause of symptoms

- What to do in this case? Unclear, could treat or not treat.

- THUS, LAB TESTING SHOULD NOT BE DONE WHEN THERE IS A LOW INDEX OF SUSPICION FOR LYME.
# Lyme Disease Treatment Options

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage for adults</th>
<th>Dosage for children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred oral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500 mg 3 times per day&lt;sup&gt;a&lt;/sup&gt;</td>
<td>50 mg/kg per day in 3 divided doses (maximum, 500 mg per dose)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg twice per day&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Not recommended for children aged &lt;8 years</td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>500 mg twice per day</td>
<td>30 mg/kg per day in 2 divided doses (maximum, 500 mg per dose)</td>
</tr>
<tr>
<td><strong>Alternative oral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selected macrolides&lt;sup&gt;c&lt;/sup&gt;</td>
<td>For recommended dosing regimens, see footnote &lt;sup&gt;d&lt;/sup&gt; in table 3</td>
<td>For recommended dosing regimens, see footnote in table 3</td>
</tr>
<tr>
<td><strong>Preferred parenteral regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>2 g intravenously once per day</td>
<td>50–75 mg/kg intravenously per day in a single dose (maximum, 2 g)</td>
</tr>
<tr>
<td><strong>Alternative parenteral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>2 g intravenously every 8 h&lt;sup&gt;d&lt;/sup&gt;</td>
<td>150–200 mg/kg per day intravenously in 3–4 divided doses (maximum, 6 g per day)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>18–24 million U per day intravenously, divided every 4 h&lt;sup&gt;d&lt;/sup&gt;</td>
<td>200,000–400,000 U/kg per day divided every 4 h&lt;sup&gt;d&lt;/sup&gt; (not to exceed 18–24 million U per day)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Although a higher dosage given twice per day might be equally as effective, in view of the absence of data on efficacy, twice-daily administration is not recommended.

<sup>b</sup> Tetracyclines are relatively contraindicated in pregnant or lactating women and in children <8 years of age.

<sup>c</sup> Because of their lower efficacy, macrolides are reserved for patients who are unable to take or who are intolerant of tetracyclines, penicillins, and cephalosporins.

<sup>d</sup> Dosage should be reduced for patients with impaired renal function.
## Lyme Disease Treatment Duration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Duration, days (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tick bite in the United States</td>
<td>Doxycycline, 200 mg in a single dose&lt;sup&gt;a,b&lt;/sup&gt;, (4 mg/kg in children ≥8 years of age) and/or observation</td>
<td>...</td>
</tr>
<tr>
<td>Erythema migrans</td>
<td>Oral regimen&lt;sup&gt;c,d&lt;/sup&gt;</td>
<td>14 (14–21)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Early neurologic disease</td>
<td></td>
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<tr>
<td>Meningitis or radiculopathy</td>
<td>Parenteral regimen&lt;sup&gt;c,f&lt;/sup&gt;</td>
<td>14 (10–28)</td>
</tr>
<tr>
<td>Cranial nerve palsy&lt;sup&gt;a,g&lt;/sup&gt;</td>
<td>Oral regimen&lt;sup&gt;c&lt;/sup&gt;</td>
<td>14 (14–21)</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>Oral regimen&lt;sup&gt;a,c,h&lt;/sup&gt; or parenteral regimen&lt;sup&gt;a,c,h&lt;/sup&gt;</td>
<td>14 (14–21)</td>
</tr>
<tr>
<td>Borrelial lymphocytoma</td>
<td>Oral regimen&lt;sup&gt;c,d&lt;/sup&gt;</td>
<td>14 (14–21)</td>
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<tr>
<td>Late disease</td>
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<tr>
<td>Arthritis without neurologic disease</td>
<td>Oral regimen&lt;sup&gt;c&lt;/sup&gt;</td>
<td>28</td>
</tr>
<tr>
<td>Recurrent arthritis after oral regimen</td>
<td>Oral regimen&lt;sup&gt;a,c&lt;/sup&gt; or parenteral regimen&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>28 (14–28)</td>
</tr>
<tr>
<td>Antibiotic-refractory arthritis&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Symptomatic therapy&lt;sup&gt;1&lt;/sup&gt;</td>
<td>...</td>
</tr>
<tr>
<td>Central or peripheral nervous system disease</td>
<td>Parenteral regimen&lt;sup&gt;c&lt;/sup&gt;</td>
<td>14 (14–28)</td>
</tr>
<tr>
<td>Acrodermatitis chronica atrophicans</td>
<td>Oral regimen&lt;sup&gt;c&lt;/sup&gt;</td>
<td>21 (14–28)</td>
</tr>
<tr>
<td>Post–Lyme disease syndrome</td>
<td>Consider and evaluate other potential causes of symptoms; if none is found, then administer symptomatic therapy&lt;sup&gt;a&lt;/sup&gt;</td>
<td>...</td>
</tr>
</tbody>
</table>
Lyme Disease Antibiotics

- Lyme Disease is a bacteria. Antibiotics work.
  - 10-21 Days for Early Infections (Doxycycline)
  - 14-28 Days for Early Disseminated (Doxycycline or Ceftriaxone IV)
  - 2nd course of antibiotics almost never needed
  - However, with a longer duration of an untreated infection, most symptoms may persist after treatment (autoimmune)
Did the Doctor give me right diagnosis?
- Diagnosis is almost always done without laboratory testing because early testing for PCR is 70% negative and bacteria are very difficult to identify in culture.

How do I know I’m cured?
- About 10-15% of people continue to have symptoms after adequate treatment with antibiotics.
- There is no test for cure of Lyme Disease.

If I test positive for B. Burgdorferi, does it mean I need to be treated for Lyme Disease?
- Several false positive cases from an inaccurate test (IgM, IgG, EIA), and people can have LD-like symptoms with several other diseases.
## TABLE 1. Summary of Lyme Disease Information Given by 19 Websites

<table>
<thead>
<tr>
<th>Website</th>
<th>Tick Bites</th>
<th>LD Diagnosis</th>
<th>Serology</th>
<th>Other Tests</th>
<th>Chronic LD</th>
<th>Treatment</th>
<th>Pregnancy</th>
<th>Breast-feeding</th>
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<tbody>
<tr>
<td><a href="http://www.acponline.org">www.acponline.org</a></td>
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<td><a href="http://www.cdc.gov">www.cdc.gov</a></td>
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<td><a href="http://www.fda.gov">www.fda.gov</a></td>
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<td><a href="http://www.healingwell.com">www.healingwell.com</a></td>
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<td><a href="http://www.hopkins-arthritis.com">www.hopkins-arthritis.com</a></td>
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<td><a href="http://www.igenex.com">www.igenex.com</a></td>
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<td><a href="http://www.intelihealth.com">www.intelihealth.com</a></td>
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<td><a href="http://www.lyme.org">www.lyme.org</a></td>
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<td><a href="http://www.webmd.com">www.webmd.com</a></td>
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</tbody>
</table>

LD indicates Lyme disease; A, accurate; I, inaccurate; —, not discussed or found.

Cooper JD, Feder HM Jr., Pediatr Infect Dis J. 2004;12:1105
Slide taken from Dr. Michael Melia, June 2013 VDH Lyme Disease Presentation
Rocky Mountain Spotted Fever (RMSF)

- **Cause:** Bacterium *Rickettsia Rickettsii*
- **Vectors:** American Dog Tick, Rocky Mountain Wood Tick, Brown Dog Tick
- **Symptoms:** fever, rash, headache
- **Late rash appearance (90%)**
- **Starts wrists/forearms/ankles ➔ trunk, palm, soles**
Reportable Diseases: Eastern Shore 2012

<table>
<thead>
<tr>
<th>Disease</th>
<th>Reported Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chlamydia</td>
<td>357</td>
</tr>
<tr>
<td>2. Gonorrhea</td>
<td>55</td>
</tr>
<tr>
<td>3. Salmonellosis</td>
<td>27</td>
</tr>
<tr>
<td>4. Campylobacter</td>
<td>11</td>
</tr>
<tr>
<td>5. Lyme Disease</td>
<td>9</td>
</tr>
<tr>
<td>6. Rocky Mountain Spotted Fever</td>
<td>8</td>
</tr>
<tr>
<td>7. HIV/AIDS</td>
<td>4</td>
</tr>
<tr>
<td>8. Elevated Lead Levels in Children</td>
<td>3</td>
</tr>
<tr>
<td>8. Pertussis</td>
<td>3</td>
</tr>
<tr>
<td>10. Tuberculosis</td>
<td>2</td>
</tr>
</tbody>
</table>
RMSF Incidence and Fatality

www.cdc.gov
RMSF Incidence
Lyme Disease vs RMSF Incidence on Eastern Shore

Virginia Monthly Morbidity Surveillance Report
RMSF Geography

Cases per million

- NN
- 0.2-1.5
- 0
- 1.5-19
- 19-63

www.cdc.gov
RMSF Seasonality: 1993-2010

The graph shows the percentage of RMSF cases reported by month of onset. The highest number of cases is reported in the months of June and July, with a significant drop in cases in February and January. The graph indicates a peak in RMSF cases during the summer months.
RMSF Persons at Risk: 2000-2010

www.cdc.gov
RMSF Diagnosis

- Most difficult to diagnose of all the common tick-borne disease because:
  - Symptoms are variable
  - Symptoms are similar to other tick-borne disease
  - Detection of antibodies usually negative first 7-10 days
  - Rash appears late
  - Can be fatal if not treated within first 5 days

- Lab Findings: anemia, thrombocytopenia, hyponatremia, elevated LFTs

- Lab Confirmation: PCR (70% sensitivity), IFA antibodies
RMSF Treatment

- Doxycycline 100 mg BID x 3 days after fever subsides or clinical improvement. Typically 7-14 days.
- Alternative: Chloramphenicol (pregnancy)
Tularemia

- Cause: Bacterium Francisella tularensis
- Vectors: Ticks, Deer Flies, Skin Contact, Ingestion of Water, Lab Exposure, Inhalation of Aerosols
- Symptoms:
  - Ulcer at site of exposure + gland swelling (handling)
  - Glandular (bite)
  - Oculoglandular (eye)
  - Oropharyngeal (eating or drinking)
  - Pneumonic (inhalation)
Tularemia Diagnosis and Treatment

- **Diagnosis:** epidemiologic link + symptoms + PCR/antibody titers
- **Treatment:** Streptomycin, Gentamicin, Doxycycline, or Ciprofloxacin x 10-21 days
- Almost all patients recovery completely
Tularemia Incidence 2001-2010
In Virginia, we have had 14 cases of Tularemia in past 10 years, 1 in this year. On the Eastern Shore, we have had 1 case of Tularemia (Northampton County 2007.)
Special Considerations

- Nationwide shortage of Doxycycline since January 2013 due to increased demand and manufacturing issues
- Doxycycline should still be the only drug for prophylaxis of Lyme Disease
- Doxycycline should still be used to treat suspected rickettsial infections (RMSF, LD, Ehrlichiosis, Anaplasmosis); no other drugs have been proven to limit fatalities as effectively