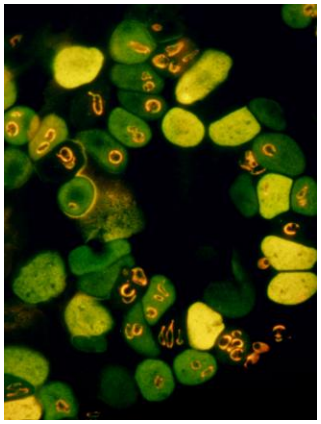
Progress Towards an Intervention to Prevent Transfusion-Transmitted *Babesia*

David A. Leiby, PhD

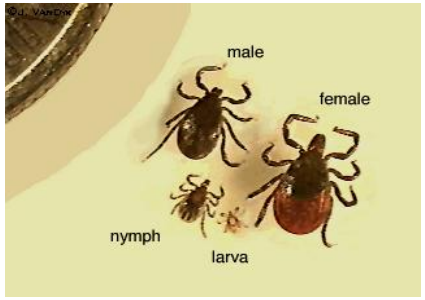
Transmissible Diseases Department
American Red Cross Holland Laboratory
and
Department of Microbiology and Tropical Medicine
George Washington University

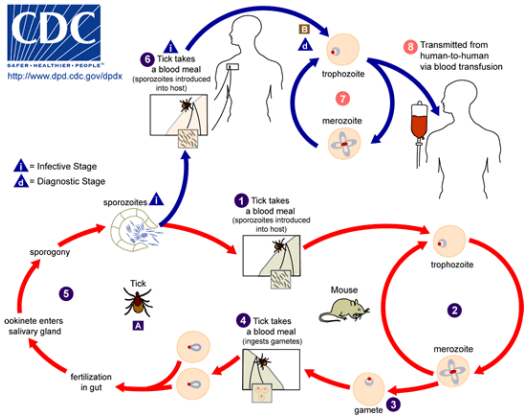
American Red Cross

Babesia spp.



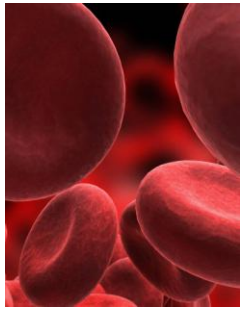
- agents of human babesiosis:
  - *B. microti*, *B. divergens* & *B. duncani*
  - *CA-1, MO-1, EU-1, KO-1,TW-1, etc.*
- infect red blood cells, but occasionally found extracellular
- transmitted by *Ixodes* ticks (aka, the deer tick)
  - often same species that locally transmits Lyme borreliosis
- generally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





American Red Cross

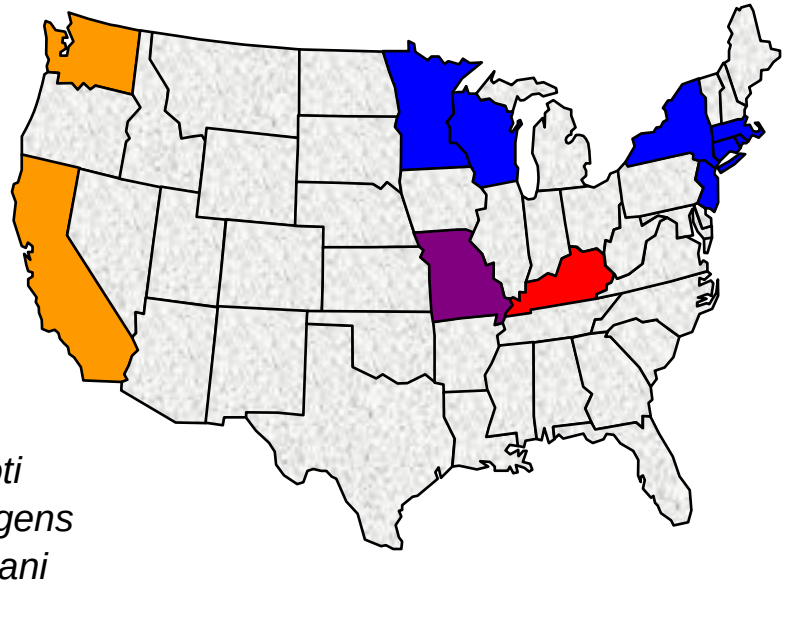
B. microti: Survival In Blood Products



- survives in red cells maintained at 4^{o}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

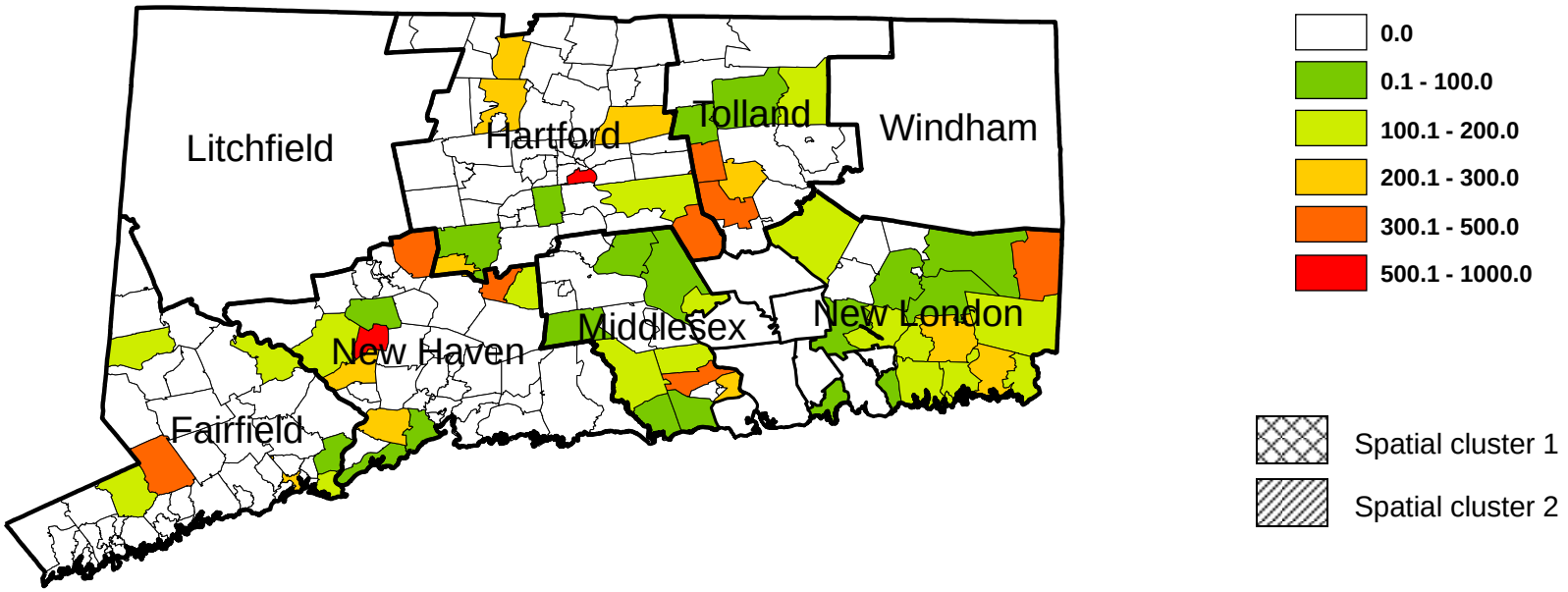
Babesia in the U.S.

- 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*



American Red Cross

Seroprevalence in Connecticut



Johnson et al., Transfusion 2009;49:2574-2582

American Red Cross

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

American Red Cross

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)

American Red Cross

Transfusion-Transmitted *Babesia*

> 100 cases associated with *B. microti*

3 cases associated with *B. duncani*

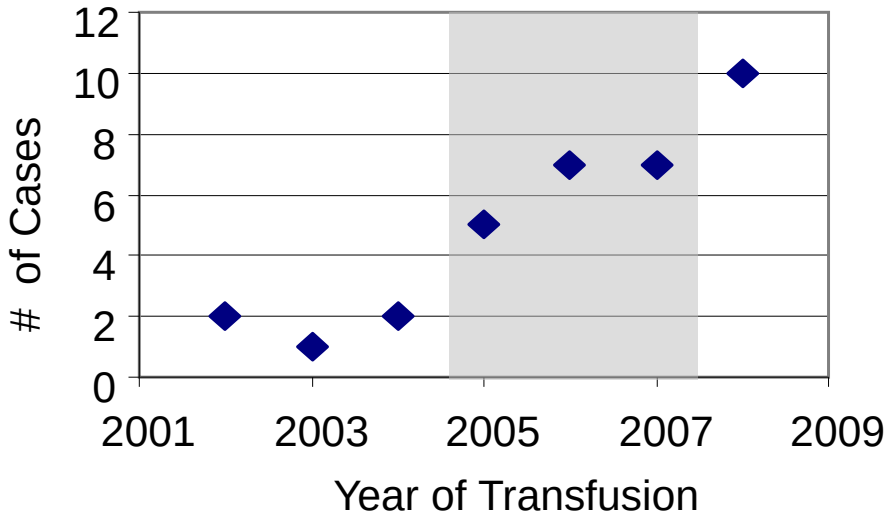
0 cases associated with other species, types, strains, etc.

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)



Tonnetti et al., Transfusion 2009;49:2557-2563

American Red Cross

Recipient Data

- 13 (68%) were 61-84 years old
- 2 (11%) ≤ 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

Tonnetti et al., Transfusion 2009;49:2557-2563

American Red Cross

Donor Data

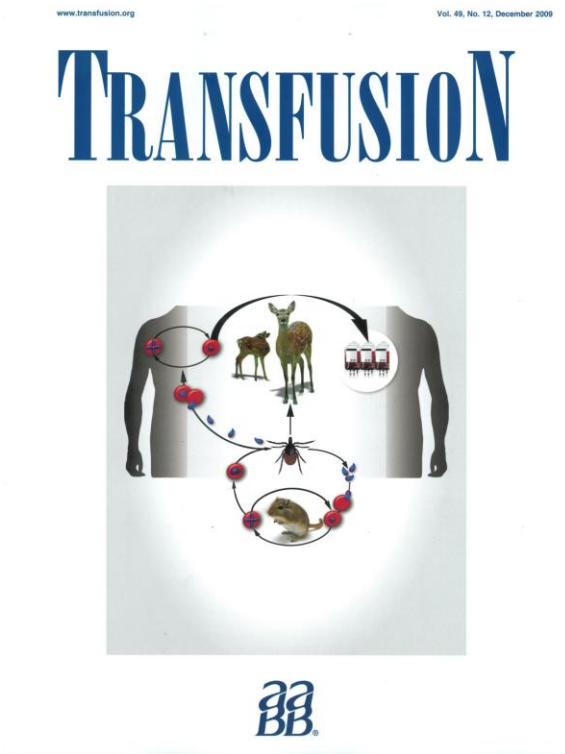
- 18 donors implicated
- all IFA positive; only 1 PCR positive
- 12 residents of endemic areas (8 CT, 3 NJ & 1 MA)
- 4 traveled to endemic areas
- - OH to CT, OH to NJ, IN to WI, VA to CT
- - 2 implicated in fatal cases
- 1 lost to follow-up & 1 unclear travel history
- none recalled symptoms, only 3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

Tonnetti et al., Transfusion 2009;49:2557-2563

American Red Cross

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≥12)



American Red Cross

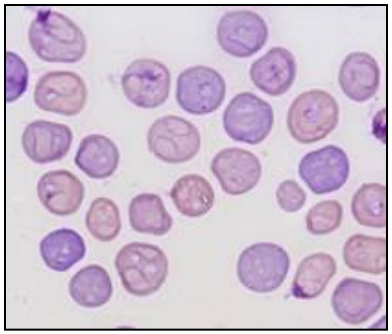
Mitigation Strategies

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

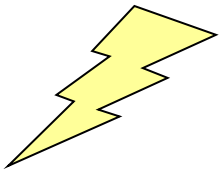
*** currently in use**

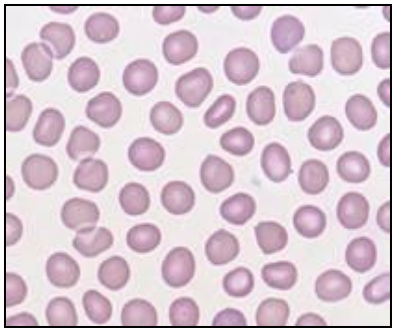
Pathogen Reduction

- 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

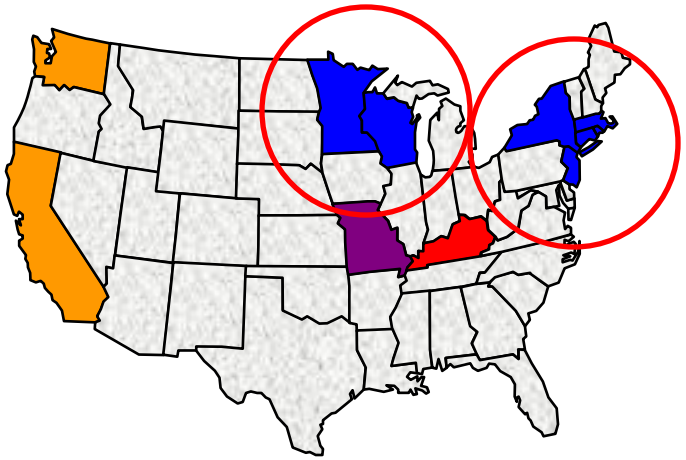




riboflavin + UV

Blood Screening Approaches

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



. . . if we only had a test!

American Red Cross

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