The blood supply: How we prevent acute and delayed transfusion transmitted infections

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Transfusion Camp
2021-11-19

Canadian Blood Services
BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES

Acknowledgment of Traditional Territory

The University of Alberta respectfully acknowledges that we are located on Treaty 6 territory, a traditional gathering place for diverse Indigenous peoples including the Cree, Blackfoot, Métis, Nakota Sioux, Iroquois, Dene, Ojibway/ Saulteaux/Anishinaabe, Inuit, and many others whose histories, languages, and cultures continue to influence our vibrant community.

Survey

In your opinion, which process is key in protecting the blood supply?

A. Donor health and risk screening
B. Transmissible diseases testing
C. Quality processes during production
D. Vigilance activities
E. Surveillance and engagement with public health and infectious diseases experts
F. A multifactorial approach utilizing more than one of A-E
G. Something else

Key points to impress on you about transmissible diseases risks in Canada

- Because of the way blood products are produced (including 7 day platelets) the **highest transfusion-transmitted infectious disease risk is bacterial sepsis from platelets**
- With donor selection and testing, the **risk for transfusion transmission of important blood-borne viruses** including Human immunodeficiency virus, hepatitis B virus, Hepatitis C virus, Human T-lymphotropic virus, and West Nile virus) **is extremely low**
- Donor deferrals play an important role in limiting transfusion-transmission risks when no blood screening test is done
- A variety of processes are utilized to track and respond to infectious diseases threats- then develop risk assessments

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Background

Canada- geographically “big”, ethno-socially-culturally diverse and always changing

This is Canada in the Winter

This is Canada in the Winter

A blood operator needs to be vigilant across a multifactorial risk environment

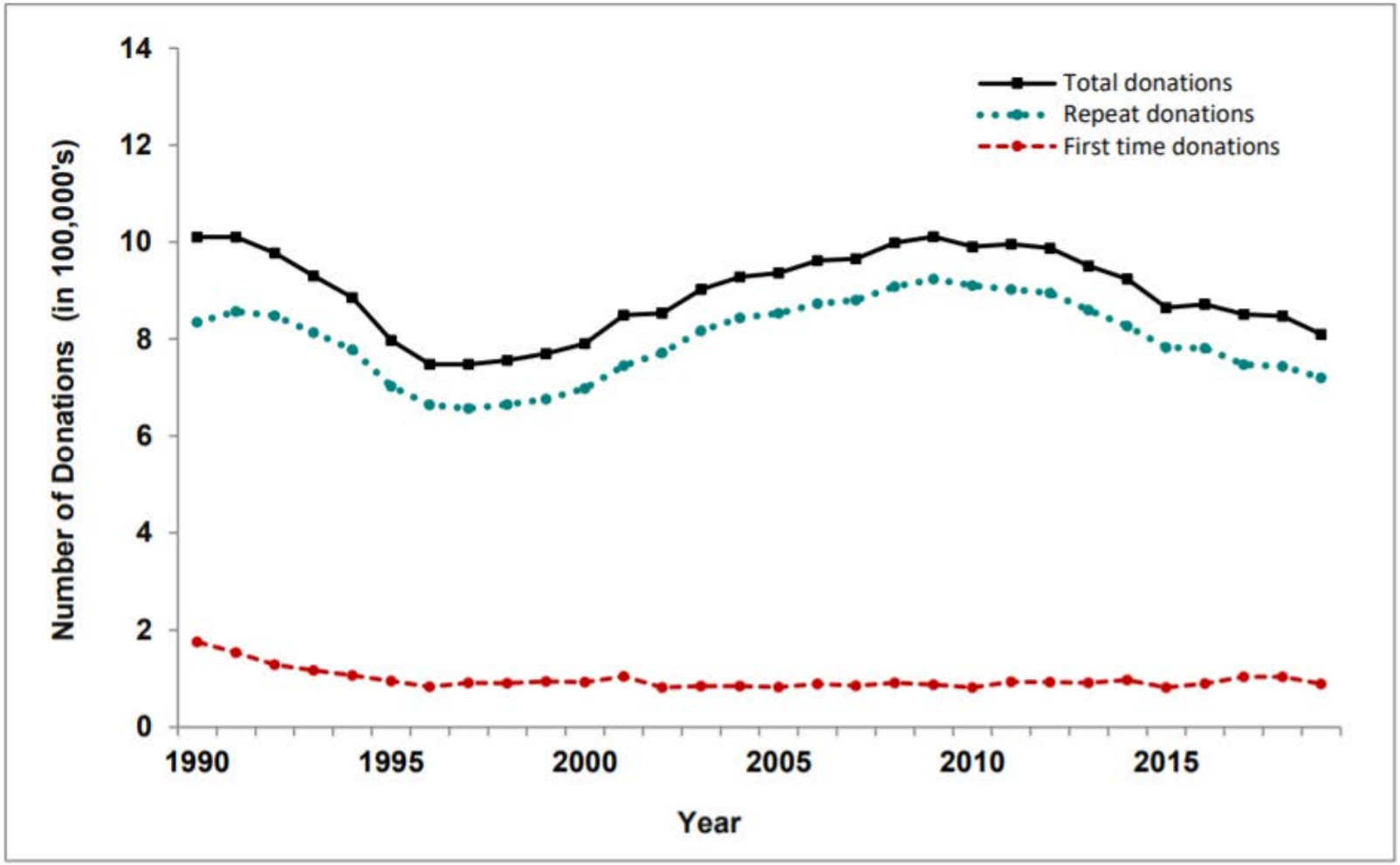
Blood collections at Canadian Blood Services

- Approximately 850,000 donations per year from about 400,000 donors (of which 80,000 are first-time donors)
- Aged 17 and older From all provinces except Quebec
- From all major cities and most smaller cities and surrounding areas- most of these are in the “South”

5514 km, 3426 miles

42°N to 83°N **53°W to 141°W**

Most Canadian blood donors are repeat donors



https://professionaleducation.blood.ca/sites/msi/files/surveillance_report_2019_en.pdf

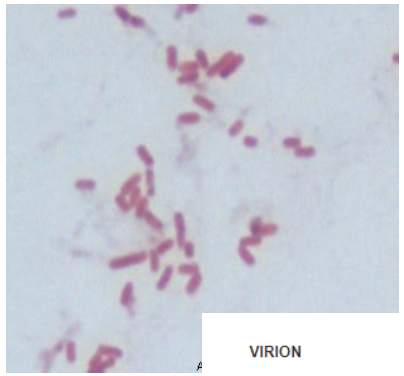
Transfusion transmitted infections

Transfusion transmitted infections

Bacterial sepsis- Acute

➢Presents acutely (with fever) during or up to 4 hours post transfusion

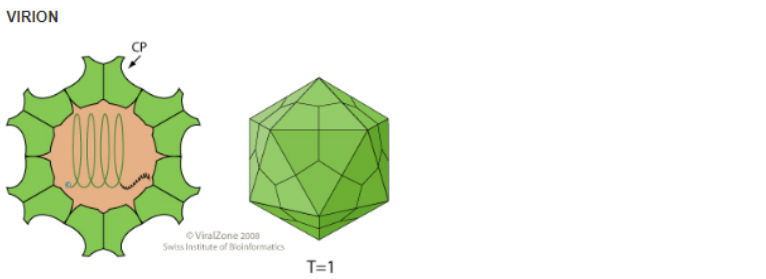
➢Platelets the most common source (stored at room temperature to preserve function)



Viral or parasitic infection – Delayed

➢Presents (with specific symptoms) weeks to months post transfusion

➢RBCs, platelets, plasma, cryoprecipitate can be the source



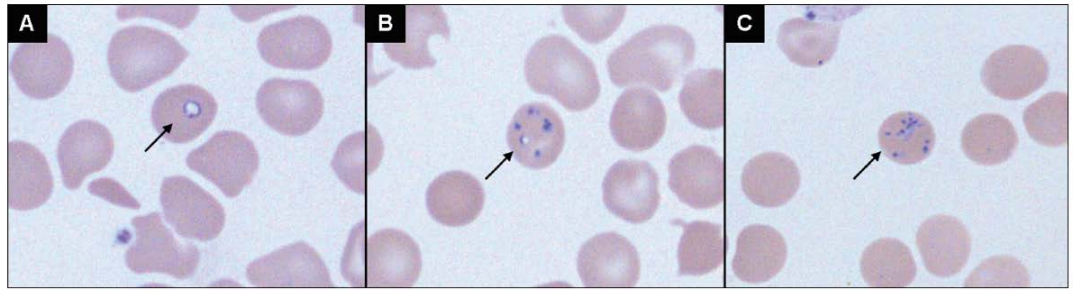


Figure 1) Babesia *species in a thin blood smear stained with Giemsa (oil, original magnification ×1000). Vacuolated intraerythrocytic form* **(A)**, *multiple forms within erythrocyte* **(B)** *and tetrads* **(C)** *are indicated*

https://viralzone.expasy.org/714

https://www.cdc.gov/parasites/babesiosis/diagnosis.html

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.

Non-bacterial transfusion transmitted infections causing delayed symptom onset- weeks to months after infection

Viruses

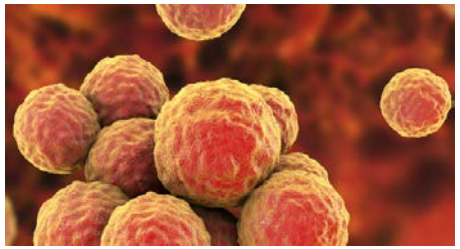
- Human immunodeficiency virus 1/2
- Hepatitis B virus
- Hepatitis C virus
- Human T lymphotropic virus
- West Nile virus
- Cytomegalovirus
- Hepatitis E virus
- Dengue virus
- Zika virus

Parasites

- *Babesia species*
- *Plasmodium falciparum* (Malaria)
- *Trypanosoma cruzi* (Chagas Disease)

Not all infection risks are equivalent

Symptomatic bacterial sepsis: platelets 1/10,000

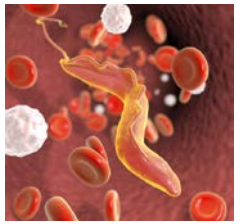


Death- bacterial sepsis: platelet 1/200,000

Death- bacterial sepsis: RBCs 1/500,000

Transmission of **West Nile virus <1/1,000,000**

Transmission of Chagas per unit component 1/4,000,000



Transmission of HBV 1/7,5,000,000

Transmission of **HTLV 1/7,600,000**

Transmission of **HCV 1/13,000,000**

Transmission of **HIV 1/21,000,000**

Rates of infections diseases positivity in donor are very low (2019)

Characteristic	Number of Donations	Percent of Donations	HIV		HCV		HBV		HTLV		Syphilis	
			Pos	Rate	Pos	Rate	Pos	Rate	Pos	Rate	Pos	Rate
Donor status												
First time	88,596	11.1	2	2.3	43	48.5	60	67.7	5	5.6	20	22.6
Repeat	712,685	88.9	2	0.3	2	0.3	8	1.1	2	0.3	13	1.8
Total	**801,281**	**100**	**4**	**0.5**	**45**	**5.6**	**68**	**8.5**	**7**	**0.9**	**33**	**4.1**

General pop: HIV (6/100,000; 2018), HCV (33.6/100,000; 2018); HBV acute (0.52/100,000; 2018), HBV chronic (10.6/100,000), Infectious syphilis (11.2/100,000; 2017)

https://professionaleducation.blood.ca/sites/msi/files/surveillance_report_2019_en.pdf
https://www.canada.ca/en/public-health/services/publications/diseases-conditions/summary-estimates-hiv-incidence-prevalence-canadas-progress-90-90-90.html
https://www.canada.ca/en/public-health/services/publications/diseases-conditions/report-hepatitis-b-c-canada-2018.html
https://www.canada.ca/en/public-health/services/diseases/hepatitis-c/surveillance-hepatitis-c.html
https://www.canada.ca/en/services/health/publications/diseases-conditions/syphilis-epidemiological-report.html

Blood safety for reducing risk for transfusion-transmitted diseases multiple approaches

How do we ensure blood safety?

Donor engagement and trust
Record of Donation
Donor selection criteria

Surveillance, donor studies and Risk assessments
Planned donor surveillance
Case studies
Risk assessments and risk-based decision making

Plan Do Study Act

Good processes
Standardization
Training
Documentation
Traceability
Donor arm prep.

Laboratory testing
HIV
HBV
HCV
HTLV
Syphilis
West Nile
Chagas
CMV
Bacterial detection (platelets)

Vigilance
Information gathering
Literature searches
Grey-literature monitoring
Peer engagement
Matrix developments

Donor screening reduces risk prior to laboratory testing for transfusion-transmissible diseases

Donor questionnaire for blood, platelets and plasma

Donor health assessment questionnaire – completed on line, 24 hours pre-donation, or in clinic.

Donor asked about their

- Health
- Medication
- Travel
- Lifestyle

Wellness

The following questions ask about your wellness today.

1. Are you feeling well today?
2. Do you have a _____?
   - flu
   - sore throat
   - fever
   - infection

Drugs, vaccines

The following questions ask about medications and shots you may have taken.

1. In the last 3 days have you taken medication, including Aspirin?(vitamins and birth control are excluded)
2. In the last month have you taken any of the following medications? (Click for more info)
   - Accutane
   - Epuris
   - Clarus
   - Isotretinoin
   - Toctino
   - Henzeme
   - Alitretinoin
   - Proscar
   - Propecia
   - Finasteride
3. In the last 3 months have you had a vaccination?
4. In the last 4 months have you taken any medication to prevent HIV infection such as pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP)?
5. In the last 6 months have you taken any of the following medications?
   - Avodart
   - Jalyn
   - Dutasteride
6. In the last 12 months have you had a rabies shot or a shot for exposure to hepatitis B?
7. Have you ever taken any of the following medications?
   - Tegison
   - Soriatane
   - Human pituitary growth hormone

General Medical

The following questions are about your medical history

1. Do you have diabetes?
2. In the last 3 days have you had dental work?
3. In the last 14 days have you been exposed to someone with suspected or confirmed COVID-19?
4. In the last 28 days have you had COVID-19?
5. In the last 6 months have you consulted a doctor for a health problem, had surgery or medical treatment?
6. In the last 6 months have you been pregnant? (female donors)
7. In the last 6 months have you had hepatitis?
8. In the last 6 months have you received blood or blood products?
9. In the last 12 months have you had a graft?
10. In the last 12 months have you had close contact with a person who has had hepatitis or yellow jaundice?
11. Since 1980, did you receive a blood transfusion or blood product in the United Kingdom, France or elsewhere in Europe?
12. Have you ever had malaria?
13. Have you ever been pregnant, miscarried or had an abortion? (female plasma/platelet donors)
14. Have you ever had a positive test for the HIV/AIDS virus?
15. Have you ever had epilepsy or fainting?
16. Have you ever had a coma or stroke?
17. Have you ever had problems with your heart or lungs?

https://www.blood.ca/en/blood/donating-blood/donor-questionnaire

Donor education about infectious diseases risks

- Donors are asked to read a pamphlet

➢What you must know to give blood)

➢Explaining the donation process

➢Testing that will be done on their blood and the obligatory provincial requirements for reporting certain test results to public health authorities

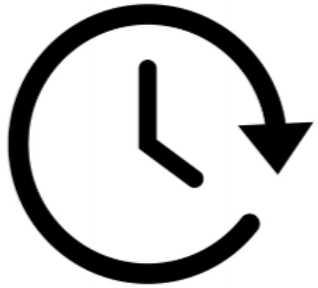
- The pamphlet also explains

➢the transfusion-transmission risk factors for human immunodeficiency virus (HIV) and hepatitis

➢informs donors that testing may fail to identify individuals who are in the early stages of infection

Deferrals

or



- Depending on the magnitude of the risk, donors may be deferred temporarily or indefinitely.
- For example

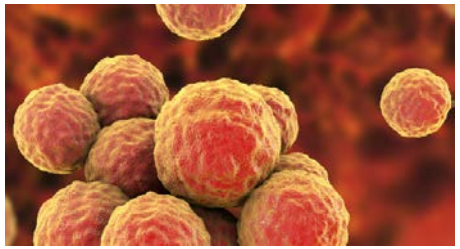
➢ people who have taken illegal drugs by injection are indefinitely deferred

➢ travelers to a region outside Canada, Continental U.S. and Western Europe are deferred for 21 days for Zika virus risk.

Laboratory testing to reduce risks of acute transfusion transmitted infections due to bacterial contamination of platelet units

Not all infection risks are equivalent

Symptomatic bacterial sepsis: platelets 1/10,000



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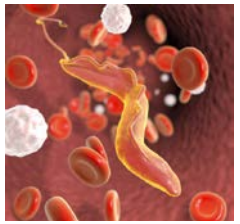

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Platelet bacterial testing

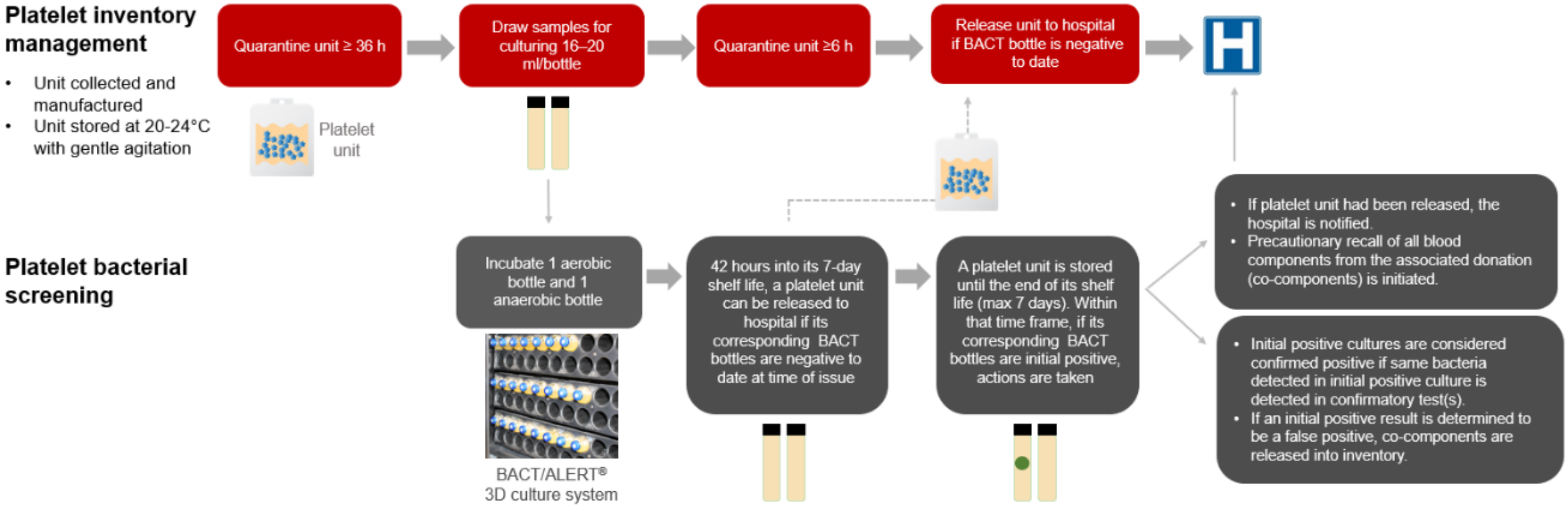


Figure 1: Platelet bacterial testing at Canadian Blood Services.

Canadian Blood Services BLOOD PLASMA STEM CELLS ORGANS & TISSUES

https://professionaleducation.blood.ca/en/transfusion/publications/faq-canadian-blood-services-platelet-bacterial-testing

Once an initial positive bacterial culture is identified, what steps are undertaken by Canadian Blood Services?

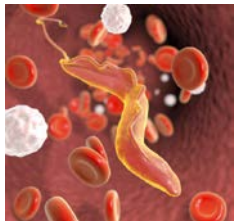
- Following an initial positive bacterial culture, Canadian Blood Services conducts additional testing of the positive platelet culture and of the original component and companion components (if applicable/ available).
- The testing is performed at a Canadian Blood Services laboratory.
- The timeline for this additional testing by Canadian Blood Services may extend to several weeks after the product recall.
- *Although additional testing results are not intended for patient clinical management, Canadian Blood Services will report results of follow-up Gram stain and bacterial identification to hospitals as soon as available for all associated transfused components.*

Laboratory testing to reduce risks of transfusion transmitted infections due to viruses, Chagas and Syphilis

Relative risks for transmissible diseases in transfusion: very rare

Transmission of **West Nile virus <1/1,000,000**

Transmission of Chagas per unit component 1/4,000,000



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Transmission of **HTLV 1/7,600,000**

Transmission of **HCV 1/13,000,000**

Transmission of **HIV 1/21,000,000**

Infectious marker testing for all donations at CBS

Agent	Assay	Window Period (days)
HIV	anti-HIV-1/2 HIV-1 p24 HIV-1/2 NAT	8
HCV	anti-HCV HCV NAT	4.1
HBV	HBsAg anti-HBc HBV NAT	22.4
HTLV	anti-HTLV I/II	51
Syphilis	Antibody	na

- serological tests are performed on individual donor samples, duplicate repeat runs on positives
- NAT is performed on pools of 6 samples from with resolution of reactive pools down to individual specimen
- all screening tests done prior to product release

Other testing
West Nile NAT: Mosquito season and non-mosquito season travellers
Chagas serology: At risk donors
Cytomegalovirus serology: Intrauterine transfusion

na = not available

O'Brien SF
Transfusion Apheresis Science
2017;56(3):389

Implications of a repeat reactive screen tests

- Don’t wait for confirmation
- If one of these two serology repeats is reactive, or the NAT repeats from the individual test

➢ the donation is discarded

➢ additional testing is performed to determine the true status of the donor for donor notification and counselling and for donor reentry purposes

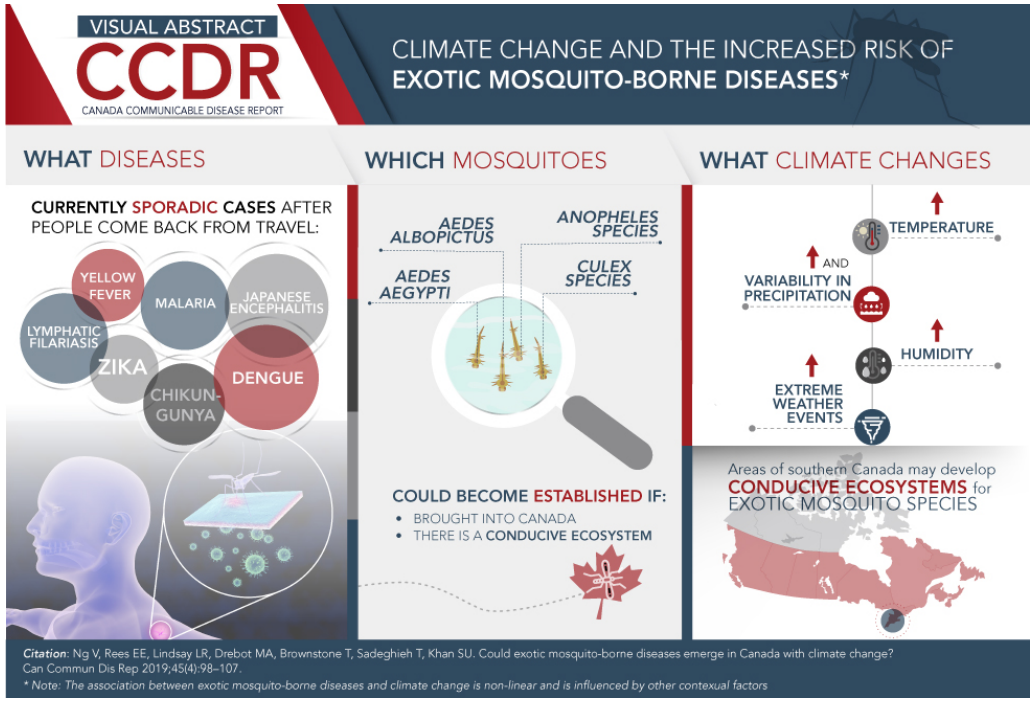
➢ Depending on the viral marker, inventory retrieval of blood products from previous donations and notification of the hospitals that received blood products from previous donations (lookback process) may be performed.

Poll question: CBS tests all donations for which pathogens?

A. HIV, HBV, HCV, syphilis, CMV
B. HIV, HBV, HCV, Chagas antibody
C. HIV, HBV, HCV
D. HIV, HBV, HBC, Zika virus

Other non-tested agents and the infectious diseases matrix

Emerging pathogens are tracked by Canadian Blood Services




WINDSOR | News

Invasive mosquito identified in Windsor: WECHU

CTV Windsor
Published Monday, June 28, 2021 4:25PM EDT
Last Updated Monday, June 28, 2021 4:27PM EDT

This 2003 photo provided by the Centers for Disease Control and Prevention shows a female Aedes albopictus mosquito acquiring a blood meal from a human host. (James Gathany/Centers for Disease Control and Prevention via AP)

In 2021, *Aedes albopictus* was trapped within city limits of Windsor Ontario

Windsor, ON, Canada Lat Long Coordinates Info.

Country	Canada
Latitude	42.317432
Longitude	-83.026772
DMS Lat	42° 19' 2.7552" N
DMS Long	83° 1' 36.3792" W

Crescent City California, USA
41.7558° N, 124.2026° W

https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2019-45/issue-4-april-4-2019/article-4-exotic-mosquito-borne-diseases-climate-change.html

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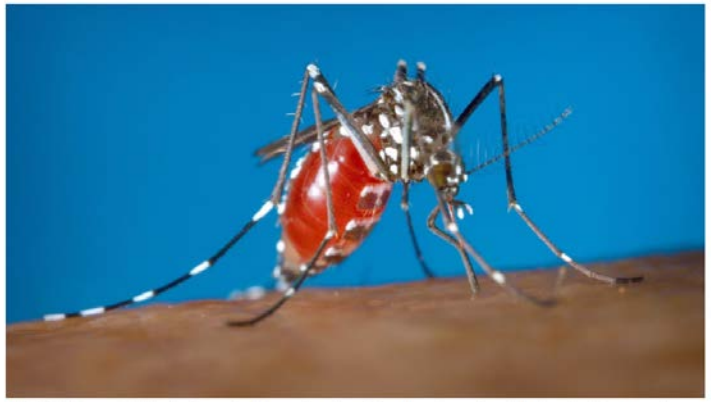


This 2003 photo provided by the Centers for Disease Control and Prevention shows a female Aedes albopictus mosquito acquiring a blood meal from a human host. (James Gathany/Centers for Disease Control and Prevention via AP)

- *Ae. albopictus* can support the transmission of epidemic arboviruses (e.g., chikungunya, dengue, and Zika viruses) and zoonotic arboviruses
- Experimental vector competence studies and viral genome detection or isolation in nature indicated that *Ae. albopictus* can transmit several enzootic arboviruses (e.g., La Crosse Virus, West Nile Virus, Eastern equine encephalomyelitis, Cache Valley Virus, Keystone Virus, Potosi Virus, Tensaw Virus, Chandipura, Jamestown Canyon, Orungo, Rift Valley, Ross River, Oropuche virus, Mayaro virus, and yellow fever virus (YFV)

https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2019-45/issue-4-april-4-2019/article-4-exotic-mosquito-borne-diseases-climate-change.html

Poll question: If you saw this news article what would you do?

A. Search the peer reviewed literature
B. Do other online searches and search the ”non-peer reviewed literature”
C. Talk to a local expert
D. Talk to a national expert
E. Start documenting what you see
F. A combination of A-E
G. Something else

The infectious diseases matrix

- Canadian Blood Services maintains an infectious disease matrix which is constantly updated and analysed regularly (daily for specific pathogens) as new information becomes available from a variety of sources:

➢ peer-reviewed publications

➢ non-peer reviewed scientific information

➢ news media

➢ information from scientific meetings and teleconferences

➢ person-to-person discussions with peers.

The press release activated the highlighted activities

What pathogens are currently on the matrix

- *Babesia*
- California serogroup viruses
- Chikungunya virus
- Dengue virus
- Ebola virus
- Hepatitis E virus
- Avian influenza viruses-quick summary
- *Plasmodium* (Malaria)
- SARS-CoV-2
- Variant Creutzfeldt Disease (vCJD)
- Yellow fever virus
- Zika virus

What information is on the infectious disease matrix?

- The matrix includes an extensive list of enveloped mosquito-borne viruses as well as other potential risk agents.
- It details when each agent would be present in blood, possibility of transfusion transmission, if there is documented evidence of donor infection, any consequences of infection, epidemiology, identification of low risk donors, impact of measures on supply and actions other blood providers have taken or are considering.
- The matrix is a living document that is shared with Canadian Blood Services leadership formally on a quarterly basis but is available to anyone at Canadian Blood Services on request.

Mosquito-borne viruses- enveloped

Variable	Zika virus[a]	Yellow fever virus[a]
Agent present in blood	Viremia may range 7-21 days, highest 3-5 days after onset of illness;	High viremia 3-6 days post-infection; lower titers up to 17 days after illness onset
Transfusion transmitted	Only 4 cases reported in Brazil	Likely. Vaccine strain also transmissible
Presence in donors	42/1505 donors positive during outbreak in French Polynesia; 50/12 million tested, confirmed positive donors in U.S. Most travel related	Not documented
Consequences of infection	Fever, rash, conjunctivitis, arthralgias; Causes microcephaly and other neurological defects in fetus	Fever, jaundice. Severe cases with organ failure, hemorrhage. High mortality in these cases.
Vaccine present	No	Yes
Epidemiology	Endemic in Asia, Africa; Outbreak in South America, Caribbean 2015-16; Small number endemic cases Florida, Texas; Outbreak in Americas has waned; No cases since March 2017 in Canada. 2012-12-27 Promed Mail report identified activity in 2018 in Mexico/South America, Caribbean, and India.	Endemic in Asia, Africa, South America; Recent large outbreak continues with a in Brazil. Mass vaccination campaigns being carried out
Diagnostic testing available	Serology, NAT	Serology, NAT
Impact of measures on supply	Impact on donations first year of implementation (approx. 1% donor loss). 21 day travel deferral	None
Other blood suppliers	Universal ID/ NAT in US as of 2016 – mandated by FDA. Currently under review to switch to MP testing, similar to WNV strategy	No donor testing for Yellow Fever

a. No Health Canada-approved donor screening test; b. low risk donors- 21 day travel deferral for outside Canada, continental US, Europe c. Leukodepletion ineffective; d. Pathogen reduction effective .

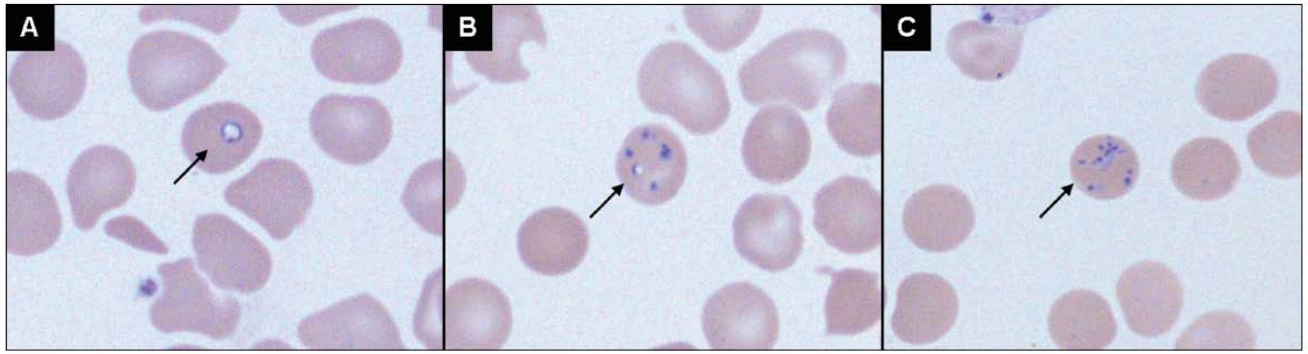
TD surveillance, public health engagements and risk assesement projects at CBS: *Babesia* as an example

Risk assessments and case studies: *Babesia*

- Tonnetti L., et al Prevalence of Babesia in Canadian blood donors: June-October 2018. Transfusion. 2019 Oct;59(10):3171-3176. doi: 10.1111/trf.15470. Epub 2019 Aug 5. PMID: 31385317.
- O'Brien SF et al. Risk of transfusion-transmitted *Babesia microti* in Canada. Transfusion. 2021 Jul 17. doi: 10.1111/trf.16595. Epub ahead of print. PMID: 34272882.
- Drews SJ et al. *Babesia microti* in a Canadian blood donor and lookback in a red blood cell recipient. Vox Sang. 2021 Aug 31. doi: 10.1111/vox.13198. Epub ahead of print. PMID: 34462920.

Babesia microbiology- the causative agent

- Intra-erythrocytic protozoan parasite; although can be visualized outside erythrocyte
- *Babesia microti* (North America and Europe)
- *B. duncani* formerly called WA1 (North America)
- *B. divergens*-like parasites (North America)
- *B. divergens* (Europe)
- Other species globally



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https://www.cdc.gov/parasites/babesiosis/diagnosis.html

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Babesia: What you need to know

- Natural transmission: Black-legged tick- genus *Ixodes*
- **Human-to-human transmission is well recognized to occur via contaminated blood transfusions**
- A 2013 study showed zero *Babesia* positives in donors, but the risk management strategy identified the need to repeat the study again in 5 years time

https://www.cdc.gov/parasites/babesiosis/biology.html

Babesia prevalence in Canada and risks to blood supply

2018 NAT and Serosurvey

- The prevalence of 0.002%-0.007% in our study is slightly less than seroprevalence rates in non-mandated US states of Arizona and Oklahoma, and several logs less than prevalence in mandated states (0.12%-0.75%)

2020 Risk Assessment

- The likelihood of clinically relevant TTB is low.
- In the base scenario 0.5 (0.01, 1.75), *B. microti*-NAT-positive donations would be expected per year, with 0.08 (0, 0.38) recipients suffering clinically significant TTB (1 every 12.5 years).
- Testing would have very little utility in Canada at this time.
- Ongoing pathogen surveillance in tick vectors is important as *B. microti* prevalence appears to be slowly increasing in Canada.

Don’t let your guard down and engage broadly

Received: 14 July 2021 | Revised: 9 August 2021 | Accepted: 9 August 2021
DOI: 10.1111/vox.13198

SHORT REPORT

Vox Sanguinis ISBT International Society of Blood Transfusion

Babesia microti in a Canadian blood donor and lookback in a red blood cell recipient

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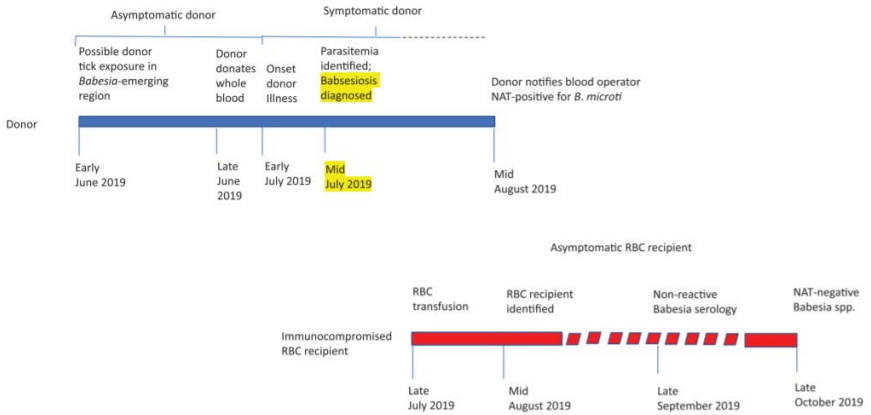


FIGURE 1 Time course for the investigation of a *Babesia microti*–infected blood donor and a recipient of red blood cells (RBCs). Key timings for investigation of the infected donor are in the top half of the figure. Key timings for the investigation of the immunocompromised RBC recipient are in the bottom half of the figure. No transfusion transmission of *B. microti* via donor RBCs was identified in this investigation [Colour figure can be viewed at wileyonlinelibrary.com]

Investigation involved

- Transfusion Medicine experts
- Infectious Diseases experts
- Medical/Clinical Microbiology experts
- Epidemiology experts
- Provincial Laboratory Directors
- Lookback/traceback team
- Canadian Blood Services
- Local and reference pathology laboratory in donor province
- Provincial laboratories in donor and recipient provinces
- Tropical Disease Unit in the Division of Infectious Diseases
  Toronto General Hospital
- National Centre for Parasitology
- National Microbiology Laboratory

No transfusion transmitted babesiosis occurred

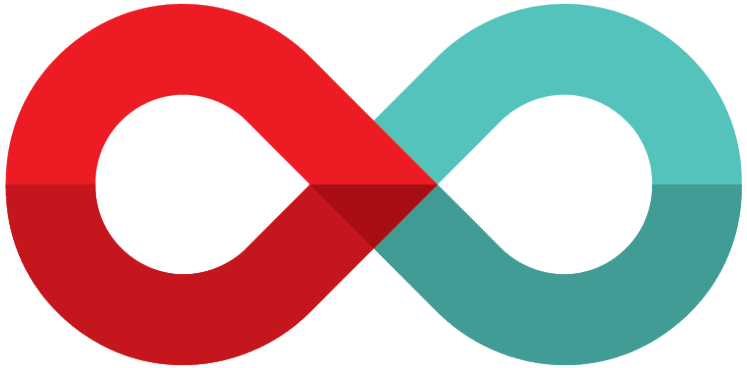
Conclusions and take-away points

Key point to impress on you about transmissible diseases risks in Canada

- Because of the way blood products are produced (including 7 day platelets) the **highest transfusion-transmitted infectious disease risk is bacterial sepsis from platelets**

Conclusions

- With donor selection and testing, the **risk for transfusion transmission of important blood-borne viruses** including Human immunodeficiency virus, hepatitis B virus, Hepatitis C virus, Human T-lymphotropic virus, and West Nile virus) **is extremely low**
- Donor deferrals play an important role in limiting transfusion-transmission risks when no blood screening test is done
- Other proactive surveillance approaches allow for Canadian Blood Services to track infectious diseases activity and make decisions on how best to protect the blood supply



Canadian Blood Services

BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES