# Acute and delayed transfusion transmitted infections

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Transfusion Camp Day 2
August 28, 2020

Canadian Blood Services
BLOOD PLASMA STEM CELLS ORGANS & TISSUES

# Objectives

- You will be able to list the key pathogens of concern to the Canadian blood supply.
- You will be able to explain to a patient the risk of getting HIV or Hepatitis C from a blood transfusion.
- You will have an understanding of how blood suppliers assess and mitigate risk of emerging infectious diseases to the blood supply.

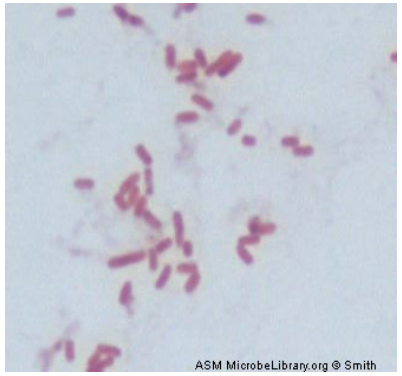
# Key points to impress on you

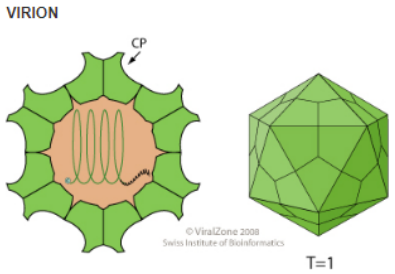
- With donor selection and testing, the **risk for transfusion transmission of important blood-borne viruses** including Human immunodeficiency virus, hepatitis B virus, Hepatitis C virus, Human T-lymphotropic virus, and West Nile virus) **is extremely low**
- With donor selection and testing, the **risk for transfusion transmission of the parasite *Trypanosoma cruzi* (Chagas) is also extremely low**
- Because of the way blood products are produced (including 7 day platelets) the **highest transfusion-transmitted infectious disease risk is bacterial sepsis from platelets**
- Donor deferrals play an important role in limiting transfusion-transmission risks when no blood screening test is done
- Think about donor and recipient health issues

# 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




Non-enveloped, spherical, about 32-34 nm in diameter. The RNA genome is enclosed within a capsid that is composed of 60 capsid proteins, assembled into a T=1 icosahedral particle.

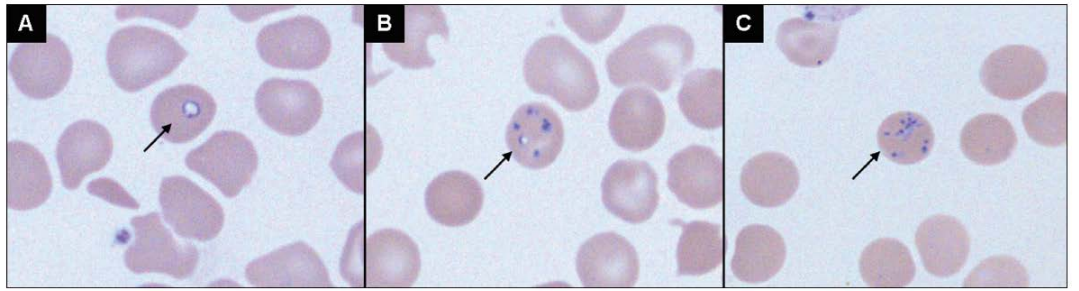



**Figure 1)** Babesia *species in a thin blood smear stained with Giemsa (oil, original magnification ×1000). Vacuolated intraerythrocytic form* (**A**), *multiple forms within erythrocyte* (**B**) *and tetrads* (**C**) *are indicated*

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

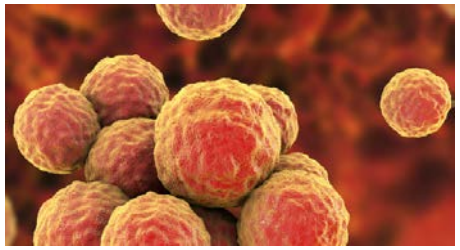
- Human immunodeficiency virus 1/2
- Hepatitis B virus
- Hepatitis C virus
- Human T lymphotropic virus
- West Nile virus
- Cytomegalovirus
- Hepatitis E virus
- Dengue virus
- Zika virus

Parasites

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

# Not all infection risks are equivalent

**Symptomatic bacterial sepsis: platelets 1/10,000**

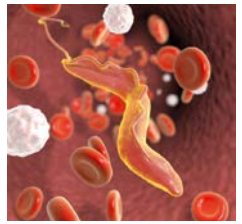



**Death- bacterial sepsis: platelet 1/200,000**

**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**

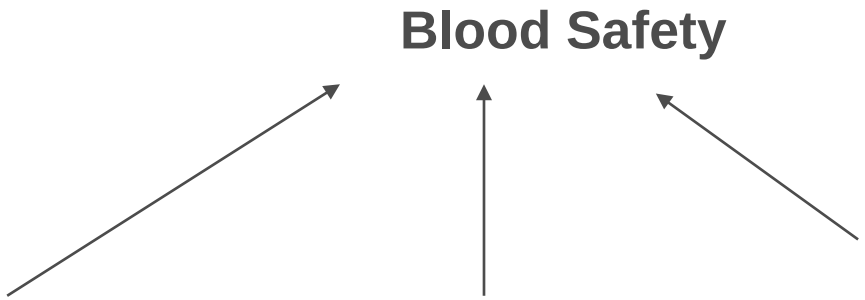
**Transmission** of **HTLV 1/7,600,000**

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

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

# Blood safety for TD uses multiple approaches

# Components of blood safety




## Donor Selection

Record of Donation
Donor selection criteria

## Donor Testing

| | |
|---|---|
| HIV | West Nile |
| HBV | Chagas |
| HCV | CMV |
| HTLV | Bacterial detection (platelets) |
| Syphilis | |

## Good Manufacturing Practices (GMP)

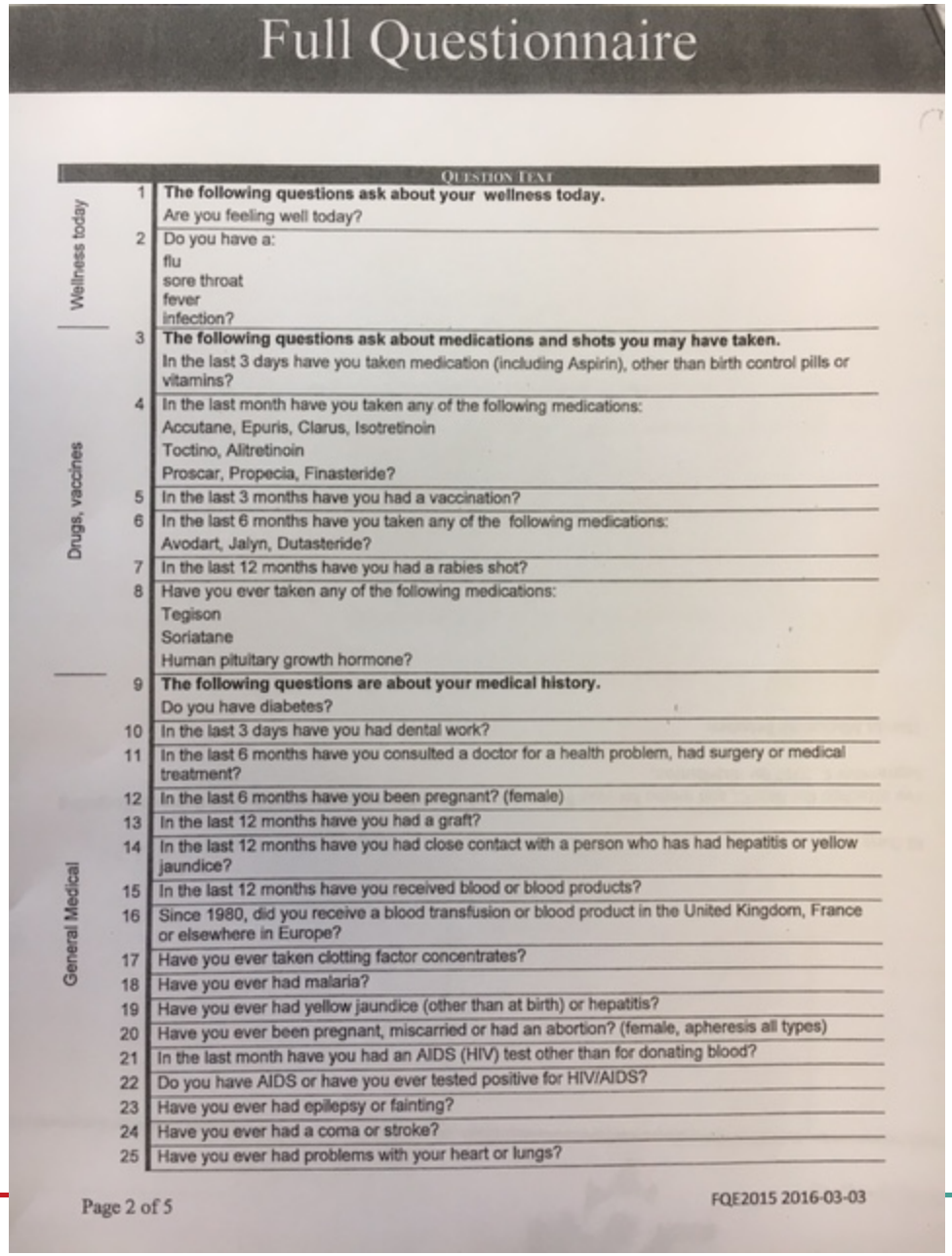
Standardization
Training
Documentation
Traceability
Donor arm prep.

# Donor screening reduces risk prior to testing

# Donor Selection

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

- Donor asked about their
  - *Health*
  - *Medication*
  - *Travel*
  - *Lifestyle*



Full Questionnaire

| | | Question Text |
|---|---|---|
| Wellness today | 1 | **The following questions ask about your wellness today.** Are you feeling well today? |
| | 2 | Do you have a: flu sore throat fever infection? |
| Drugs, vaccines | 3 | **The following questions ask about medications and shots you may have taken.** In the last 3 days have you taken medication (including Aspirin), other than birth control pills or vitamins? |
| | 4 | In the last month have you taken any of the following medications: Accutane, Epuris, Clarus, Isotretinoin Toctino, Alitretinoin Proscar, Propecia, Finasteride? |
| | 5 | In the last 3 months have you had a vaccination? |
| | 6 | In the last 6 months have you taken any of the following medications: Avodart, Jalyn, Dutasteride? |
| | 7 | In the last 12 months have you had a rabies shot? |
| | 8 | Have you ever taken any of the following medications: Tegison Soriatane Human pituitary growth hormone? |
| General Medical | 9 | **The following questions are about your medical history.** Do you have diabetes? |
| | 10 | In the last 3 days have you had dental work? |
| | 11 | In the last 6 months have you consulted a doctor for a health problem, had surgery or medical treatment? |
| | 12 | In the last 6 months have you been pregnant? (female) |
| | 13 | In the last 12 months have you had a graft? |
| | 14 | In the last 12 months have you had close contact with a person who has had hepatitis or yellow jaundice? |
| | 15 | In the last 12 months have you received blood or blood products? |
| | 16 | Since 1980, did you receive a blood transfusion or blood product in the United Kingdom, France or elsewhere in Europe? |
| | 17 | Have you ever taken clotting factor concentrates? |
| | 18 | Have you ever had malaria? |
| | 19 | Have you ever had yellow jaundice (other than at birth) or hepatitis? |
| | 20 | Have you ever been pregnant, miscarried or had an abortion? (female, apheresis all types) |
| | 21 | In the last month have you had an AIDS (HIV) test other than for donating blood? |
| | 22 | Do you have AIDS or have you ever tested positive for HIV/AIDS? |
| | 23 | Have you ever had epilepsy or fainting? |
| | 24 | Have you ever had a coma or stroke? |
| | 25 | Have you ever had problems with your heart or lungs? |

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# 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

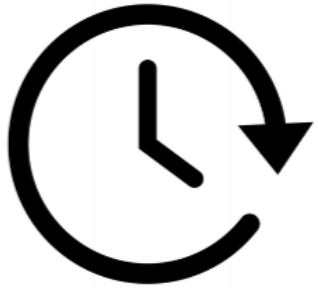
- The pamphlet also explains

➢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.

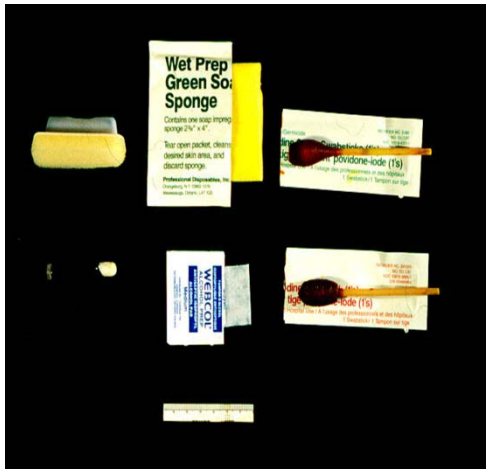
# Laboratory testing to reduce risks of acute transfusion transmitted infections due to bacterial contamination of platelet units

# Canadian Blood services platelets have a 7-day shelf life at room temperature

- In 2017 Canadian Blood services extended platelet concentrate shelf-life from 5 to 7 days.

# Key actions to prevent bacterial contamination of all platelet units

- Skin disinfection at donation site (arm prep)
- Diversion of first 40ml of blood (and skin plug where bacteria are most likely to be found) to a pouch used for donor testing




# Detection and confirmation of bacterial contamination of all platelet units

Detect

Aerobic & anaerobic culture

**Platelets recultured, discarded**

Confirm- by bacterial culture and ID

- **Co-components quarantined, released to inventory if platelets not contaminated**

Culture bottles incubated for 6 days

So maximum culture time can be > shelf-life .

# Confirmatory testing: Most commonly implicated bacteria in platelet contamination (7 day platelets)

## Anaerobes

*Cutibacterium acnes* (skin flora)
- pools ∽ 70%
- apheresis ∽ 70%

*Staphylococcus saccharolyticus* (skin flora)
- pools ∽ 5-10%
- apheresis ∽ 5%

## Facultative anaerobes

Coagulase negative *Staphylococcus epidermidis* (skin flora)
- pools ∽ 5-10%
- apheresis < 5%

Coagulase negative *Staphylococcus*
- pools ∽ 5-10%
- apheresis ∽ 5%

Remainder of isolates are anaerobic and facultative anaerobic colonizers of skin, respiratory tract and GI tract

Sandra Ramirez-Arcos 2020

# Common causes of transfusion-transmitted bacterial infections (US, 2010-2016)

| Infection type | Pathogen | Number of cases | Number of cases where pathogen was identified by a facility in unit or donor | Associated component type* | | | |
|---|---|---|---|---|---|---|---|
| | | | | Red blood cell | Whole blood derived platelet | Apheresis platelet | Plasma† |
| Bacterial | Gram-positive | | | | | | |
| | *Staphylococcus aureus* | 14 | 9 | 2 | 2 | 10 | |
| | *Staphylococcus*, non-aureus‡ | 8 | 5 | 1 | 1 | 6 | |
| | *Streptococcus*, viridans group | 4 | 4 | | | 4 | |
| | *Bacillus* spp. | 1 | 1 | | | | 1 |
| | *Corynebacterium* spp. | 1 | | 1 | | | |
| | *Enterococcus faecalis* | 1 | | 1 | | | |
| | Gram-negative | | | | | | |
| | *Escherichia coli* | 3 | 2 | 1 | 1 | 1 | |
| | *Acinetobacter* spp. | 2 | 2 | | | 2 | |
| | *Achromobacter* spp. | 1 | 1 | | | 1 | |
| | *Brevundimonas diminuta* | 1 | 1 | | | 1 | |
| | *Pseudomonas fluorescens* | 1 | 1 | 1 | | | |
| | *Ralstonia picketti* | 1 | 1 | | | 1 | |
| | Gram-negative rods | 1 | | | | 1 | |

Canadian Blood Services BLOOD PLASMA STEM CELLS ORGANS & TISSUES

Haas, Transfus Med Rev. 2019 April ; 33(2): 84–91. doi:10.1016/j.tmrv.2019.01.001.

# Possible further actions for Medical Officers in response to confirmed positive bacterial testing: Pooled platelets

| *Platelet Bacterial Isolates* | | | |
|---|---|---|---|
| **Species** | **Bacterial characteristics** | **Special considerations** | **Call donor?** |
| ***Cutibacterium acnes*** | Known skin commensal | Can act as a pathogen after bacterial seeding and can be considered opportunistic, causing either superficial or deep/invasive infections. It can cause numerous infections, including but not limited to breast infections, skin abscesses, infective endocarditis, and device-related infections.<br><br>This organism is a strict anaerobe and does not proliferate during platelet storage, therefore it cannot reach clinically significant levels in platelets | No |
| **Anaerobic coagulase negative *Staphylococcus saccharolyticus*** | frequently colonizes the rectum and genitourinary tract, in an age- and season-dependent manner (preferentially in summer and fall) | *S. saccharolyticus* has been associated prosthetic valve endocarditis and prosthetic joint infections.<br><br>This organism is a strict anaerobe and does not proliferate during platelet storage, therefore it cannot reach clinically significant levels in platelets. | No on first time<br><br>Consider if repeat positive |
| **Staphylococcus aureus1** | Present in the nose (usually temporarily) of about 30% of healthy adults and on the skin of about 20%. The percentages are higher for people who are patients in a hospital or who work there. | Commonly associated with skin infections, often causing abscesses. Can cause bacteremia, endocarditis and osteomyelitis. Can accumulate on medical devices in the body, such as artificial heart valves or joints, heart pacemakers, and catheters inserted through the skin into blood vessels. | Yes |

Canadian Blood Services BLOOD PLASMA STEM CELLS ORGANS & TISSUES

MOs need to use clinical judgement

Zeller, M., Drews, S.J., Ramirez-Arcos, S. 2019

# Poll question: Which is the correct answer?

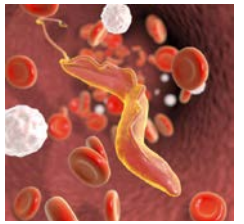
A. 75% of all platelets are tested.
B. Platelets are not released until testing results are known.
C. Platelet samples are incubated for a total of 48 hours.
D. All platelets are tested but platelets may be released and transfused prior to final bacterial testing results.

# Transmissible disease testing to reduce risk of delayed transfusion-transmitted infections

# 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**



**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**

# Infectious marker testing for all donations at CBS

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

1 Mosquito season and travellers
2 At risk donors
na = not available

- 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



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.

# Screening vs Confirmatory Testing

- Screen Tests are designed to be highly sensitive
  - *goal is to not miss any positives*

    *however*
  - *false reactive results can occur even when the donor was never exposed to the particular infection*
- Confirmatory Testing is highly specific

  This is used for :
  - *Donor counselling*
  - *Reporting to public health*
  - *Initiating Lookback*
- Some examples of confirmatory testing are NAT testing for HIV, Western blot for HCV (only if NAT negative), immunoflourescence, microhaemagglutination (chagas and syphilis). Chagas and syphilis confirmatory testing performed by reference laboratories.

- Donors are deferred from donation based on screening test results.
- Donors with certain false positive tests (HIV, HCV, HBsAg) are permitted to enter the Donor Re-entry Programme and can come back in 6 months to try again.

# 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

# Emerging pathogens and the blood supply

# Other pathogens of interest for blood operators

- **Babesiosis** - protozoan parasite (tick borne)
- **Hepatitis E – virus**
- **Zika Virus**

- vCJD (variant Creutzfeld Jacob Disease) – prion
- Malaria - protozoan parasite (mosquito borne)
- Dengue – virus (mosquito borne)
- Chikungunya – virus
- Yellow fever - virus

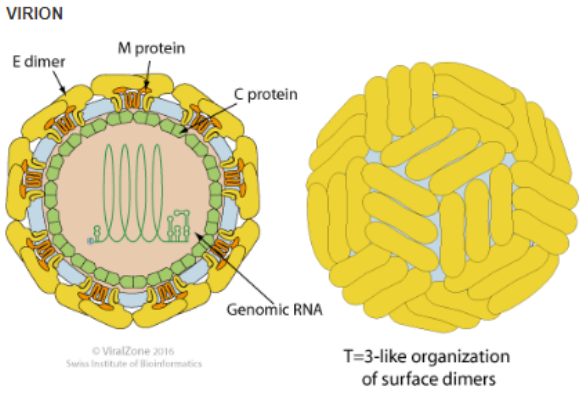
# Zika virus: a vector borne-illness with transfusion potential

- *Disease*

➢ Most infections asymptomatic or mild (fever, maculopapular rash, headache, arthralgia, and conjunctivitis)

➢ Guillain-Barré syndrome/neurological complications

➢ Infection during pregnancy: microcephaly, severe congenital defects, and infant death




Enveloped, spherical, about 50 nm in diameter. The surface proteins are arranged in an icosahedral-like symmetry.

*Aedes aegypti* > *Aedes albopictus*

Also transmit

- Chikungunya virus
- Dengue virus
- Yellow fever virus

https://viralzone.expasy.org/6756
https://www.cdc.gov/dengue/entomologyecology/index.html

# Double duty for a Zika deferral: reducing risk for Dengue virus, Chikungunya virus and Yellow fever virus

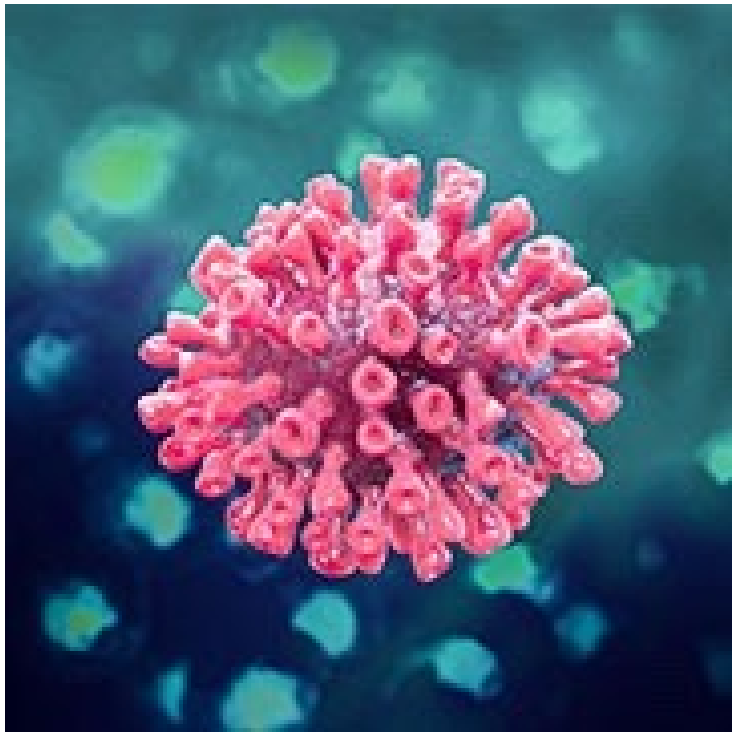
- 21-day deferral on return from high risk area **(High risk= any non-North America and Non-Europe)**
- 56-day deferral after full recover of laboratory confirmed case

# Poll question: The Zika virus deferral may also protect the blood supply from which other pathogens?

A. Dengue virus
B. Yellow fever
C. Chikungunya virus
D. All of the above

# SARS-CoV-2: the virus causing COVID-19

- SARS-CoV-2 is a betacoronavirus.
- Zoonotic origin: initial cases linked to a wet market in Wuhan, China.
- Transmitted by droplets and contact
- No evidence that transfusion transmissible (Leblanc et al., readings)



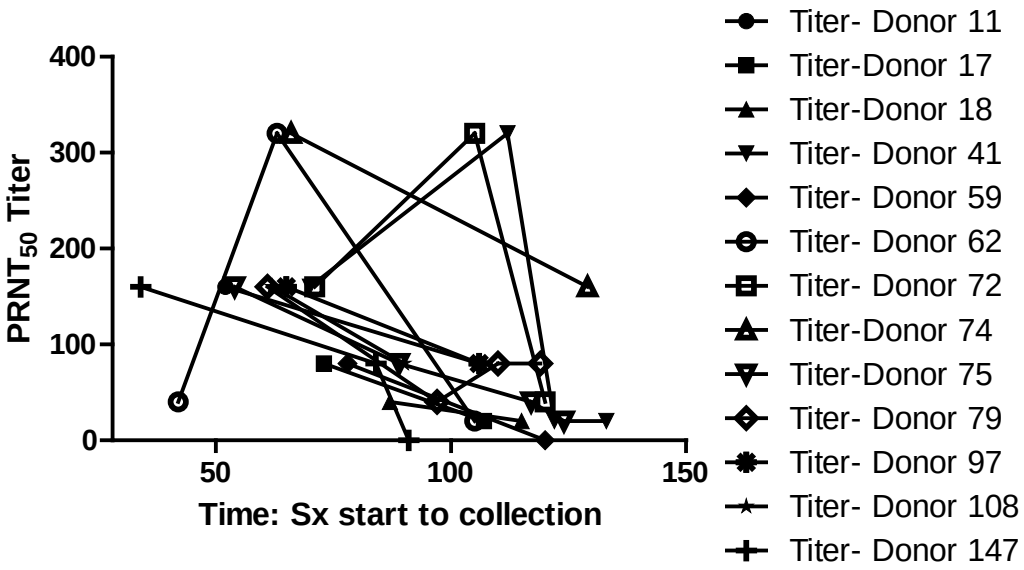


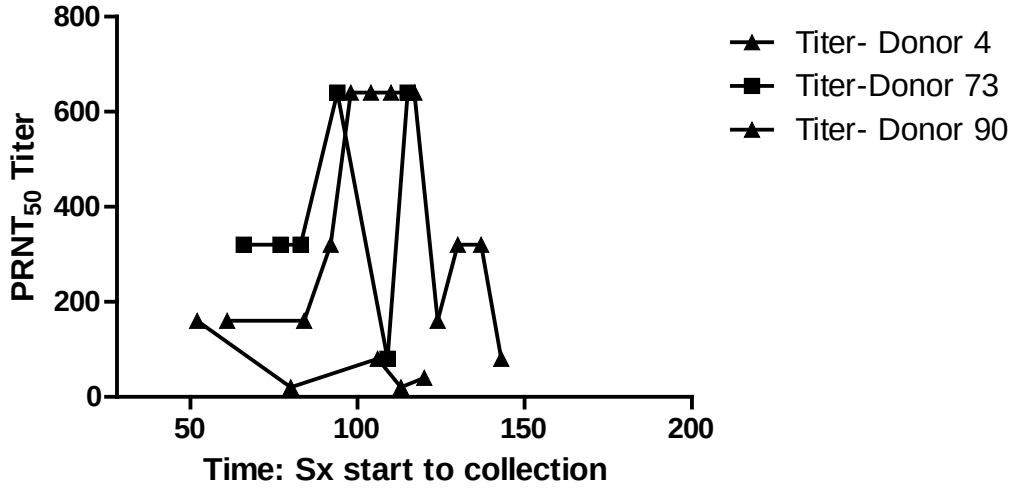
1. Zhou, P. et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* https://doi.org/10.1038/s41586-020-2012-7 (2020).

# Canadian Blood Services and COVID-19

- CBS involved with
  - Immunity taskforce seroprevalence and cross site validation work
  - CIHR correlates of immunity work
  - Provides convalescent plasma products to clinical trials

# Strong correlation between the decline in SARS-CoV-2 antibody titers and time after symptoms onset



# Readings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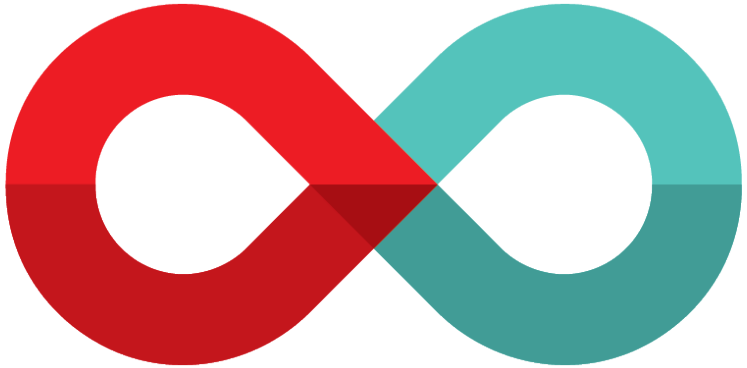

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