EXPERIENCE WITH SCREENING DONORS FOR BABESIA MICROTI IN AN ENDEMIC AREA

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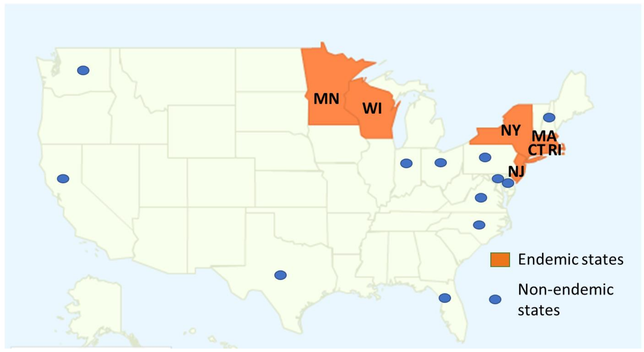
INTRODUCTION/ABSTRACT

Babesia is a tick borne intra-erythrocytic parasite. Babesia is responsible for transfusion transmitted babesiosis (TTB). Donor deferral based on the health history did not adequately mitigate the issue. Currently, there is no FDA approved blood screening test for babesia. However two platforms are available for screening under an (investigational new drug) IND.

GEOGRAPHIC DISTRIBUTION OF 159 TTB CASES [1]



OBJECTIVES

Evaluate the effects of donor screening for babesia in an endemic area

- Determine the proportion of donors that test positive for babesia throughout the first year and summer of second year after implementation in New York
- Compare the number of TTB cases per unit collected before implementation of screening (2008 – 2016) to the number of TTB cases per unit collected in the first 16 months of screening

MATERIALS AND METHODS

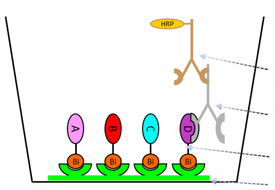
From May 2016-March 2017 donors were screened by Enzyme Immunoassay for a combination IgG and IgM antibodies to Babesia microti under US FDA Investigational New Drug Program (IND). The samples were tested by Creative Testing Solutions (CTS, Phoenix, AZ). Serum samples were collected from blood donors to perform the test. A signal/Cut off value (S/CO) ≥1 was considered positive. Repeat-reactive samples were defined as those with at least two of three reactive (S/CO≥1.0) results. Donors with repeat reactive results were indefinitely deferred from blood donation and lookback performed on previous collections from the previous year.

We used the following case criteria to determine Babesia infection in patients: Diagnosed Babesia infection confirmed by laboratory testing. Parasitologic evidence included observation of Babesia organisms on peripheral blood smear or detection of Babesia deoxyribonucleic acid (DNA) by a molecular method. Serologic evidence included positive results (titer ≥ 256) by indirect fluorescent antibody (IFA) or Immunoglobin G (IgG) immunoblot. Additional criteria for TTB were: 1) receipt of a blood component within a plausible time frame and 2) absence of evidence that another route was more likely than transfusion. A TTB case was considered definite if an extant segment demonstrated evidence of infection. A TTB case was considered probable if linked, in a plausible time frame, to a donor found positive by nucleic acid testing or a titer ≥ 64 on serologic testing on a specimen collected subsequently. A TTB case was considered possible if no donor was implicated, but it was not possible to test all donors, and the patient had no other plausible risk. If all associated donors were seronegative or the patient's infection pre-dated any transfusion(s), the case was excluded as transfusion transmitted. Cases not linked to transfusion or transplantation were considered community acquired.

Statistical analysis was performed using Prism software (GraphPad, San Diego, CA). 95% confidence intervals (95% CI) for proportions were calculated using the Wilson/Brown hybrid method. P values were calculated using Fisher's exact test.

B. microti ELISA Assay Format [2]

Multiple peptides combined in one assay well



Assay Principle

- Anti-human IgG+IgM-HRP Conjugate
- Serum Antibody
- Biotinylated Peptide
- Streptavidin-coated Plate

EIA Kit

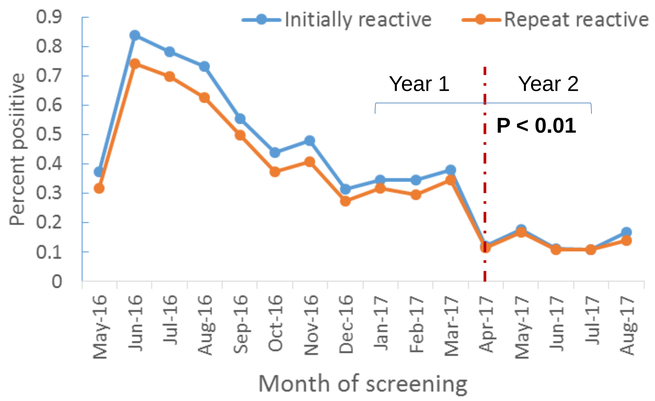
- Ready to use reagents
- 96 well microplate format
- ~3 hours turnaround time
- Suitable for manual or high-throughput automated operation

RESULTS

Patterns of donor reactivity during the first 16 months of babesia screening: Of the 439,274 donors who were tested by our donor center to date, 1,765 (0.402%) were initially reactive and 1,559 (0.355%) were repeat reactive. A seasonal pattern in the prevalence was observed during the first year of screening with the highest number of donors being positive in summer, and then progressively declining during the fall and winter months. During the first year of screening (May 2016 – April 2017) babesia screening led to permanent deferrals of 0.43% (95% CI, 0.41 – 0.45) of donors for repeat reactive serology (1416 deferrals / 329853 donations). During the second year of screening, including the peak summer months of babesia transmission (May – August 2017), donor deferral rates for babesia decreased to 0.13% (95% CI, 0.11 – 0.15) of donors (143 deferrals /109421 donations). P < 0.01, Fisher's exact test

Date	Number tested	Number initially reactive	% Initially reactive	Number repeat reactive	% Repeat reactive
May-16	19,800	74	0.374	63	0.318
Jun-16	33,358	280	0.839	248	0.743
Jul-16	29,908	234	0.782	209	0.699
Aug-16	28,128	206	0.732	176	0.626
Sep-16	27,093	150	0.554	135	0.498
Oct-16	27,308	120	0.439	102	0.374
Nov-16	27,624	133	0.481	113	0.409
Dec-16	30,675	96	0.313	84	0.274
Jan-17	26,520	92	0.347	84	0.317
Feb-17	24,654	85	0.345	73	0.296
Mar-17	28,501	108	0.379	99	0.347
Apr-17	26,284	32	0.122	30	0.114
May-17	26,403	47	0.178	44	0.167
Jun-17	28,322	32	0.113	31	0.109
Jul-17	26,756	29	0.108	29	0.108
Aug-17	27,940	47	0.168	39	0.14

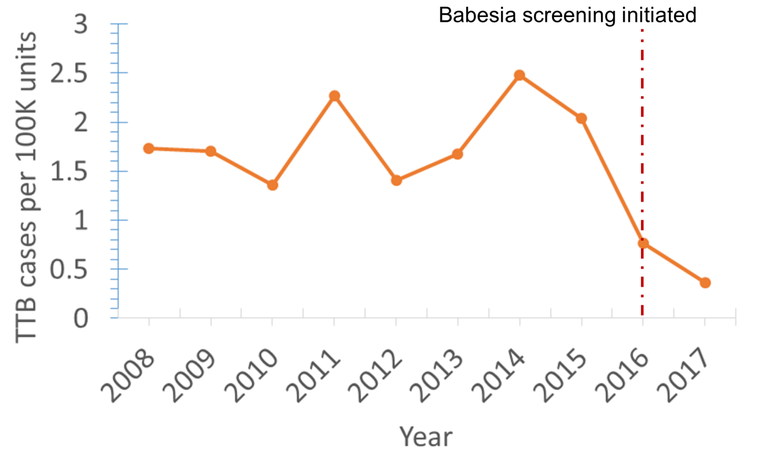
PERCENTAGE OF DONORS REACTIVE FOR BABESIA BY MONTH



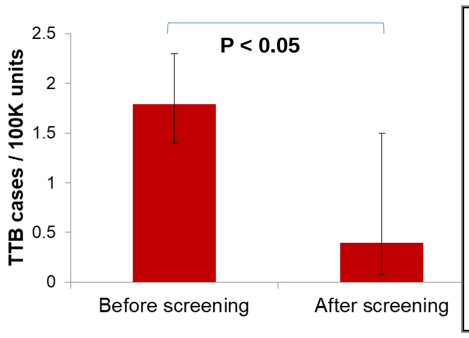
Effect of babesia screening on occurrence of TTB: There were two cases of TTB reported from our center during the period of active screening (green boxes) – one in 2016 and one in 2017. In both cases samples from the donors were sent to the state where Immunofluoresence assays were positive (combination of IgG, IgM and IgA). The other 2 TTB cases in 2016 occurred prior to initiation of screening

Year	BabesiaCases	RBC collections	TTB cases per 100K units
2008	8	462960	1.728011059
2009	8	470182	1.701468793
2010	6	441250	1.359773371
2011	10	441275	2.266160557
2012	6	427100	1.404823226
2013	7	419137	1.670098321
2014	10	404016	2.475149499
2015	8	393150	2.034846751
2016	3	393040	0.763281091
2017	1	279000	0.358422939

TTB CASES PER 100,000 COLLECTED UNITS IN THE YEARS LEADING UP TO AND AFTER INITIATION OF BABESIA SCREENING



TTB cases per 100K units collected by year before and after babesia screening: In the 7 years and 4 months prior to implementation of babesia donor screening there were 1.79 TTB cases per 100,000 units collected (65 TTB cases / 3.63 x 10^6 units). In the 16 months after implementation of babesia donor screening (May 2016) there were 0.40 TTB cases per 100,000 units collected (2 TTB cases / 5.03 x 10^5 units).



Comparison of TTB cases per 100K units before and after babesia screening: After initiation of screening TTB cases declined from 1.79 (2.3 – 1.4) / 100K units to 0.4 (1.5 – 0.071) / 100K units. Data are presented as the proportion with 95% Confidence intervals calculated using the Wilson/Brown hybrid method. The P value was calculated using Fisher's exact test.

CONCLUSIONS

-- Our data confirm a decreased incidence in TTB with the use of serological donor babesia screening from 1.79 (95% CI, 2.3 – 1.4) TTB cases per 100K RBC units collected before screening (2008 – May 2016) to 0.40 (1.5 – 0.071) TTB cases per 100,00 RBC units collected after screening (May 2016 – Aug. 2017).

-- Two breakthrough cases out of 439,274 units tested have been observed since initiation of screening. Possible explanations of breakthrough cases include window period donations and sensitivity limitations of the screening assay.

-- Since initiation of screening, donor deferrals for babesia have declined from 0.43% (0.41 – 0.45) of donors (1416 deferrals / 329853 donations) during the first year (May 2016 – April 2017) to 0.13% (0.11 – 0.15) of donors (143 deferrals /109421 donations) during the second year to date (May 2017 – August 2017). This decline may reflect the permanent removal of repeat reactive donors from the donor pool, or perhaps decreased babesia transmission in 2017 compared to previous years. Correlation with babesia surveillance data from 2017 is needed to address the latter possibility.

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