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

1. Zhou X, Xia S, Huang JL, Tambo E, Zhuge HX, Zhou XN. Human babesiosis, an emerging tick-borne disease in the People's Republic of China. *Parasit Vectors* 2014; **7**: 509.
2. Jiang JF, Zheng YC, Jiang RR, et al. Epidemiological, clinical, and laboratory characteristics of 48 cases of "Babesia venatorum" infection in China: a descriptive study. *Lancet Infect Dis* 2015; **15**(2): 196-203.
3. Zhou X, Li SG, Wang JZ, et al. Emergence of human babesiosis along the border of China with Myanmar: detection by PCR and confirmation by sequencing. *Emerg Microbes Infect* 2014; **3**(8): e55.
4. Ai CX, Wen YX, Zhang YG, et al. Clinical manifestations and epidemiological characteristics of Lyme disease in Hailin county, Heilongjiang Province, China. *Ann N Y Acad Sci* 1988; **539**: 302-13.
4 Hong SH, Anu D, Jeong YI, et al. Molecular detection and seroprevalence of Babesia microti among stock farmers in Khutul City, Selenge Province, Mongolia. *Korean J Parasitol* 2014; **52**(4): 443-7.

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

People's Republic of China

Site Selection

Collections in Heilongjiang (Babesia has already been demonstrated)
Testing at Institute of Blood Transfusion **in** Chengdu

Study Design and Methods

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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