Human Babesiosis

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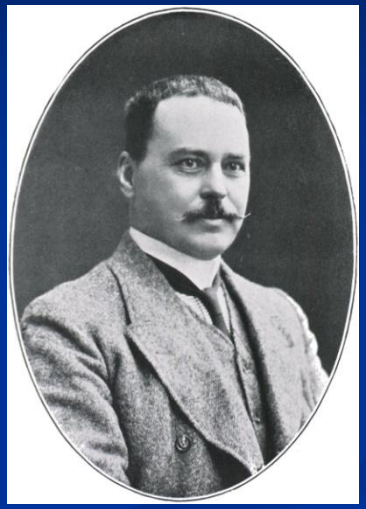
Babesiosis

An emerging zoonotic infection caused by an intraerythrocytic protozoan of the *Babesia* genus

Victor Babes

Dawn of Medical Entomology

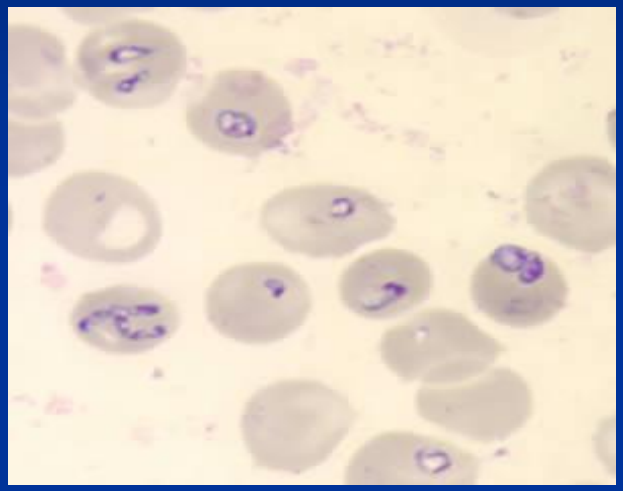
- 1898 Sir Ronald Ross and Sir Patrick Manson's malaria theory
- 1889 Theobald Smith, MD, and F.L. Kilbourne, DVM, discovered *Babesia bigemina* causing Texas cattle fever

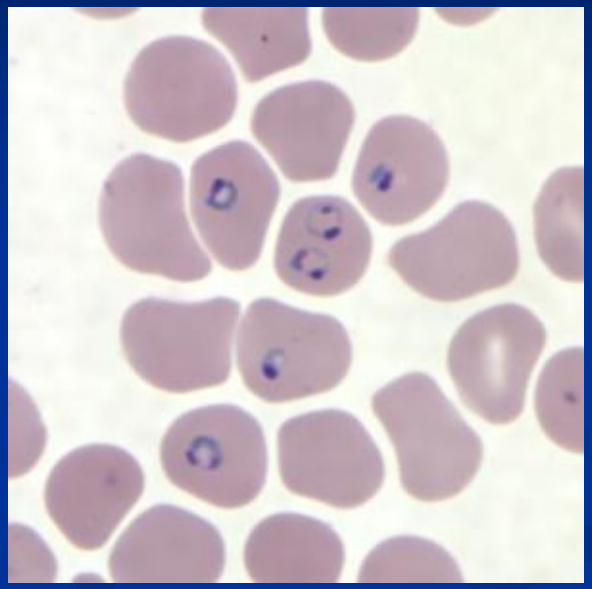


Patrick Manson

Theobald Smith

Babesia vs Plasmodia

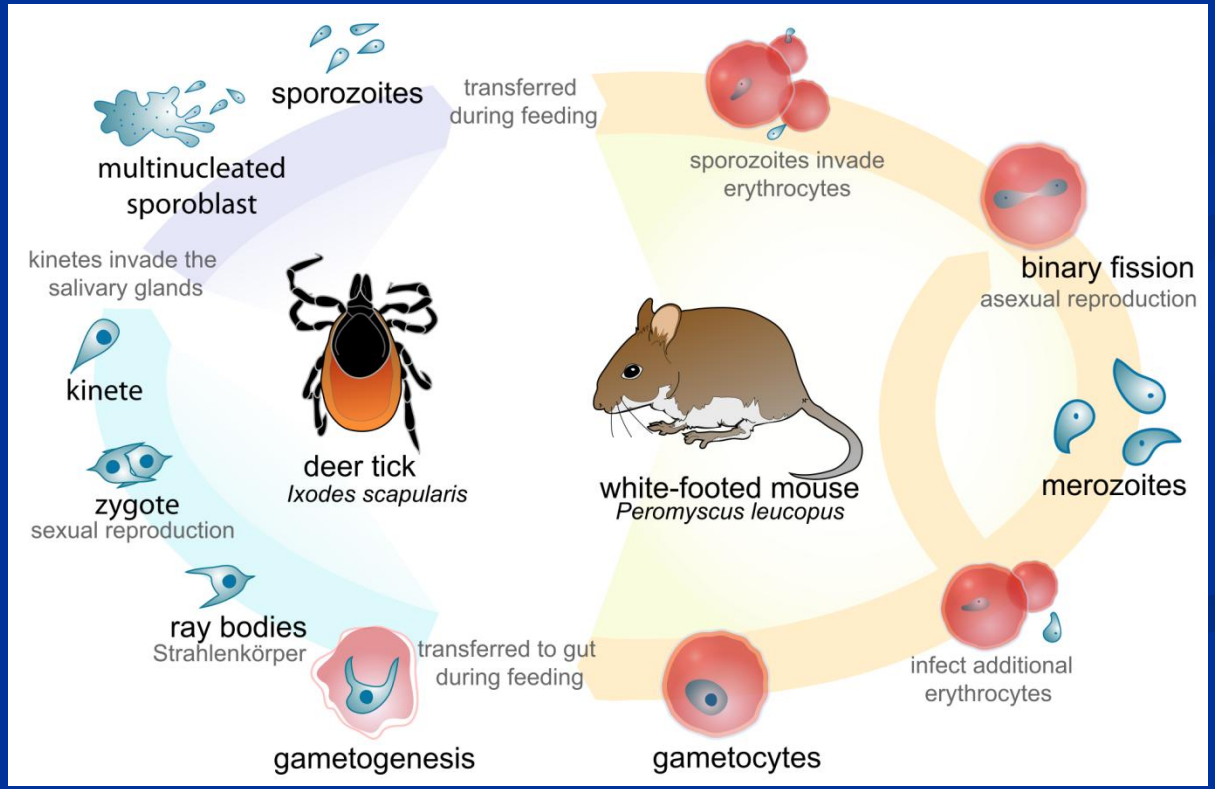




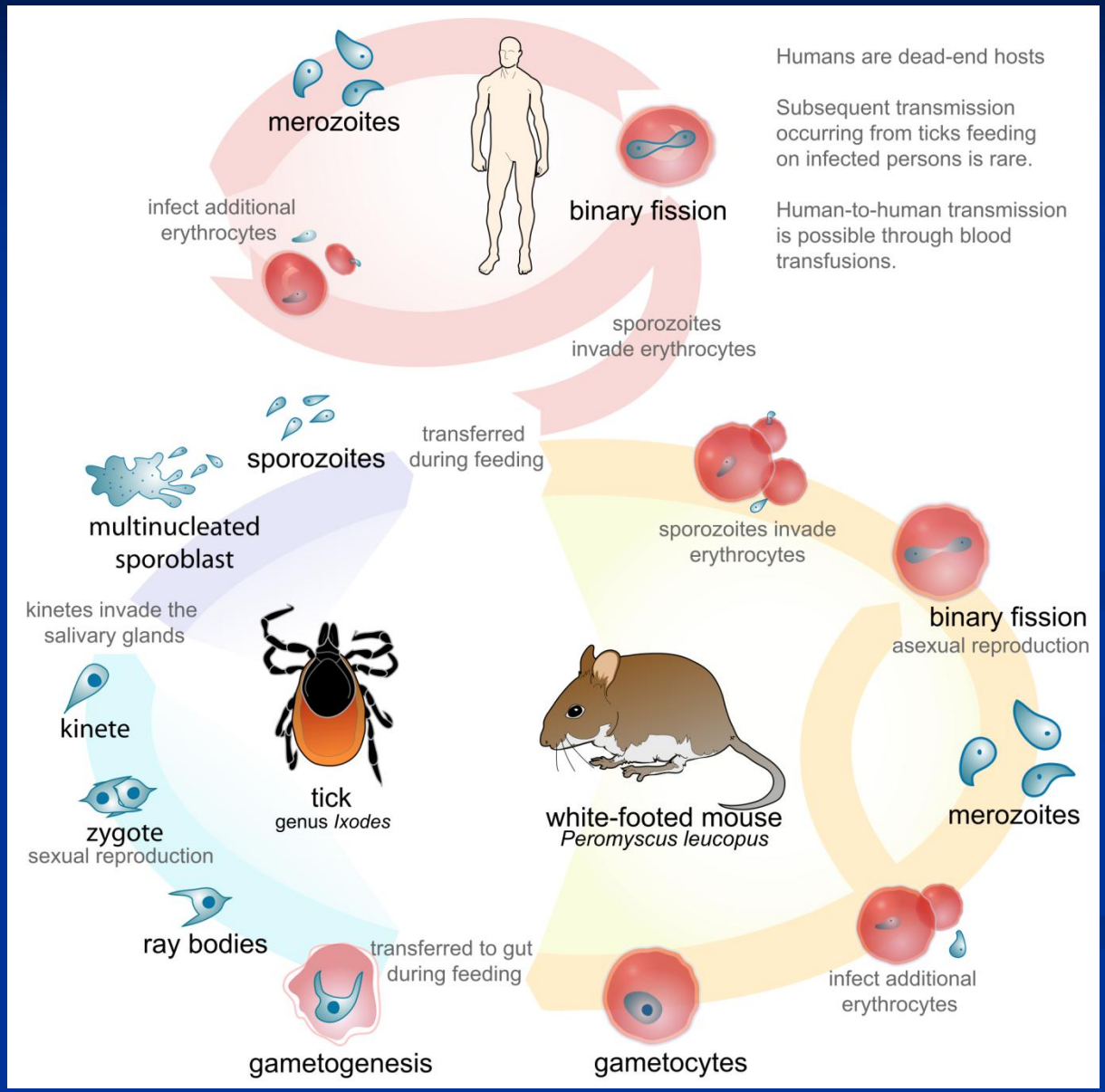
Distinguishing features:

- *Babesia* are pleomorphic
- can be vacuolated
- do not produce pigment

Wildlife cycle



Emerging Zoonosis



One Medicine and Babesiosis

- 1957 1st human case in Yugoslavia
- 1969 Nantucket fever in humans
- 1976 white-footed mice *B. microti* reservoir

Human Babesiosis

- Most cases in US are asymptomatic

- Symptoms can include:

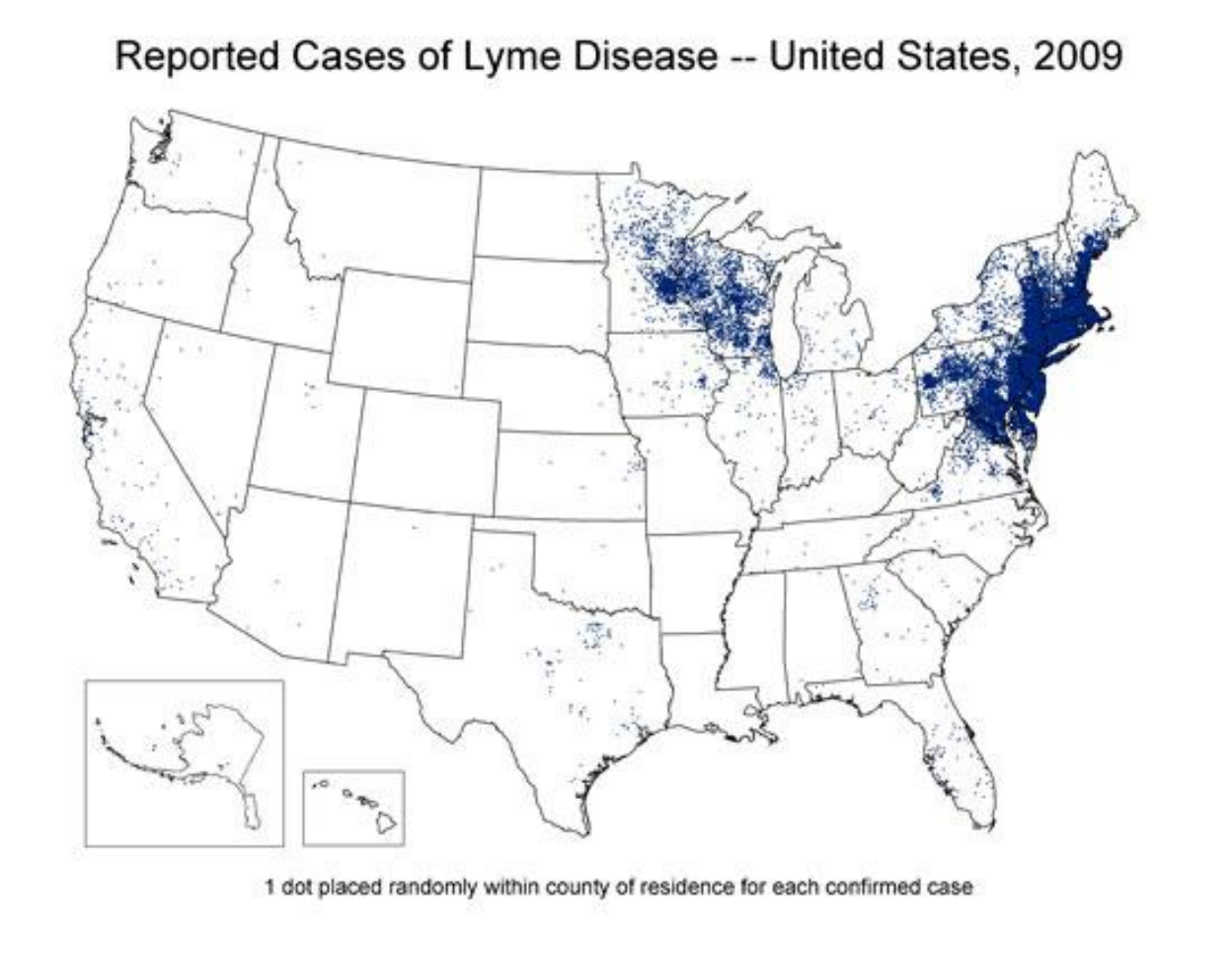
  - cyclic fever
  - chills
  - myalgia
  - fatigue
  - enlargement of liver and/or spleen
  - hemolytic anemia
  - hemoglobinuria

Babesiosis vs Lyme Disease

Vector = Ixodid ticks

Reservoir = white
footed mice and others

Co-infection



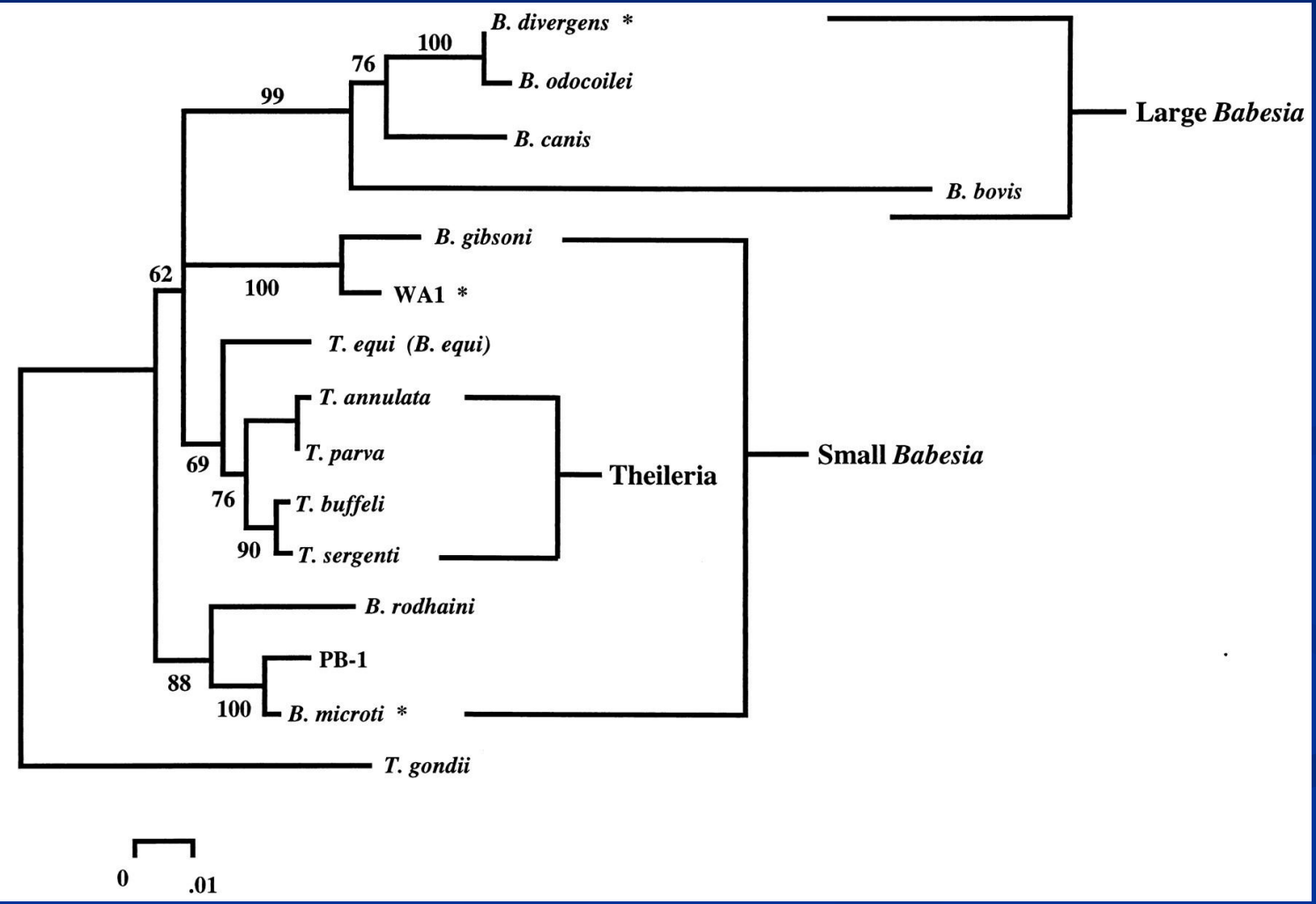
Zoonotic species

- *B. microti* most common cause in the US
  - endemic in Northeast
  - cases in Midwest and Northwest
- *B. duncani* (formerly *B.* WA-1)
  - isolated from patients in WA and CA
- MO-1
  - isolated from patients in WA, MO and KY
- *B. divergens*
  - causes most European cases

Piroplasms in Wildlife

- *Babesia odecoilei*
- *Theileria cervi*

Phylogeny of Piroplasms



Prevalence

- Hundreds of cases reported annually
- 9 deaths from blood transfusion 1997-2007

Risk Factors for Severe Cases

- Immunodeficiency
- Elderly
- Splenectomy
- Co-infection with other tick-borne diseases

Co-infection

TABLE 1. Symptoms associated with Lyme disease and babesiosis[a]

Symptom	% of patients surveyed exhibiting the indicated symptoms		
	Lyme disease (n = 214)	Babesiosis (n = 10)	Both (n = 26)
Fatigue	49	60	81
Headache	42	60	77
Erythema migrans	85	0	62
Fever	42	80	58
Sweats	11	20	46
Chills	23	50	42
Myalgia	31	20	38
Anorexia	14	10	31
Arthralgia	36	50	27
Emotional lability	7	0	23
Nausea	5	10	23
Neck stiffness	21	30	23
Multiple EM	14	0	19
Cough	10	20	15
Sore throat	9	20	15
Conjunctivitis	3	0	12
Splenomegaly	0	10	8
Vomiting	4	0	8
Joint swelling	3	0	4

Homer et al. 2000 *Clin. Micro. Rev.* 13(3): 451-469

Diagnosis

- Serology
- Blood smear
- PCR
- Inoculation of hamsters

Treatment

- Clindamycin and Quinine
- Toxicities significant: hearing loss, syncope, hypotension, GI distress
- Alternatives: atovaquone and azithromycin
- In very serious cases: erythrocyte exchange transfusion

Blood safety

- *Babesia* can cause chronic asymptomatic parasitemia

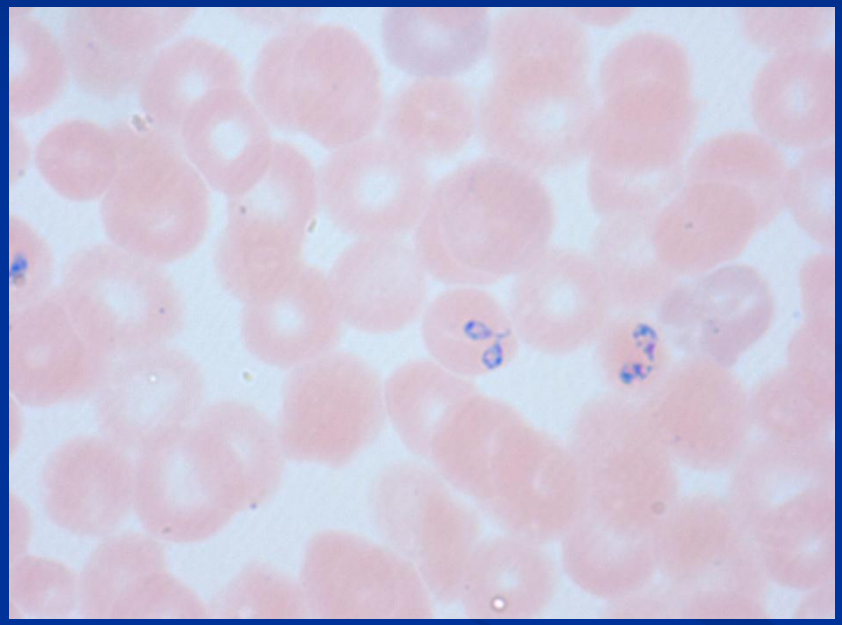
Case Study: Tennessee

Patient information

- 43 y.o. male
- Idiopathic thrombocytopenic purpura
  - Splenectomy in 2003
  - Rituxumab
- Hunted deer in middle Tennessee property
- No report of tick bite

Patient isolate

- Blood smear positive
- Mongolid jird inoculation negative
- IFA negative (*B. microti*, *B. duncani*, *B. divergens*)
- PCR negative for *B. microti*
- PCR positive for *Babesia* genus
  - 4% difference from other *Babesia* spp.
  - Nearest relative *Babesia* from Chinese ruminants



December 2008

S_x onset

July 2009

Blood-smear confirmation

PCR

T_x with quinine and clindamycin

S_x resolution

November 2009

Deer sampled

Tick dragging

February 2010

Rabbits sampled

Animal Specimen Processing

- White-tailed deer

  - serum separated from whole blood

  - DNA extracted from blood cells

- Eastern cotton-tailed rabbits

  - serum separated from whole blood

  - DNA extracted from spleens

Molecular Testing

- Deer blood, rabbit spleen and tick DNA:

  - screened for *Babesia spp*. using PIRO primers

  - amplify fragments from the 18S rRNA gene

- Positive samples sequenced to ID species

Serological Testing

- Indirect immunofluorescence assays
  - *B. microti*
  - *B. odocoilei*
  - MO-1
- IFA positive titer ≥ 1:64

Molecular Results

- 7/166 (4%) *Ix. scapularis - B. odocoilei*
- 0/5 deer blood DNA
- 1/8 rabbit spleen DNA - MO-1

Serology Results

- Deer serum

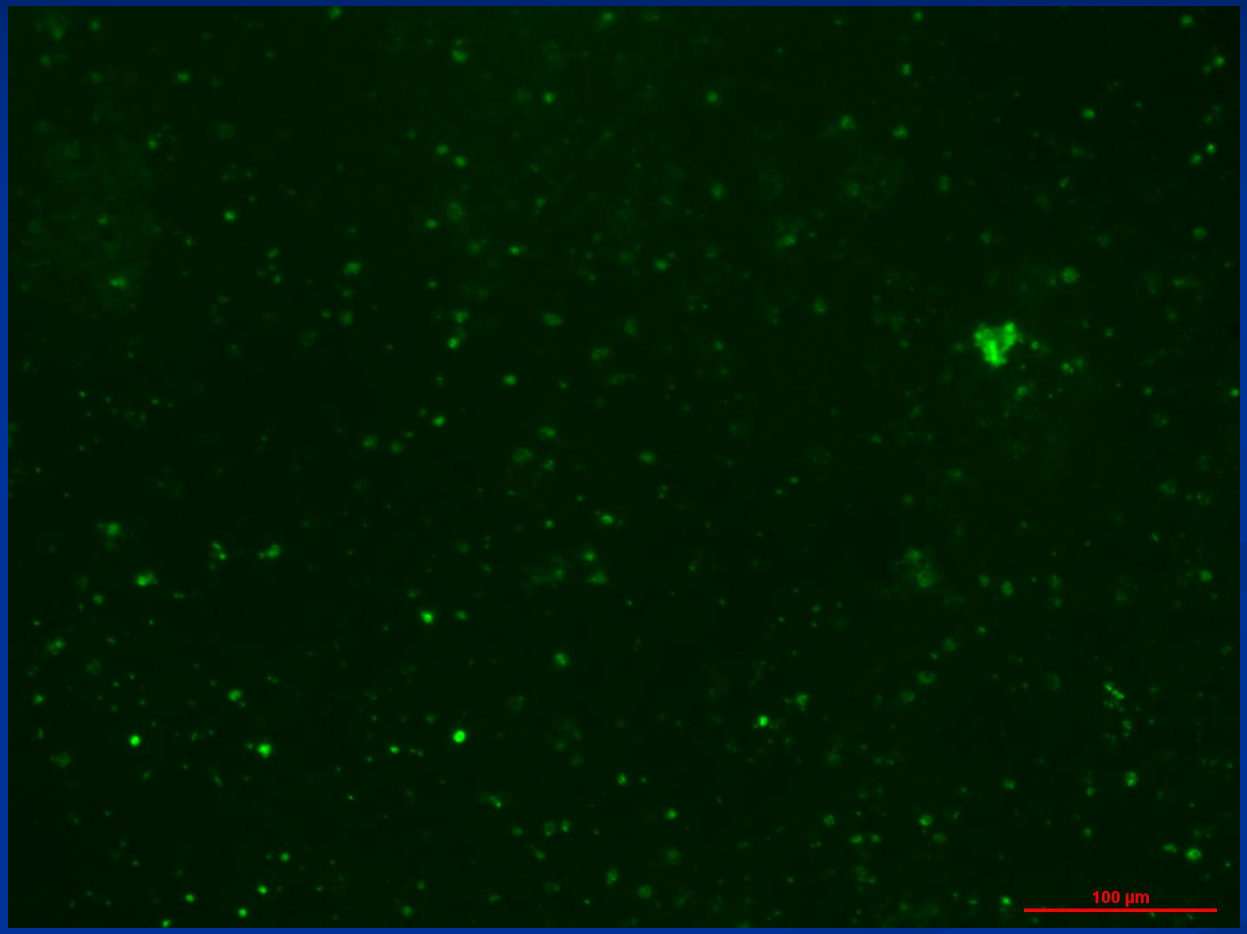
  - 4/5 antibodies reactive to *B. odocoilei*

- Rabbit serum

  - 2/7 antibodies reactive to *B. odocoilei*

  - 3/7 antibodies reactive to MO-1

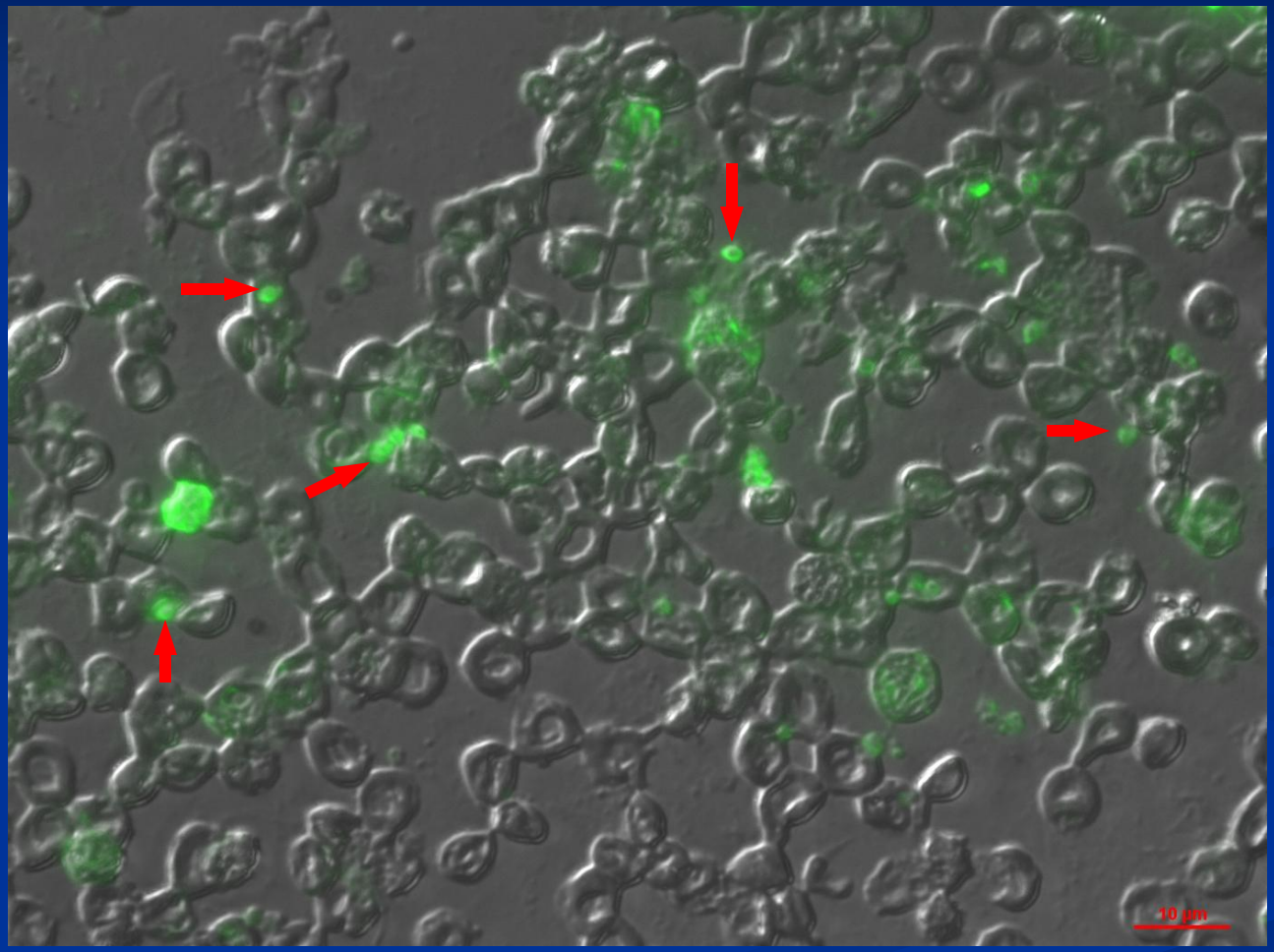
MO-1 antibodies in rabbit sera



Fluorescent image at 400X

Dilution 1:128

MO-1 antibodies in rabbit sera



Bright field and fluorescent image overlay at 1000X

Dilution 1:64

Results Summary

	Ticks	White-tailed deer	Eastern cottontail rabbits
B. odocoilei	√	√	√
MO-1			√

B. odocoilei

- Isolated in *I. scapularis* ticks
- Deer and rabbit sera reactive to antigen
- Shows link
  - parasites likely circulating *I. scapularis* ↔ wildlife
  - *I. scapularis* potentially transmitting other *Babesia*

Theileria cervi

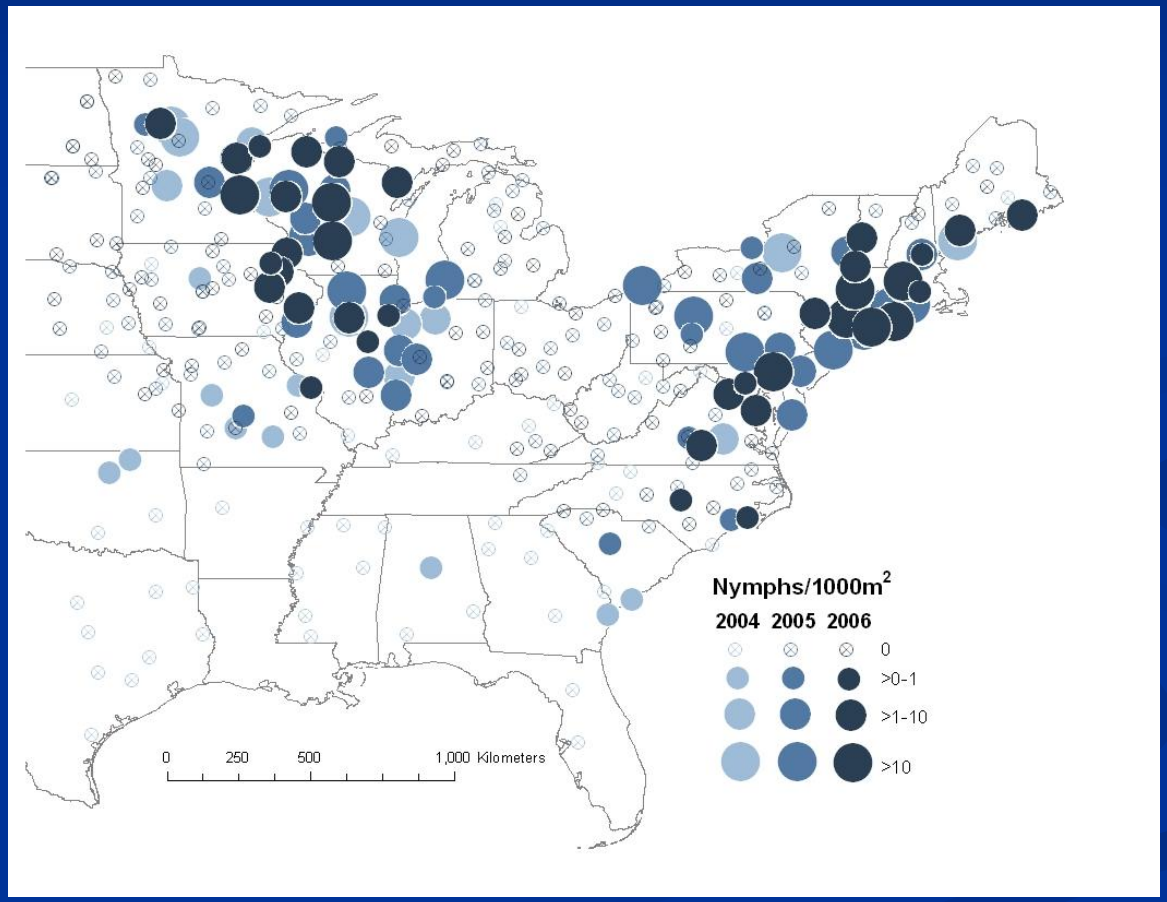
- 3/5 deer positive blood by PCR
- 24/128 (14%) deer ticks positive

MO-1

- Rabbits exposed to MO-1
- MO-1 causes severe disease in the US
- risk of exposure TN residents
- risk of exposure to blood transfusion patients

- physician awareness is imperative

Density of host-seeking *I. scapularis* nymphs (2004 – 2006)



Data by M Diuk-Wasser, Yale Univ. & Risk Map Study Grp

Reporting

- April, 2010: reportable to TDH
- January, 2011: nationally notifiable

Prevention

- Educate public about reducing tick exposure
- Screening blood donations
- Educate physicians, veterinarians and other public health officials

Action Plan

- Report to local health authority
- Investigate cases
  - Pathogen
  - Vector
  - Reservoir
- Investigate blood-transfusion acquired cases
  - Donor
  - Recipient
- Consider possibility of co-infection

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