Babesia in People’s Republic of China

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Babesiosis: an emerging infectious disease

- Babesiosis is the clinical illness that follows infection with Babesia species
  - *tick-borne* protozoan parasite
  - *Intra-erythrocytic*, morphologically similar to malaria
  - Over 100 species that infect vertebrate hosts

- Overwhelming *majority* of cases caused by *B.microti*
  - *B.microti* widely endemic Northeast and Upper Midwestern United States
  - Limited global surveillance

- Clinical
  - *Mild febrile illness*: immunocompetent
  - *Severe disease* in selected patient subsets i.e. immunocompromise, age, asplenia
  - hemolytic anemia, renal-, cardiorespiratory failure and death

Over-representation of high risk subsets among transfusion recipients
Associated fatality rate with TTB ➔ 18%
Transfusion Transmitted Babesiosis (TTB) in the United States

• **Increase in naturally acquired and TTB**
  – Non-seasonal and not geographically restricted

• **Total of 205 cases of TTB since 1979 with 32 fatalities**
  – Likely undercounts cases

• Transfusion transmissible via **ANY RBC containing product**
  – liquid stored or frozen deglycerolized RBCs
  – whole blood-derived platelets (n=4)

• **Tolerates standard storage and processing**
  – Refrigeration
  – Leukoreduction: many cases
  – Irradiation: at least 10 cases

**PERCEPTION**
Babesiosis perceived to be confined to the US
Babesia and International Blood banking

- Most **ubiquitous** genus of parasite
  - diverse geography and animal vectors
- **B. microti** poses greatest transfusion risk
  - Cases of *B. microti* and *B. microti*-like infections have been reported in America, Europe and Asia Pacific
- Growing recognition and improved diagnostics
  - increase in surveillance and hemovigilance
Babesia in China

• **Babesia has been demonstrated in China**
  - Northeast\(^1,2\) and Southwest China\(^3\) → malaria endemic in the latter
  - Local reports of Babesia microti in Chinese literature
  - Historical reporting of Lyme disease in Heilongjiang\(^4\) (shared vector with Babesia)

• **Babesia in Asia**
  - One B. *microti* surveillance study in Mongolia\(^5\)
    - 7% seroprevalence
    - 3% PCR positivity
  - Neighboring PRC

**Uncertain risk to Chinese blood supply**

Specific Aims

RESEARCH QUESTION
1. What is the seroprevalence of B. microti in a sample of Chinese blood donors?
2. What is the rate of Babesia parasitemia as evidenced by detectable Babesia DNA in a sample of Chinese blood donors?

SPECIFIC AIMS
1a. To determine the B. microti seroprevalence in a sample of blood donors in People’s Republic of China (PRC)
1b. To construct a laboratory sample set to enable molecular evaluation for evidence of Babesia parasitemia (B. microti, Venatorum, divergens and duncani DNA) in a sample of Chinese Blood donors*

*Molecular testing to be conducted using supplemental funding support
Collections in **Heilongjiang** (Babesia has already been demonstrated) Testing at **Institute of Blood Transfusion in Chengdu**
Pilot Study (n=1000-2000)

- Routine sample collection from community blood donors
  - Under extant donor consent
- Samples processed on-site and stored pending shipment
- **Deidentified** samples sent to IBT in Chengdu for batched testing
  - IFA (prepared at ARC) to detect antibodies against B. *microti*
    - Slides shipped to PRC
  - Aliquots saved on seroreactive donors for molecular testing

Eligibility

**Inclusion criteria:**
- All community blood donors who present during the enrollment period (red blood cells or whole blood)

**Exclusion:**
- Those individuals who do not meet eligibility criteria for community blood donation.
- Direct or autologous blood donors.
- Apheresis platelet and plasma donors
Ethics

• IRB application underway
• Standard **donor consent**
• Batched deidentified testing: **No notification and deferral**
  – The study reagents (e.g. IFA slides) are not SDA approved (FDA equivalent in China) ➔ may only be used for research purposes.
  – Consistent with current, routine practice in PRC
• Clinical interpretation limited
  – Need ancillary testing (blood smear, PCR and clinical history)
  – E.g., Seroreactivity present in past exposure with resolution and active parasitemia
• Molecular testing planned in the future
  – Current study lacks the resources for real time ancillary measures such as PCR/TMA
Limitations

- **Infrastructure:** Dr. Hua Shan has a longstanding research program in PRC through REDS-III International and IBT.
- **Testing and QC:** Testing performed locally in China at IBT.
- **Sample size, site selection, funding and bias:**
  - The sample size determined by available funding.
  - Sites **not broadly representative** selected given probability of tick bone infection (intentional selection bias).
  - Site selected rural areas, there is potential for population migration, which could dilute out risk detracts from the ability to identify high-risk areas.
- **Interpretation of test results:**
  - IFA ONLY that is specific for B. *microti*.
  - **Limited serological cross-reactivity** between Babesia species.
  - Unlikely to capture other species of Babesia (e.g. B. *venatorum*), which have been reported in PRC.
- **Seasonality:**
  - Naturally acquired Babesiosis (i.e. tick-bite) is **seasonal** but seroreactivity ± parasitemia is observed throughout the year.
Conclusions and Future directions

**New tools**

- **Serology**
  - AFIA (Immugen) and ELISA (Immunetics) for *B. microti*

- **Molecular**
  - TMA (Hologic, Inc) → 4 species

- **Antigen Panels (FDA)**

- **Pathogen Reduction**
  - Mirasol (Terumo)

- **Next Steps**
  - IRB approval pending

- **Future directions**
  - Broader surveillance locally as well as outside of the US → scope for collaboration
  - If Babesia is present → recipient tracing studies
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