Human Babesiosis

Abelardo C. Moncayo, Ph.D.
Director, Vector-Borne Diseases
Tennessee Department of Health
Babesiosis

An emerging zoonotic infection caused by an intraerythrocytic protozoan of the *Babesia* genus

Victor Babes
Dawn of Medical Entomology

- 1898 Sir Ronald Ross and Sir Patrick Manson’s malaria theory
- 1889 Theobald Smith, MD, and F.L. Kilbourne, DVM, discovered *Babesia bigemina* causing Texas cattle fever
Babesia vs Plasmodia

Distinguishing features:

- *Babesia* are pleomorphic
- can be vacuolated
- do not produce pigment
Emerging Zoonosis

Humans are dead-end hosts
Subsequent transmission occurring from ticks feeding on infected persons is rare.
Human-to-human transmission possible through blood transfusions.
One Medicine and Babesiosis

- 1957 1st human case in Yugoslavia
- 1969 Nantucket fever in humans
- 1976 white-footed mice *B. microti* reservoir
Human Babesiosis

- Most cases in US are asymptomatic

- Symptoms can include:
  - cyclic fever
  - chills
  - myalgia
  - fatigue
  - enlargement of liver and/or spleen
  - hemolytic anemia
  - hemoglobinuria
Babesiosis vs Lyme Disease

Vector = Ixodid ticks

Reservoir = white footed mice and others
Co-infection

Reported Cases of Lyme Disease -- United States, 2009

1 dot placed randomly within county of residence for each confirmed case.
Zoonotic species

- *B. microti* most common cause in the US
  - endemic in Northeast
  - cases in Midwest and Northwest

- *B. duncani* (formerly *B. WA-1*)
  - isolated from patients in WA and CA

- MO-1
  - isolated from patients in WA, MO and KY

- *B. divergens*
  - causes most European cases
Piroplasms in Wildlife

- *Babesia odocoilei*
- *Theileria cervi*
Phylogeny of Piroplasms

The diagram illustrates the evolutionary relationships among different species of piroplasms. The tree is divided into two main branches: Large Babesia and Small Babesia. Key species include:

- B. divergens *
- B. odocoilei
- B. canis
- B. gibsoni
- WA1 *
- T. equi (B. equi)
- T. annulata
- T. parva
- T. buffeli
- T. sergenti
- B. rodhaini
- PB-1 *
- B. microti *
- T. gondii

The numbers on the branches indicate the bootstrap support values, with percentages above 70% indicating strong support for the branching pattern.
Prevalence

- Hundreds of cases reported annually
- 9 deaths from blood transfusion 1997-2007
Risk Factors for Severe Cases

- Immunodeficiency
- Elderly
- Splenectomy
- Co-infection with other tick-borne diseases
Co-infection


<table>
<thead>
<tr>
<th>Symptom</th>
<th>% of patients surveyed exhibiting the indicated symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td><em>(n = 214)</em></td>
</tr>
<tr>
<td>Fatigue</td>
<td>49</td>
</tr>
<tr>
<td>Headache</td>
<td>42</td>
</tr>
<tr>
<td>Erythema migrans</td>
<td>85</td>
</tr>
<tr>
<td>Fever</td>
<td>42</td>
</tr>
<tr>
<td>Sweats</td>
<td>11</td>
</tr>
<tr>
<td>Chills</td>
<td>23</td>
</tr>
<tr>
<td>Myalgia</td>
<td>31</td>
</tr>
<tr>
<td>Anorexia</td>
<td>14</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>36</td>
</tr>
<tr>
<td>Emotional lability</td>
<td>7</td>
</tr>
<tr>
<td>Nausea</td>
<td>5</td>
</tr>
<tr>
<td>Neck stiffness</td>
<td>21</td>
</tr>
<tr>
<td>Multiple EM</td>
<td>14</td>
</tr>
<tr>
<td>Cough</td>
<td>10</td>
</tr>
<tr>
<td>Sore throat</td>
<td>9</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4</td>
</tr>
<tr>
<td>Joint swelling</td>
<td>3</td>
</tr>
</tbody>
</table>
Diagnosis

- Serology
- Blood smear
- PCR
- Inoculation of hamsters
Treatment

- Clindamycin and Quinine
- Toxicities significant: hearing loss, syncope, hypotension, GI distress
- Alternatives: atovaquone and azithromycin
- In very serious cases: erythrocyte exchange transfusion
Blood safety

- *Babesia* can cause chronic asymptomatic parasitemia
Case Study: Tennessee
Patient information

- 43 y.o. male
- Idiopathic thrombocytopenic purpura
  - Splenectomy in 2003
  - Rituxumab
- Hunted deer in middle Tennessee property
- No report of tick bite
Patient isolate

- Blood smear positive
- Mongolid jird inoculation negative
- IFA negative (\textit{B. microti}, \textit{B. duncani}, \textit{B. divergens})
- PCR negative for \textit{B. microti}
- PCR positive for \textit{Babesia} genus
  - 4\% difference from other \textit{Babesia} spp.
  - Nearest relative \textit{Babesia} from Chinese ruminants
December 2008

S_x onset

July 2009

Blood-smear confirmation
PCR
T_x with quinine and clindamycin
S_x resolution

November 2009

Deer sampled
Tick dragging

February 2010

Rabbits sampled
Animal Specimen Processing

- **White-tailed deer**
  - serum separated from whole blood
  - DNA extracted from blood cells

- **Eastern cotton-tailed rabbits**
  - serum separated from whole blood
  - DNA extracted from spleens
Molecular Testing

- Deer blood, rabbit spleen and tick DNA:
  - screened for *Babesia spp.* using PIRO primers
  - amplify fragments from the 18S rRNA gene

- Positive samples sequenced to ID species
Serological Testing

- Indirect immunofluorescence assays
  - *B. microti*
  - *B. odocoilei*
  - MO-1

- IFA positive titer $\geq 1:64$
Molecular Results

- 7/166 (4%) *Ix. scapularis* - *B. odocoilei*
- 0/5 deer blood DNA
- 1/8 rabbit spleen DNA - MO-1
Serology Results

- **Deer serum**
  - 4/5 antibodies reactive to *B. odocoilei*

- **Rabbit serum**
  - 2/7 antibodies reactive to *B. odocoilei*
  - 3/7 antibodies reactive to MO-1
MO-1 antibodies in rabbit sera

Fluorescent image at 400X

Dilution 1:128
MO-1 antibodies in rabbit sera

Bright field and fluorescent image overlay at 1000X

Dilution 1:64
## Results Summary

<table>
<thead>
<tr>
<th></th>
<th>Ticks</th>
<th>White-tailed deer</th>
<th>Eastern cottontail rabbits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>B. odocoilei</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>MO-1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
B. odocoilei

- Isolated in *I. scapularis* ticks
- Deer and rabbit sera reactive to antigen
- Shows link
  - parasites likely circulating *I. scapularis* ↔ wildlife
  - *I. scapularis* potentially transmitting other *Babesia*
Theileria cervi

- 3/5 deer positive blood by PCR
- 24/128 (14%) deer ticks positive
MO-1

- Rabbits exposed to MO-1
- MO-1 causes severe disease in the US
- risk of exposure TN residents
- risk of exposure to blood transfusion patients

- physician awareness is imperative
Density of host-seeking

Data by M Diuk-Wasser, Yale Univ. & Risk Map Study Grp
Reporting

- April, 2010: reportable to TDH
- January, 2011: nationally notifiable
Prevention

- Educate public about reducing tick exposure
- Screening blood donations
- Educate physicians, veterinarians and other public health officials
Action Plan

- Report to local health authority
- Investigate cases
  - Pathogen
  - Vector
  - Reservoir
- Investigate blood-transfusion acquired cases
  - Donor
  - Recipient
- Consider possibility of co-infection
Acknowledgements

- **TDH**
  - Dr. John R. Dunn
  - Dr. L. Rand Carpenter
  - Emily Mosites
  - Junjun Huang
  - Charissa Fritzen

- **Vanderbilt University**
  - Dr. Julian F. Hillyer
  - Jonas King

- **TWRA**
  - Roger D. Applegate

- **CDC/CGH/DPDM**
  - Dr. Barbara Herwaldt
  - Dr. Norman J. Pieniazek
  - Dr. Andrey Perelygin

- **SCWDS UGA Veterinary School**
  - Dr. Michael J. Yabsley

- **Cummings School of Veterinary Medicine at Tufts University**
  - Dr. Sam R. Telford III