

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 China³ → malaria endemic in the latter
 - Local reports of *Babesia microti* in Chinese literature
 - Historical reporting of Lyme disease in Heilongjiang⁴ (shared vector with *Babesia*)
- **Babesia in Asia**
 - One *B. microti* surveillance study in Mongolia⁵
 - 7% seroprevalence
 - 3% PCR positivity
 - Neighboring PRC

Uncertain risk to Chinese blood supply

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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.
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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?

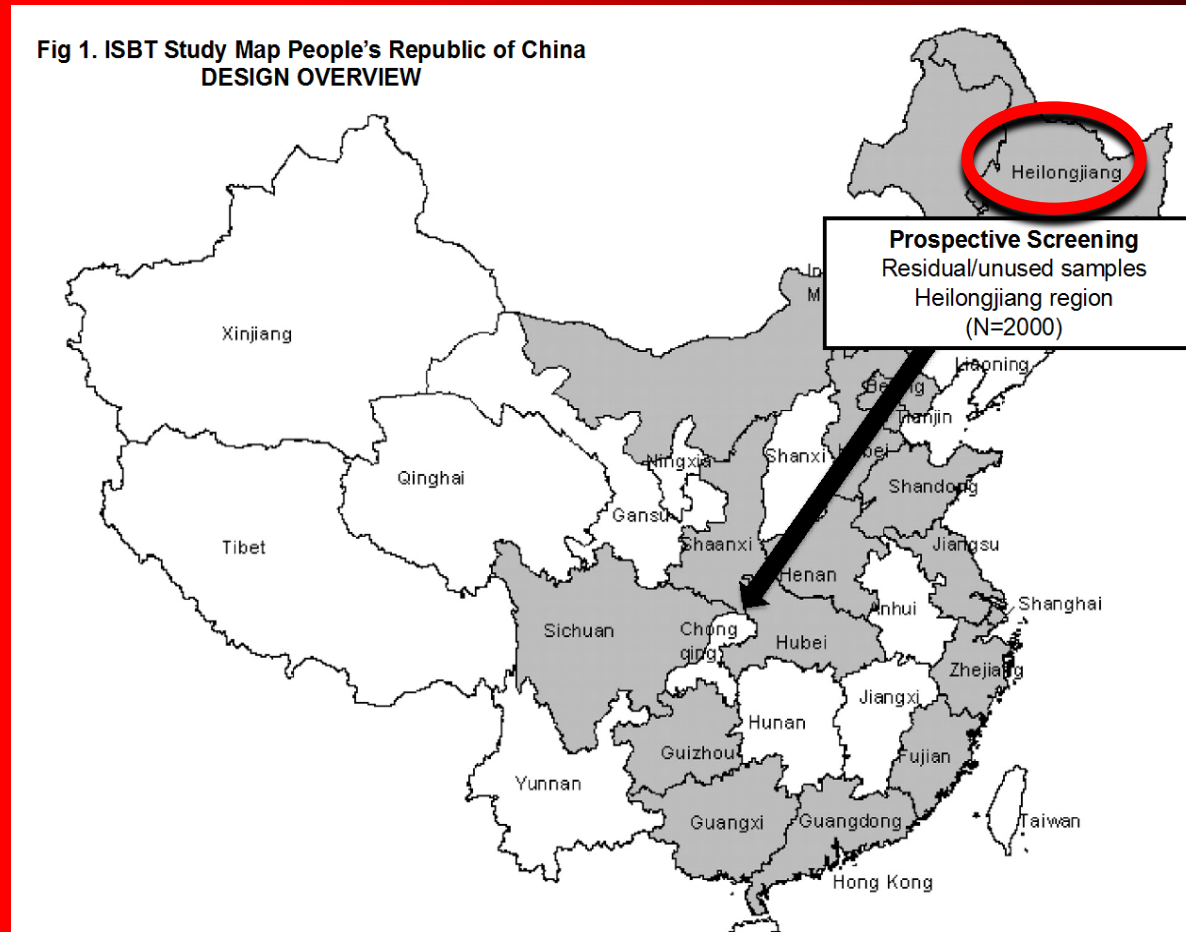
SPECIFIC AIMS

- 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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