

Progress Towards an Intervention to Prevent Transfusion-Transmitted *Babesia*

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and

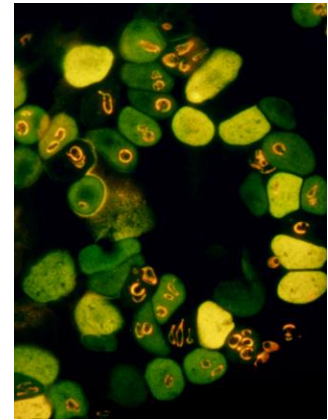
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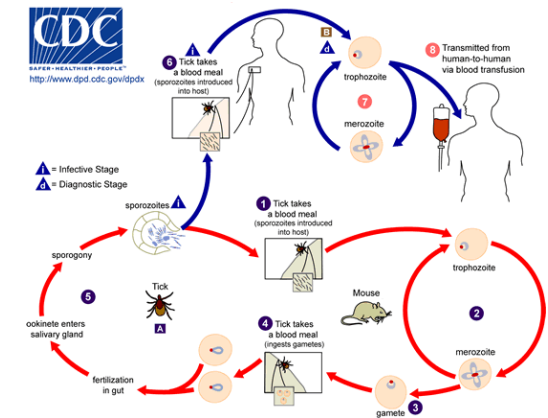
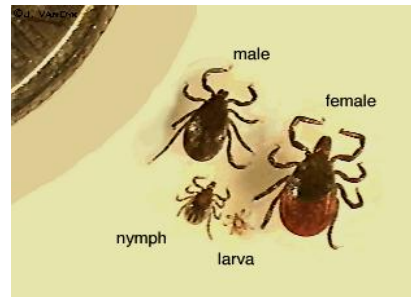


**American
Red Cross**

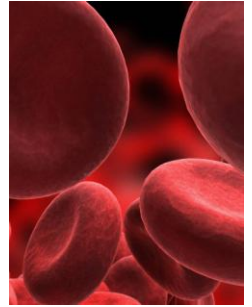
Babesia spp.



- agents of human babesiosis:
 - B. microti*, *B. divergens* & *B. duncani*
 - CA-1, MO-1, EU-1, KO-1, TW-1, etc.
- infect red blood cells, but occasionally found extracellular
- transmitted by *Ixodes* ticks (aka, the deer tick)
 - often same species that locally transmits Lyme borreliosis
- generally causes benign flu/malaria-like illness
- but can be fatal in:
 - infants
 - elderly
 - immunocompromised
 - sickle cell disease
 - asplenic



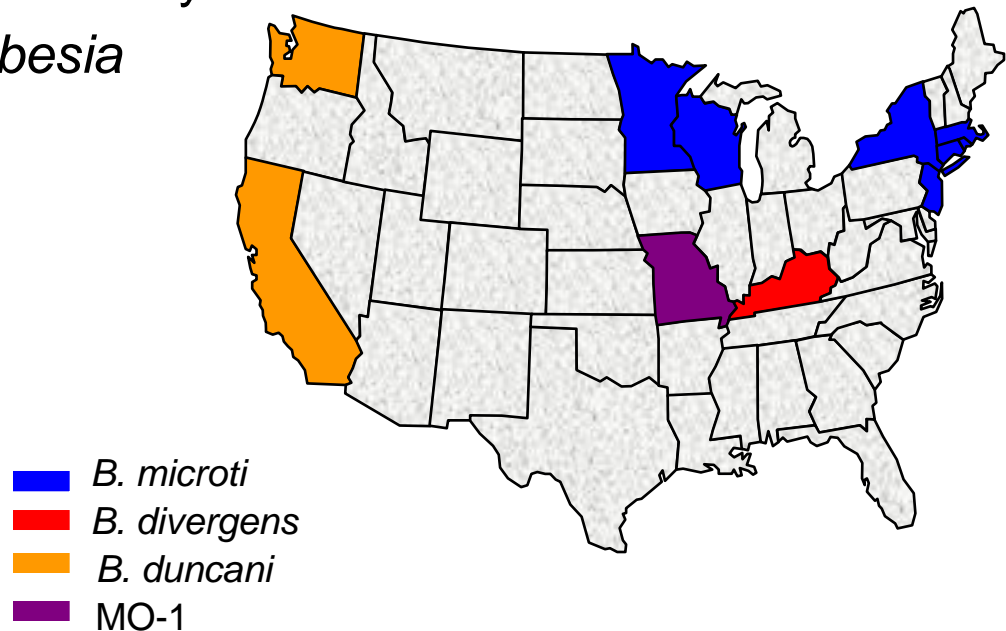
***B. microti*: Survival In Blood Products**



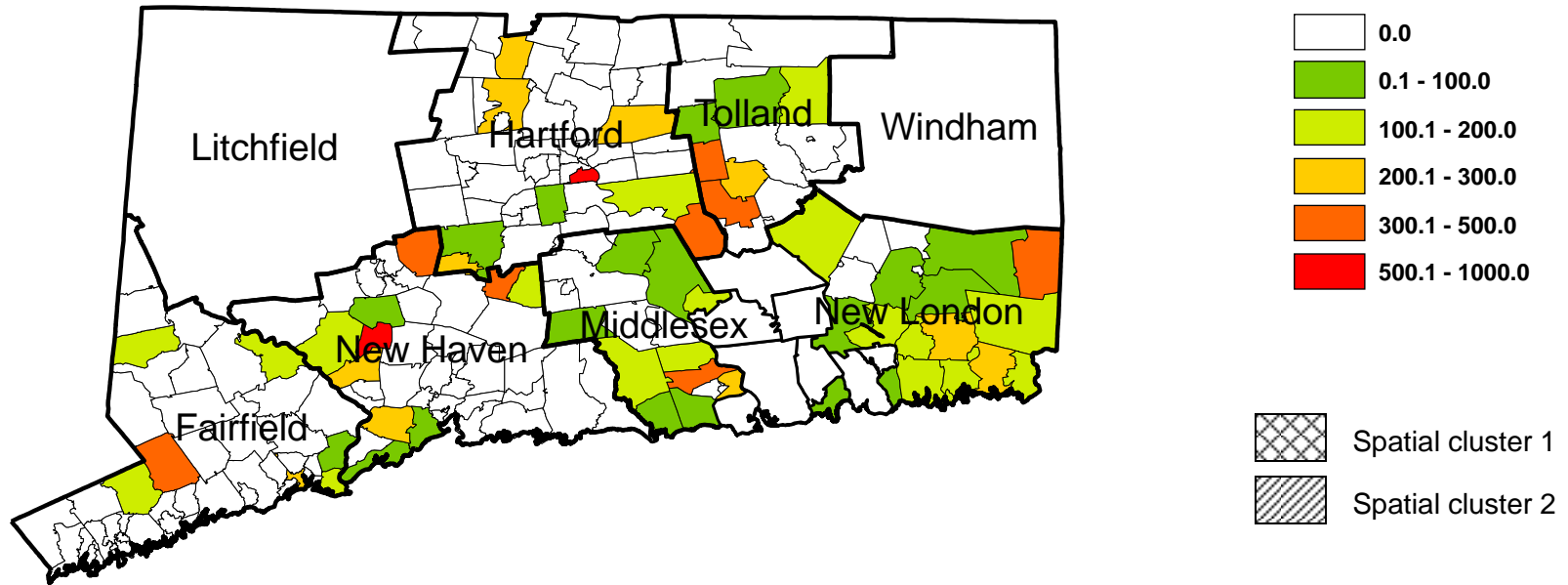
- survives in red cells maintained at 4°C
 - 21 days experimentally
 - 42 days in association with transfusion case
 - *survives indefinitely in cryopreserved red cells*
- parasite killed in frozen plasma
- extracellular parasites reported
 - pose potential issues for platelet apheresis & fresh plasma products

Babesia in the U.S.

- 1993 – *B. duncani* on West Coast
- 1996 – MO1 in Missouri
- 1999 – *B. microti* reported in New Jersey
- 2002 – *B. divergens* in Kentucky
- other miscellaneous *Babesia*



Seroprevalence in Connecticut



Seroprevalence in WI and MN

- testing 2000 samples
 - initiated in October 2010
- focused on high case prevalence counties/cities
 - based on MN Health Department data
- all samples tested by IFA
 - positive samples tested by PCR
 - no opt-out option
- tested 574 samples to date
 - 5 (0.9%) IFA positive donors

courtesy of Laura Tonnetti



Summary of 10 NCBS Transfusion Transmitted (TT) Babesia Investigations Since 7/2008

Case #	NCBS IFA ⊕ Donor	Product Involved	# of Patients Infected	Comments
1	No	RBC	0	Donor confirmed as source of Anaplasma infection. Negative for Babesia
2	Yes	Double RBC	2	1 Fatality
3	Yes	RBC	1	
4	Yes	RBC	3	Decedent and 2 Kidney txp recipients
5	Yes	RBC	1	
6	Yes	RBC	1	
7 ^{*†}	No	RBC	1	Non ARC donor was ⊕
8 [‡]	No	RBC	1	Out of Region PRTTI. Another ARC region had + donor
9	Yes	RBC	1	
10	Yes	RBC	1	
Totals	7 [*] ⊕ Donors	8 [†] NCBS Implicated RBCS	12 [‡] Patients (11 from MN Area)	

* 7NCBS ⊕ Donors but 8 MN donors as one donor was Non ARC See Case #7 above.

†8 NCBS RBCs but 9 MN RBCS because of Case #7 above .

‡ Case #8 above: Suspected NCBS RBC was exported to another ARC Region. ⊕ Patient & Donor not from MN .

9 Potential Cases of Transfusion-Transmitted Babesia

- 11 Local Patients Affected
- 8 Local Donors Implicated (1 Case Non ARC)



Transfusion-Transmitted *Babesia*

> 100 cases associated with *B. microti*

3 cases associated with *B. duncani*

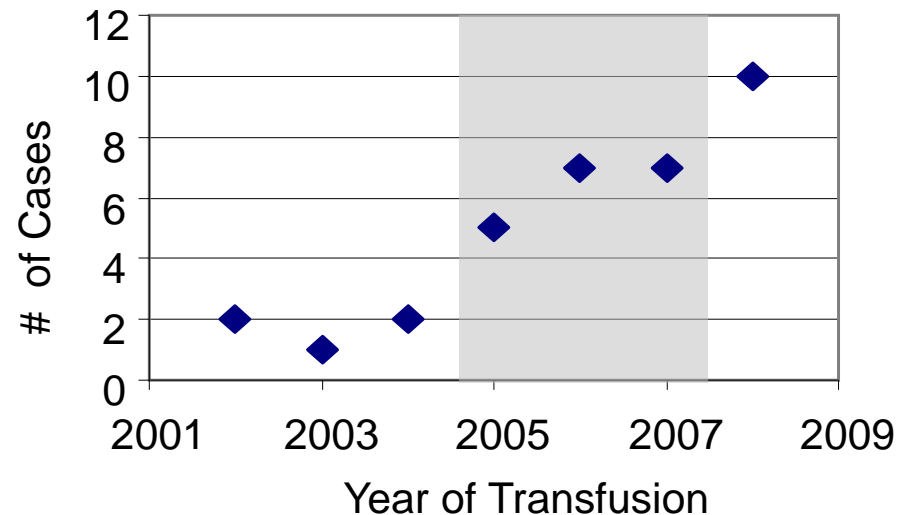
0 cases associated with other species,
types, strains, etc.

***B. microti*: Transfusion Cases**

- > 100 known cases worldwide (1979 - present)
 - 1 in Japan (autochthonous)
 - 1 in Canada (U.S. derived)
 - rest in U.S.
 - ~ 10 per year
- one possible case in Europe
 - Hildebrandt et al., Eur J Clin Microbiol Infect Dis 2007;26:595-601
- recipients - neonates to 79 years
- fatalities increasingly reported
- red cells and whole blood platelets implicated
- no licensed tests
- **gaining traction as critical blood safety issue**

ARC Hemovigilance: 2005-2007

- suspected transfusion-transmitted *B. microti* infections reported by transfusion services
- additional cases through recipient tracing
- donor follow-up samples tested by IFA and PCR
- 19 cases transfusion-transmitted *B. microti*
 - 5 fatalities
 - 18 RBC units (1 split unit)



Recipient Data

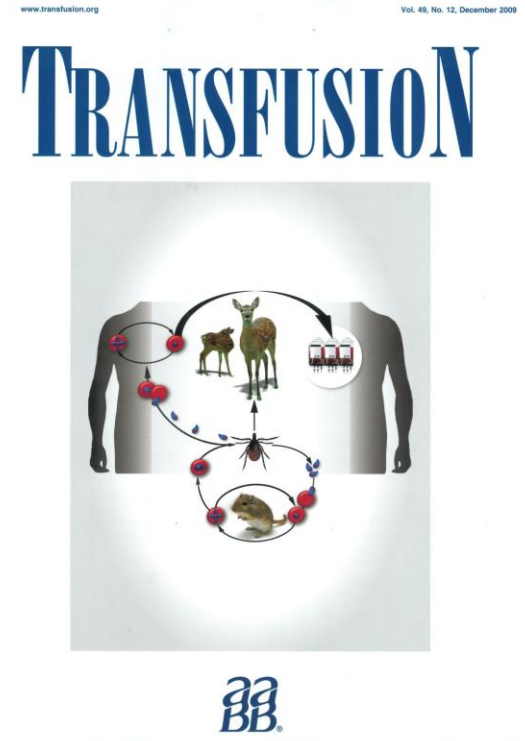
- 13 (68%) were 61-84 years old
- 2 (11%) \leq 2 years old
- 4 asplenic
- 2 had sickle cell disease (1 asplenic)
- incubation period: 23 – 384 days
- 5 of 19 (26%) died within days to weeks of diagnosis

Donor Data

- 18 donors implicated
- all IFA positive; only 1 PCR positive
- 12 residents of endemic areas (8 CT, 3 NJ & 1 MA)
- 4 traveled to endemic areas
 - - OH to CT, OH to NJ, IN to WI, VA to CT
- - 2 implicated in fatal cases
- 1 lost to follow-up & 1 unclear travel history
- none recalled symptoms, only 3 reported tick bite

Factors Driving Mitigation Efforts

- FDA Workshop
- AABB Association Bulletin
- publications
- education
- past failures to act
- babesiosis: nationally notifiable in US
- >100 transmission cases with rising fatalities ($n \geq 12$)



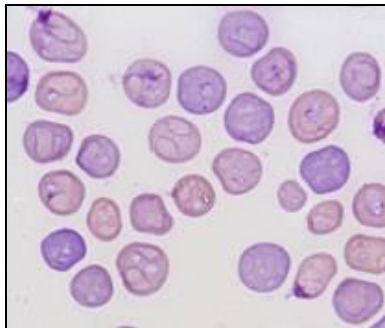
Mitigation Strategies

- UDHQ – “history of babesiosis”*
- geographic exclusion*
- risk-factor questions
- leukoreduction
- pathogen reduction
- serologic screening
 - 7 state strategy?
- nucleic acid testing
 - seasonal?

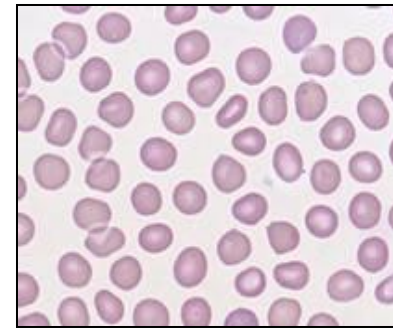
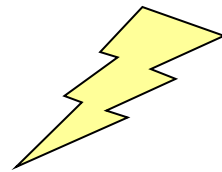
* currently in use

Pathogen Reduction

- efficacy demonstrated
 - amotosalen + UV light
 - Grellier et al., Transfusion 2008;48:1676-1684.
 - riboflavin + UV light
 - Tonnetti et al., Transfusion 2010;50:1019-1027
- studies limited to apheresis plasma and platelets
- presently, not a viable option in the absence of a whole blood methodology



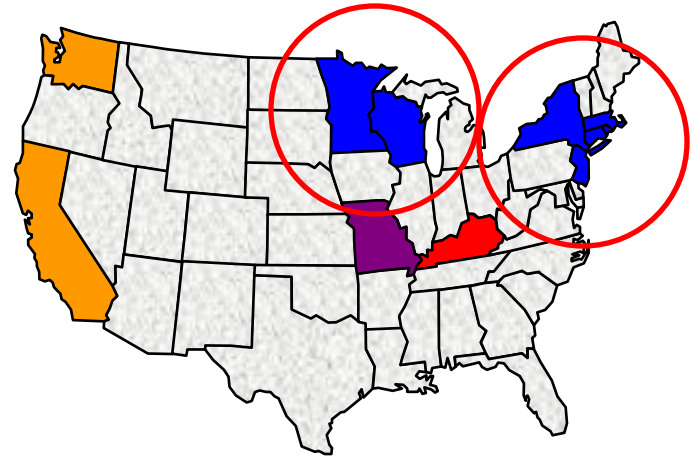
untreated



riboflavin + UV

Blood Screening Approaches

- universal screening
- regional testing
- statewide testing
- highly endemic area testing
- CMV model



. . . if we only had a test!

Piloting NAT

- pilot study of 1,000 CT donations
- collected August/October 2009 from Middlesex and New London Counties
- 1,002 tested to date:
 - 25 (2.5%) IFA positive
 - 3 (0.3%) PCR positive (2 IFA +, 1 IFA -)
 - all identified by first week of September
- 1 apparent window period infection detected
 - number likely low
 - acutely infected donors too sick to donate?
- role for NAT during tick season?

Babesia NAT Approach

- seasonally triggered
- May through September
- targets acute or “window period” infections
- technologic hurdles remain:
 - PCR sensitivity sufficient, but . . .
 - parasitemia low compared to viral infections
 - requires whole blood
 - limited volume for testing
 - considerations of concentration techniques