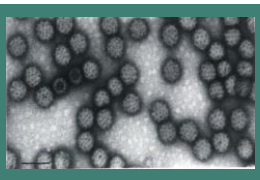
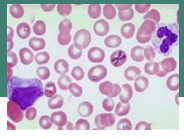
13th Annual Canadian Blood Services International Symposium

Blood-Borne Pathogens: Defend, Detect, and Destroy

Canadian Blood Services
it's in you to give



Prevalence and Risk of Blood-borne Pathogens in the Canadian Blood Supply



Dr. Margaret Fearon
Medical Director, Medical Microbiology,
Canadian Blood Services
September 26, 2015

Canadian Blood Services
it's in you to give

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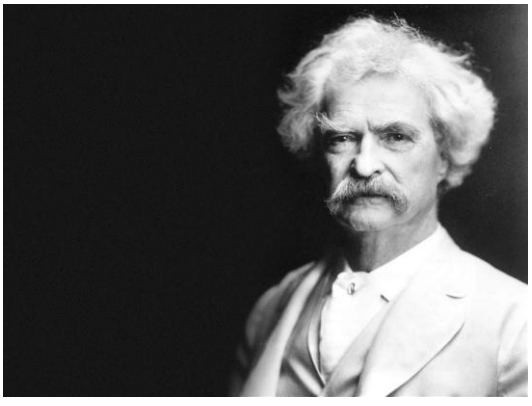

“It usually takes me two or three days to prepare an impromptu speech.”
— Mark Twain

4

Outline

- Current prevalence of 'classical' transfusion transmissible infections in CBS blood donors.
- 'New' Infectious diseases – 1999 to 2010
- Emerging, re-emerging Infectious Diseases
- How we prepare for and manage new risks.
- New paradigms for risk management

5

Confirmed TD (viruses and syphilis) Positive Allogeneic Donors 2002 – 2014

Marker	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
HBV	93	95	77	66	72	78	84	61	77	69	73	60	54
HCV	94	81	82	73	77	82	74	65	57	64	51	50	56
HIV	1	3	6	4	2	4	3	8	2	5	5	2	2
HTLVI/II	11	11	13	12	13	9	9	8	11	9	10	10	10
Syphilis	54	55	38	28	39	27	33	29	30	47	29	37	37
WNV	-	14	0	13	8	66	1	0	0	6	20	6	6

24 Chagas confirmed positive donors from May 2010 – Dec. 2014

6

Estimated residual risk in Canada using incidence rates from observed donor seroconversions 2006-2009*

Virus	Window period in days (95% CI)	Incidence rate from repeat donors (per 100,000 person years)	Residual Risk for all donors per million donations (95% CI)
HIV	9.5(8.2-10.8)	0.40	1:8
HCV	8.0(6.8-9.2)	0.56	1:6.7
HBV	38.3(33-43.7)	0.48	1:1.7

*Current incidence and residual risk of HIV, HBV and HCV at Canadian Blood Services. S.O'Brien, Q Yi,W.Fan,V.Scalia, M.Fearon, JP Allain. Vox Sanguinis 2012;103:83-86

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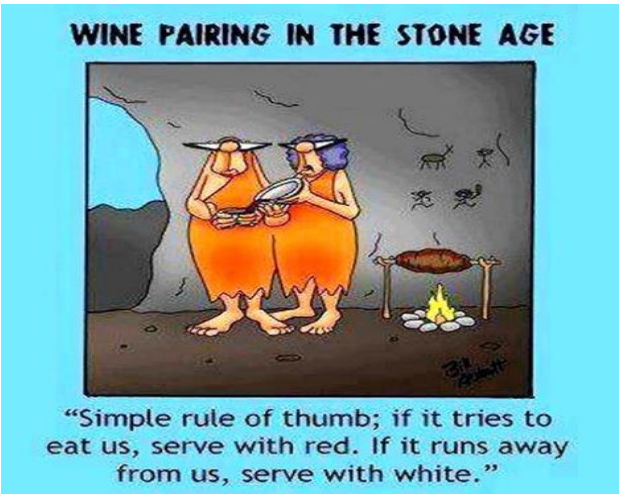

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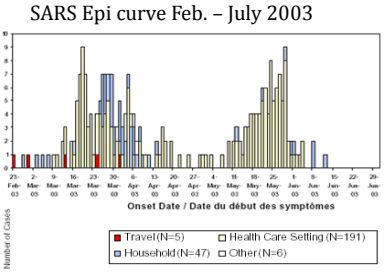
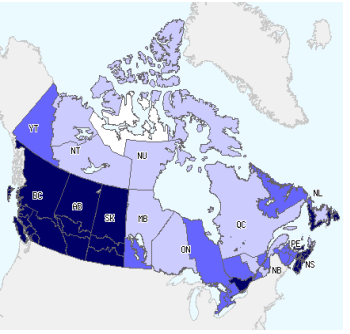
Infectious Diseases 1999 - 2010

West Nile 1999

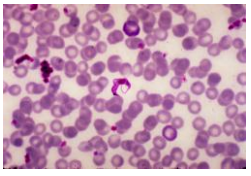
SARS 2003



Pandemic Flu 2009



Chagas Disease 2010



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New Testing Paradigms

- **West Nile virus** (Universal donor testing 2003)
  - Seasonal WNV testing (June 2015)
    - *All donors tested from June 1 to November 30*
    - *Only donors with travel outside Canada tested Dec. 1 – May 31*

- **Chagas Disease (***Trypanosoma cruzi***)** (May 2010)
  - Test donors at risk only:
    - *Born or lived in an endemic country (South America, Central America, Mexico)*
    - *Mother or maternal grandmother born or lived in an endemic country*

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Infectious Disease Outbreaks that impact Security of Supply

- **Sars, Pandemic Influenza**
  - Contingency planning for:
    - *Shortage of staff, and donors due to illness*
    - *Shortage of critical supplies*
    - *Staff and donor education*
    - *Infection control procedures in clinic*
    - *Donor deferral criteria*

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"Clearly there has been a lack of imagination about how much can go wrong."

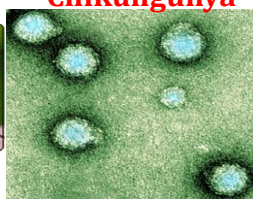
Rachel Maddow

12

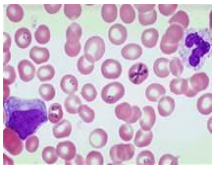
Emerging Infectious Disease Risks

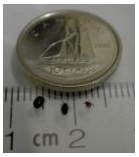
Aedes aegypti

Chikungunya



Babesia microti

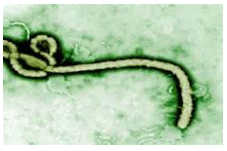




Black legged Tick (*Ixodes scapularis*)

Ebola virus outbreak West Africa 2014-15

Filovirus

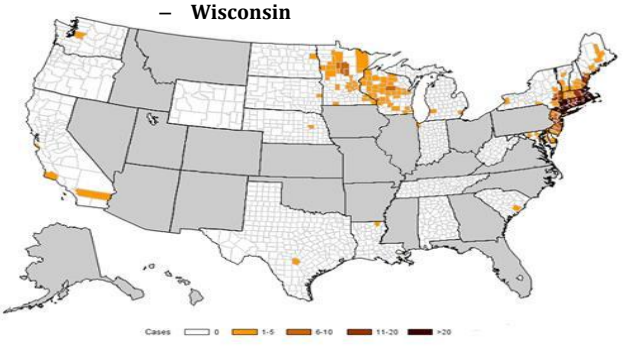


Hepatitis E

Babesiosis

- Babesiosis is caused by a protozoan parasite (Babesia microti, duncani) spread by infected ticks.
- Most infections asymptomatic or unrecognized
- Incubation 1-6wks.(9 post transfusion)
  - Flu like symptoms
  - Severe: hemolytic anemia, thrombocytopenia, renal failure, ARDS
- Overall mortality~5% (higher if at-risk)
  - i.e. immunocompromised,
  - asplenics,
  - Transfusion – transmitted cases 160 reported cases from 1979 – 2009 in the U.S., one case reported in Canada.

- Majority of U.S. Cases reported in:
  - **Connecticut**
  - **Massachusetts**
  - **Rhode Is.**
  - **New York State**
  - **New Jersey**
  - **Wisconsin**



1,762 reported cases of babesiosis by county of residence (27 states) 2013. *CDC January 2015*

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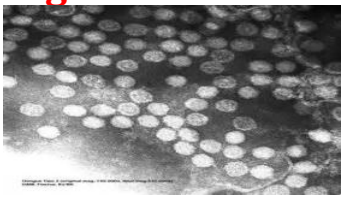
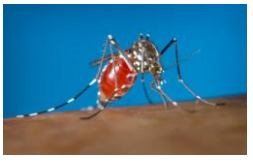
Hepatitis E

- Common viral hepatitis clinically similar to hepatitis A
- Genotypes 1 and 2 common in developing countries, generally transmitted via contaminated water.
- Travel is not the only risk factor. Endemic cases (genotypes 3 and 4) occur in developed countries.
- Contact with pigs, raw pork a risk factor?
- Prevalence in Canada is unknown.
- No cases of transfusion transmission reported in North America but cases have been reported in endemic countries and recently in the U.K.

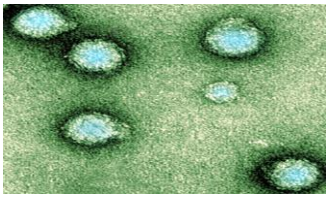
15

Dengue





Chikungunya



- Two viruses common in the tropics.
- Spread by mosquitos (*Aedes aegypti, Aedes albopictus*).
- Similar acute illness – fever, rash, muscle and joint pain. Similar incubation 3-7 days.
- **Dengue** ('breakbones fever') is currently more widespread.
- **Chikungunya** ('that which bends up') just arrived in the Caribbean in 2013.
- A few clusters of transfusion transmitted dengue reported.
- No cases of TT chikungunya reported to date.
- Current malaria travel deferral covers many but not all affected areas.

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‘In preparing for battle, I have always found that plans are useless but planning is indispensable.’

Dwight D. Eisenhower

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Preparing for Emerging Infectious Disease Risks

- **Surveillance**
  - PHAC, WHO, CDC, ProMED mail
  - Collaboration with public health:
    - *Diagnostic testing data from National Microbiology Laboratory and provincial Public Health Laboratories*
  - Collaboration with Veterinarians, Etymologists, Ornithologists
    - *Animal, Bird, Tick and Mosquito surveillance data*

- **Seroprevalence studies** on our donors

- **Donor surveys** – risk behaviours, travel

- **Risk based decision making (Alliance of Blood Operators)**

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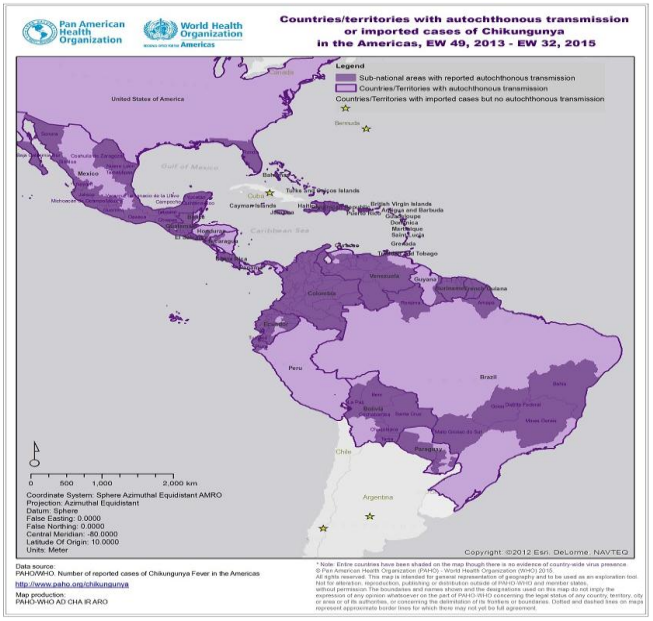
Chikungunya Surveillance



Canadian Data

Public Health Agency of Canada (National Microbiology Lab)

520 confirmed Chikungunya antibody Positive patients Jan.1 2014 - July 1, 2015 (25% (112) are PCR positive)

Travel documented for only 1/3 of cases, but of those, 90% travelled to the Caribbean.

ProMED mail

EBOLA UPDATE (110): WHO, SUSPECTED, FUNDING, RESEARCH
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A ProMED-mail post
<http://www.promedmail.org>
ProMED-mail is a program of the
International Society for Infectious Diseases <http://www.isid.org>

In this update:
[1] WHO Ebola data and statistics [data up to 20 Sep 2015] [2] WHO situation report [data to 20 Sep 2015] [3] Ebola survivors suffer complications [4] Suspected, funding, research

******
[1] WHO Ebola data and statistics (data through 20 Sep 2015)
Date: Wed 23 Sep 2015
Sources: WHO Ebola data and statistics [edited] <http://apps.who.int/gho/data/node.ebola-sitrep.ebola-summary?lang=en>

Cumulative cases & deaths as of dates shown

Case definition Cumulative cases (deaths)

Guinea -- as of 20 Sep 2015

Confirmed 3340 (2079)
Probable 453 (453)
Suspected 7 (not available)
Total 3800 (2532) [3 cases in past 21 days]

Liberia (a) -- 7 Sep 2015

Confirmed 6 (2) no additional cases
Probable 0 (not available)
Suspected (not available) (not available) Total 6 (2) [0 cases in past 21 days]

Liberia (b) -- up to 9 May 2015

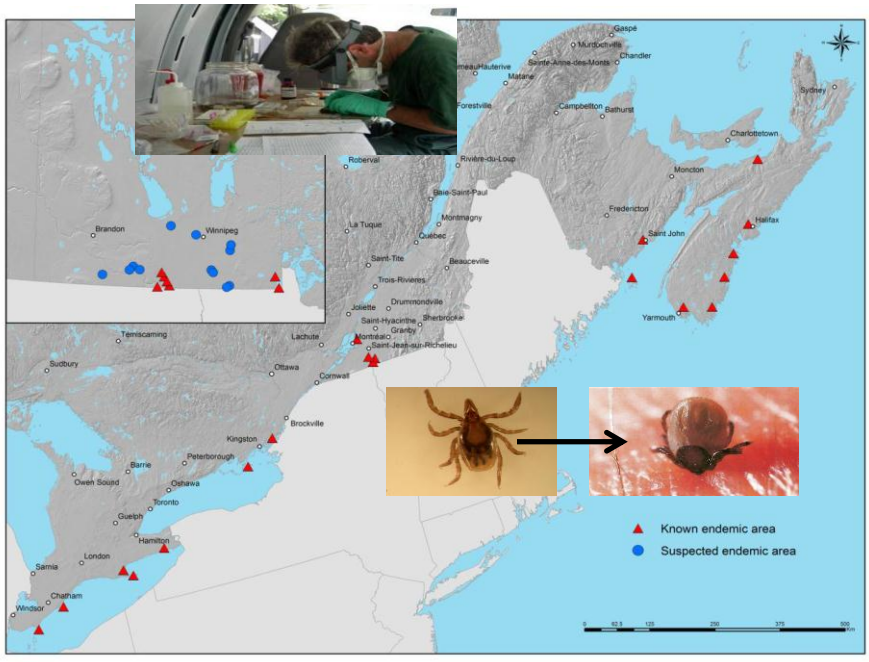
Confirmed 3151 (not available)
Probable 1879 (not available)
Suspected 5636 (not available)
Total 10 666 (4806)

Results of Active Tick Surveillance 2008-2012

Ogden N. et al
Environmental Risk from Lyme Disease in central and eastern Canada: a summary of recent surveillance information.
CCDR 2014;40:58-67

Public Health Agency of Canada | Agence de la santé publique du Canada

Known and suspected Lyme-disease endemic locations



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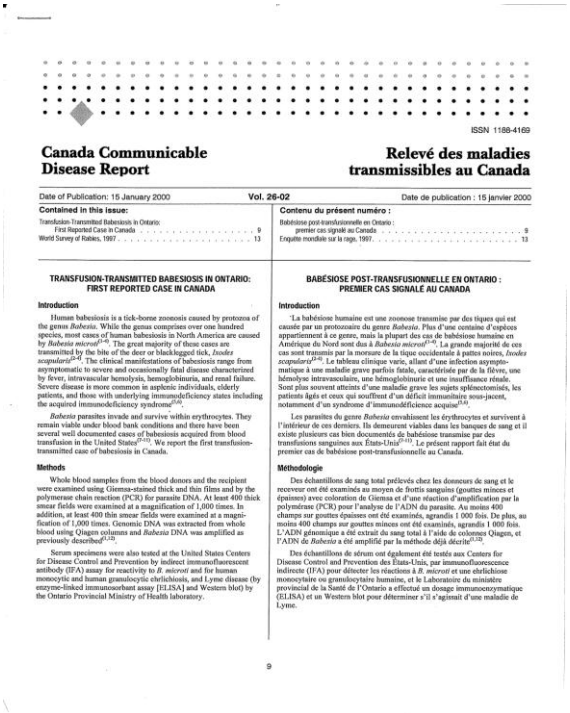


ISSN 1188-4169

Canada Communicable Disease Report

Relevé des maladies transmissibles au Canada

Date of Publication: 15 January 2000 | Vol. 26-02 | Date de publication : 15 janvier 2000

Contained in this issue:

Contenu du présent numéro :

TRANSFUSION-TRANSMITTED BABESIOSIS IN ONTARIO: FIRST REPORTED CASE IN CANADA

Introduction

Human babesiosis is a tick-borne zoonosis caused by protozoa of the genus *Babesia*. While the genus comprises over one hundred species, most cases of human babesiosis in North America are caused by *Babesia microti*[1-3]. The great majority of these cases are transmitted by the bite of the deer or blacklegged tick, *Ixodes scapularis*[2-4]. The clinical manifestations of babesiosis range from asymptomatic to severe and occasionally fatal disease characterized by fever, intravascular hemolysis, hemoglobinuria, and renal failure. Severe disease is more common in asplenic individuals, elderly patients, and those with underlying immunodeficiency states including the acquired immunodeficiency syndrome[2,5].

Babesia parasites invade and survive within erythrocytes. They remain viable under blood bank conditions and there have been several well documented cases of babesiosis acquired from blood transfusion in the United States[2,6-11]. We report the first transfusion-transmitted case of babesiosis in Canada.

Methods

Whole blood samples from the blood donors and the recipient were examined using Giemsa-stained thick and thin films and by the polymerase chain reaction (PCR) for parasite DNA. At least 400 thick smear fields were examined at a magnification of 1,000 times. In addition, at least 400 thin smear fields were examined at a magnification of 1,000 times. Genomic DNA was extracted from whole blood using Qiagen columns and *Babesia* DNA was amplified as previously described[9,12].

Serum specimens were also tested at the United States Centers for Disease Control and Prevention by indirect immunofluorescent antibody (IFA) assay for reactivity to *B. microti* and for human monocytic and human granulocytic ehrlichiosis, and Lyme disease (by enzyme-linked immunosorbant assay [ELISA] and Western blot) by the Ontario Provincial Ministry of Health laboratory.

BABÉSIOSE POST-TRANSFUSIONNELLE EN ONTARIO : PREMIER CAS SIGNALÉ AU CANADA

Introduction

La babésiose humaine est une zoonose transmise par des tiques qui est causée par un protozoaire du genre *Babesia*. Plus d'une centaine d'espèces appartiennent à ce genre, mais la plupart des cas de babésiose humaine en Amérique du Nord sont dus à *Babesia microti*[1-3]. La grande majorité de ces cas sont transmis par la morsure de la tique occidentale à pattes noires, *Ixodes scapularis*[2-4]. Le tableau clinique varie, allant d'une infection asymptomatique à une maladie grave parfois fatale, caractérisée par de la fièvre, une hémolyse intravasculaire, une hémoglobinurie et une insuffisance rénale. Sont plus souvent atteints d'une maladie grave les sujets splénectomisés, les patients âgés et ceux qui souffrent d'un déficit immunitaire sous-jacent, notamment d'un syndrome d'immunodéficience acquise[2,5].

Les parasites du genre *Babesia* envahissent les érythrocytes et survivent à l'intérieur de ces derniers. Ils demeurent viables dans les banques de sang et il existe plusieurs cas bien documentés de babésiose transmise par des transfusions sanguines aux États-Unis[2,6-11]. Le présent rapport fait état du premier cas de babésiose post-transfusionnelle au Canada.

Méthodologie

Des échantillons de sang total prélevés chez les donneurs de sang et le receveur ont été examinés au moyen de frottis sanguins (gouttes minces et épaisses) avec coloration de Giemsa et d'une réaction d'amplification par la polymérase (PCR) pour l'analyse de l'ADN du parasite. Au moins 400 champs sur gouttes épaisses ont été examinés, agrandis 1 000 fois. De plus, au moins 400 champs sur gouttes minces ont été examinés, agrandis 1 000 fois. L'ADN génomique a été extrait du sang total à l'aide de colonnes Qiagen, et l'ADN de *Babesia* a été amplifié par la méthode déjà décrite[9,12].

Des échantillons de sérum ont également été testés aux Centers for Disease Control and Prevention des États-Unis, par immunofluorescence indirecte (IFA) pour détecter les réactions à *B. microti* et une ehrlichiose monocytaire ou granulocytaire humaine, et le Laboratoire du ministère provincial de la Santé de l'Ontario a effectué un dosage immunoenzymatique (ELISA) et un Western blot pour déterminer s'il s'agissait d'une maladie de Lyme.

CASE REPORT

The first case of locally acquired tick-borne *Babesia microti* infection in Canada

Jared MP Bullard MD FRCPC[1,2,3], Arshad N Ahsanuddin MD[4], Anamarija M Perry MD[4], L Robbin Lindsay PhD[2,3], Mahmood Iranpour PhD[3], Antonia Dibernardo BSc[3], Paul G Van Caeseele MD FRCPC[1,2,3]

JMP Bullard, AN Ahsanuddin, AM Perry, et al. The first case of locally acquired tick-borne *Babesia microti* infection in Canada. Can J Infect Dis Med Microbiol 2014;25(6):e87-e89.

A child with a complicated medical history that included asplenia acquired an infection with *Babesia microti* in the summer of 2013 and had not travelled outside of Manitoba. Although the clinical findings were subtle, astute laboratory work helped to reach a preliminary identification of *Babesia* species, while reference laboratory testing confirmed the diagnosis. Blacklegged ticks (*Ixodes scapularis*) are known to transmit *Borrelia burgdorferi* and *Anaplasma phagocytophilum* in the province; however, the present case represents the first known instance of tick-borne *B microti*, both in Manitoba and in Canada. The expanding territory of the blacklegged tick increases the relevance of this emerging infection. Clinicians, laboratory medical practitioners and public health officials should be aware of *B microti* as a potential locally acquired infection in Canada.

Key Words: Babesia microti; *Babesiosis; Blacklegged ticks; Canada; Emerging infection; Local acquisition*

Le premier cas d'infection à *Babesia microti* transmis par une tique à être contracté au Canada

Un enfant ayant des antécédents médicaux complexes, qui incluaient une asplénie, a contracté une infection à *Babesia microti* pendant l'été 2013, sans avoir quitté le Manitoba. Même si les résultats cliniques étaient discrets, un travail de laboratoire astucieux a contribué à l'identification préliminaire d'une espèce de *Babesia*. Le test du laboratoire de référence a confirmé le diagnostic. On sait que les tiques occidentales à pattes noires (*Ixodes scapularis*) transmettent le *Borrelia burgdorferi* et l'*Anaplasma phagocytophilum* dans la province. Le présent cas est toutefois la première occurrence connue de *B microti* à tique, tant au Manitoba qu'au Canada. L'expansion du territoire de la tique occidentale à pattes noires renforce la pertinence de cette infection émergente. Les cliniciens, les praticiens de laboratoires médicaux et les directeurs de la santé publique devraient savoir que le *B microti* peut être transmis localement au Canada.

CASE PRESENTATION

A seven-year-old boy presented to the emergency department at the Winnipeg Children's Hospital (Winnipeg, Manitoba) on August 7, 2013, with a five-day history of fever (up to 39.5°C) and a headache. He also complained of mild anorexia and malaise. He experienced no other meningeal or respiratory tract symptoms and there was no nausea, vomiting or diarrhea. His urine output was maintained, although urine was darker than normal. He did not complain of arthralgias, arthritis or myalgias. No rash, jaundice or icterus had been noted by his parents. His medical history consisted of multiple congenital anomalies related to a midline defect syndrome that had not been formally diagnosed. These consisted of hydrocephalus treated with a ventriculoperitoneal shunt; panhypopituitarism; partially corrected tetrology of Fallot and dextrocardia; and asplenia secondary to mid-gut malrotation, which was surgically corrected at two weeks of age. The patient had travelled with his relatives to the southeast corner of Manitoba to stay at a cabin four weeks before the onset of symptoms. He did not recall specific tick bites but had numerous mosquito bites during the 48 h he was there. He did not report any other animal exposures. The patient had received blood transfusions for his surgeries during his first month of life, but not after.

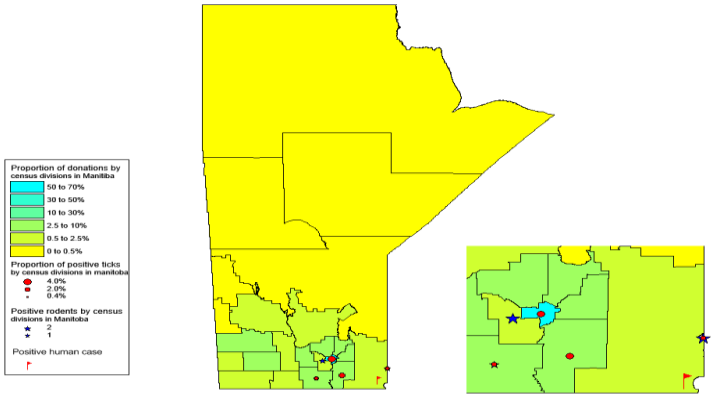
Screening blood tests, including electrolyte, urea and creatinine levels, were all within normal limits. His white blood cell count, hemoglobin and platelet levels were also normal. A manual slide review was performed due to abnormalities consistent with his asplenia, and a parasite believed to represent *Plasmodium falciparum* was noted. Blood smears were produced using the remaining blood sample. Numerous ring-form trophozoite parasites were observed within erythrocytes, and a lack of pigment and occasional tetrads/Maltese cross formations were noted (Figure 1). Based on these findings, and a lack of a significant travel history, identification was deemed to be consistent with *Babesia* species.

Twenty-four hours after initial evaluation, the patient was notified to return to the emergency department and the Pediatric Infectious Diseases Service was consulted. At this point, the patient was asymptomatic and the parasitemia level was determined to be 1%. He was diagnosed with mild babesiosis and prescribed a six-week course of atovaquone and azithromycin. Serology testing for *Borrelia burgdorferi* was ordered and found to be negative. Follow-up bloodwork was performed one week into his treatment course. At that time, the patient continued to have headache and intermittent, nonspecific abdominal pain. A mild anemia and slightly increased transaminase levels and bilirubin were noted. A blood specimen was collected and sent to the National Microbiology Laboratory for confirmation of *Babesia microti* infection, and to rule out infection with *B burgdorferi* and/or *Anaplasma phagocytophilum*. While polymerase chain reaction (PCR) was negative for the latter two organisms, real-time PCR was performed using primers that target the chaperonin-containing t-complex rtx (CCTη) (1) and subsequently confirmed using a second real-time PCR assay targeting the 18S ribosomal RNA gene (in-house/Applied Biosystems,

[1]*Cadham Provincial Laboratory, Manitoba Health;* [2]*Department of Medical Microbiology;* [3]*Department of Paediatrics and Child Health;* [4]*Department of Pathology, University of Manitoba;* [5]*Zoonotic Diseases and Special Pathogens, National Microbiology Laboratory, Winnipeg, Manitoba*

Correspondence: Dr Jared Bullard, 750 William Avenue, Winnipeg, Manitoba R3C 3Y1. Telephone 204-945-1306, fax 204-786-4770, e-mail jared.bullard@gov.mb.ca

Map of Manitoba showing active surveillance data of the percentage of *Babesia microti* positive ticks, the number of positive rodents and the 2013 human case overlaying the percentage of donations by census division.*



*Seroprevalence of *Babesia microti* infection in Canadian blood donors. O'Brien S.,Delage G.,Scalia V.,Lindsay R., Bernier F.,Dubuc S.,Germain M.,Pilot G.,Yi Q-L.,Fearon M. (submitted to Transfusion 2015/07)

Results : CBS and Héma Quebec Seroprevalence Study
Babesia microti IgG Antibody

Samples tested (n= 13,993) from July 15, 2013 – Dec. 11, 2013

No. Tested	Clinic	Babesia microti IgG Ab. Test Result	
		Negative	Positive
158	Toronto	158	0
6364	South Central Ontario	6364	0
1765	N.S./N.B.	1765	0
1775	Winnipeg	1775	0
3931	Hema Quebec	3931	0
TOTAL		13,993	0

HÉMA-QUÉBEC

Canadian Blood Services
Société canadienne du sang

Results : CBS and Héma Quebec Seroprevalence Study
Hepatitis E Antibody

Table 1: Anti-HEV Data (n = 4110)

No. Tested	Collection Site	Anti-HEV Result		Seroprevalence rate (%)
		NEG	POS	
1469	South Central Ontario	1383	86	5.85
333	N.S./N.B.	327	6	1.80
356	Winnipeg	338	18	5.06
1952	Quebec	1821	131	6.71
TOTAL		3869	241	5.86

PCR Results: Of **13,993** donors tested there were **0 PCR positives**

HÉMA-QUÉBEC

Canadian Blood Services
Société canadienne du sang

Results: CBS and Hema Quebec Seroprevalence Study

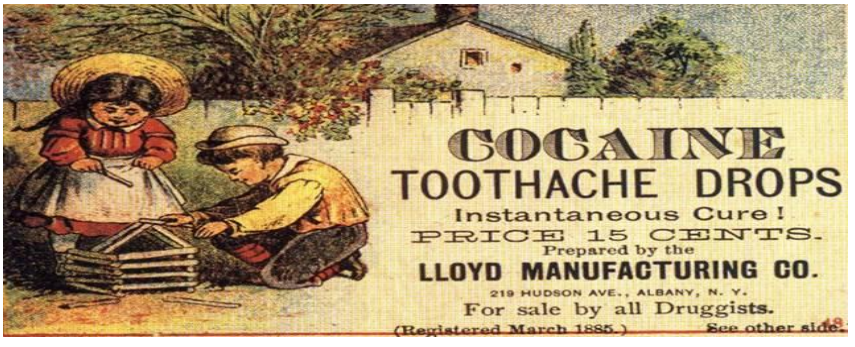
Odds ratios of positive results for antibody to hepatitis E virus by demographic variables

Estimated odds ratios of HEV antibody positive test results, by sex and age, from subset of Babesiosis Testing Study (n=2,150) and Héma-Québec data (n=1,952)

	n Positive	n Negative	% Positive	Odds Ratio	95% Confidence Intervals
Female	95	1,791	5.04	1.00	
Male	146	2,070	6.59	1.33	(1.02 - 1.74)
Under 30	15	921	1.60	1.00	
30-39	10	524	1.87	1.17	(0.52 - 2.63)
40-49	30	727	3.96	2.53	(1.35 - 4.75)
50+	186	1,689	9.92	6.76	(3.97 - 11.51)

HÉMA-QUÉBEC

Canadian Blood Services
Société canadienne du sang



CBS Donor Travel Survey 2014

Table 5 - Weighted percentages of travel destinations of all whole blood donors in the survey sample, and the projected number of donors in the donor population with travel outside Canada in the past 12 months

	All respondents (n=8,908)	CBS Donors (N=415,829)	
	% of sample	Projected Number Donors	95% C.I.
Travel destinations			
United States	48.0	199,628	(195,314 - 203,942)
Mexico	7.1	29,530	(27,312 - 31,748)
Caribbean	9.3	38,852	(36,339 - 41,365)
South America	0.7	3,035	(2,300 - 3,770)
Central America	0.5	1,984	(1,389 - 2,579)
Europe	9.8	40,625	(38,061 - 43,189)
Middle East	0.6	2,689	(1,997 - 3,381)
Africa	0.4	1,468	(956 - 1,980)
Asia	2.1	8,527	(7,303 - 9,751)
Australia / New Zealand / South Pacific	1.0	4,238	(3,371 - 5,106)

Note: A donor could select more than one travel destination.

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CBS Donor Travel Survey 2014

Table 8 - Weighted percentages and projected number of whole blood donors who would return to donate 14 or 28 days post-travel by various travel destination scenarios

	All respondents (n=8,908)	CBS Donors (N=415,829)	
	% of sample	Projected Number Donors	95% C.I.
Caribbean travel			
Return to donate within 14 days	0.5	1,984	(1,403 - 2,566)
Return to donate within 28 days	1.6	6,545	(5,557 - 7,533)
Travel outside of Canada and US			
Return to donate within 14 days	1.9	7,930	(6,781 - 9,079)
Return to donate within 28 days	5.9	24,368	(22,520 - 26,216)
Travel to AZ, CA, FL, HI, or outside of Canada and US			
Return to donate within 14 days	3.0	12,562	(11,117 - 14,007)
Return to donate within 28 days	9.1	37,967	(35,665 - 40,270)

Based on weighted percentages of travel and self-reported duration until returning to donate in the 2014 Travel Survey and projected number of donors based on number of donors in 2013

Travel outside of Canada and US included all travel destinations whether tropical or not

Estimate Risk of Transfusion Transmission of Chikungunya in Canada

- Risk Based on Cases in the Caribbean (PAHO data):

  1 in 8,659,932 donations (1 in 15,172,895 – 1 in 6,060,606)

- Risk Based on Imported Cases from the Caribbean (Laboratory Testing Data):

  1 in 11,803,847 donations (1 in 27,935,302 – 1 in 7,462,687)

ALLIANCE OF BLOOD OPERATORS'

Risk-Based Decision-Making Framework for Blood Safety

Changing the Decision-Making Paradigm

Sponsored by the ABO, a team of experts gathered to map out a strategy to change the decision-making paradigm.

A health sector focus

A consistent, standardised approach to decision-making

Evidence-based decisions using risk assessment tools

Acceptable risk based on societal considerations

Multiple sectors included in the decision-making process

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The RBDM Framework

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If you think preparedness is expensive, try disease.

Mary Daschler (paraphrased)

Canadian Blood Services

it's in you to give