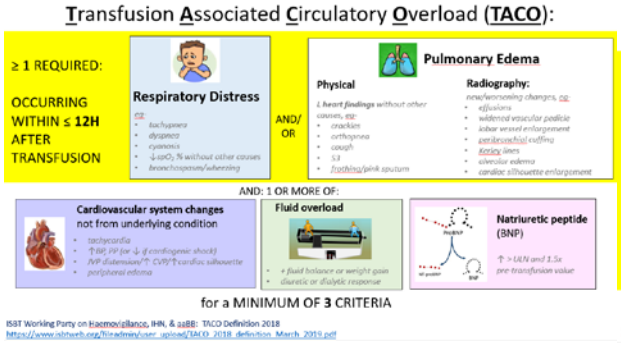
Dr. Christine Cserti-Gazdewich, Acute Non-Infectious Reactions

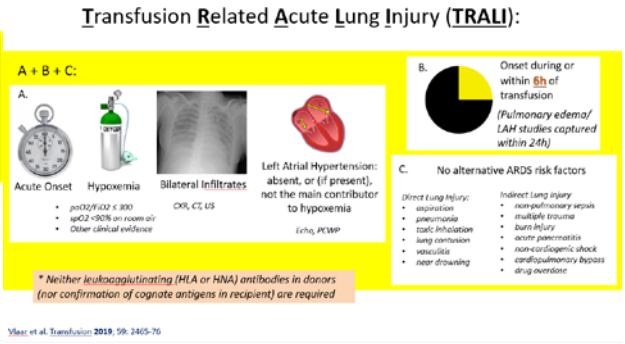
Minimum Disclosure Framework

in Layman's Terms & Logscale Frequencies

logscale		
1 2	**Common, minor events** (1 / 10^1-10^2)	non-serious **fever** non-serious **hives** make **antibodies** to donor antigens (RBC, HLA)
3 4 5	**Serious, potentially fatal events** (1 / 10^3-10^5)	**breathing trouble**: –volume-driven fluid excess –immune injury-driven fluid leaks –anaphylaxis / severe bronchospasm **bacterial contamination** of unit **botched process** (wrong sample or bag)
6	**Extremely rare events** (1 / 10^6 or less)	viral contamination of unit (**hepatitis, HIV**) **new** or **rare** (not tested-for) **bugs** fatal immune "take-over" by product

- Fever differential diagnosis
  - Low risk: FNHTR
  - High risk: bacterial contamination, bacterial sepsis, acute hemolytic transfusion reaction
- Dyspnea differential diagnosis: TACO, TRALI, Allergic, TAD





- Allergic reaction: ranges from cutaneous eruption to anaphylactic reaction
- Investigations:
  - Febriles: hemolysis, microbiology
  - Dyspneics: hemolysis, microbiology, CBS (donor ALA)
  - Hypotensives: hemolysis, microbiology
  - Anaphylactics: hemolysis, ?IgA/anti-IgA IgG
- Report all transfusion reactions to the blood bank and blood bank will report to outside channels (Canadian Blood Services, TTISS, Health Canada, etc.)

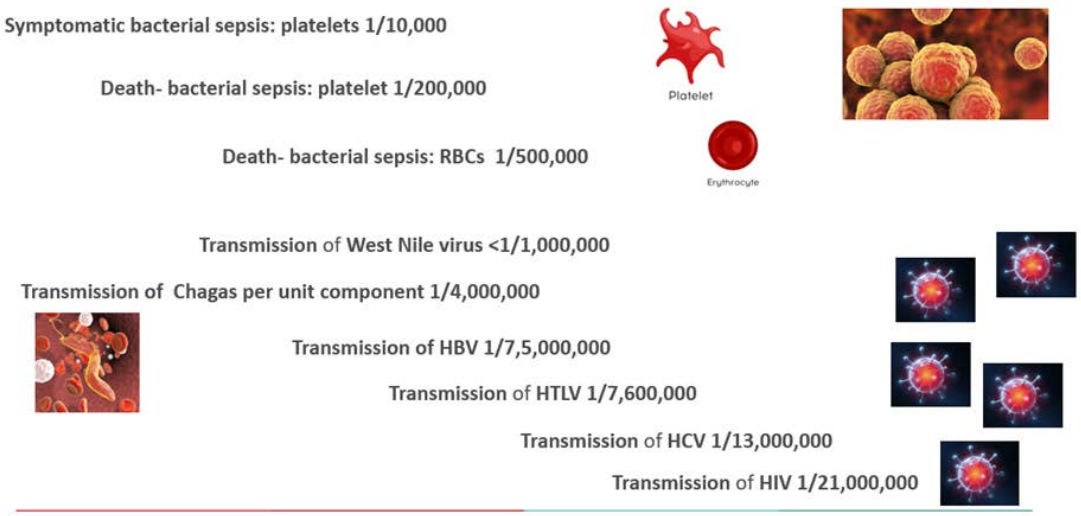
Dr. Steven Drews, Acute & Delayed Transfusion Transmitted Infections

Key Points

The most common transfusion transmitted infection is Bacterial sepsis

To reduce the risk of bacterial contamination
- Skin disinfection
- Diversion of the first 40mL of blood
- Detection of bacterial contamination in ALL platelet units

Transmission of blood borne viruses is extremely low



To reduce risk of other infections
- Donor health assessment questionnaire
- Infectious disease testing

Infectious marker testing for all donations at CBS

Agent	Assay	Window Period (days)
HIV	anti-HIV-1/2 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

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

Protecting the blood supply from transfusion-transmitted infectious diseases

Canadian Blood Services is nationally responsible for a secure system of life essentials for transfusion and transplantation that's reliable, accessible and sustainable. Processes, practices and systems are designed to ensure the quality and safety of our products and services. To safeguard the blood system (including stem cells) against existing, emerging and re-emerging pathogens, Canadian Blood Services undertakes a variety of processes and practices.
All blood transfused in Canada is collected from volunteer donors. They are sked about risk factors for transfusion-transmissible diseases. As laboratory tests have improved, the importance of the health assessment questionnaire in eliminating donors at risk for infectious diseases has decreased. However, currently, the questionnaire is the only means of excluding donors with a risk of Creutzfeldt–Jakob disease (CJD), variant CJD, Ebola virus, malaria, Zika virus, babesiosis, or leishmaniasis. Donors are not tested for these agents.

Antibody and antigen tests are done on individual donor samples while nucleic acid testing (NAT) is primarily done on pools of six samples. The multiplex assay used for NAT enables the simultaneous detection of HIV RNA, hepatitis C virus (HCV) RNA and hepatitis B virus (HBV) DNA. West Nile Virus (WNV) RNA testing is also done in pools of six samples. However, to enhance sensitivity, single unit WNV NAT may be used in selected geographic areas during outbreaks of WNV.

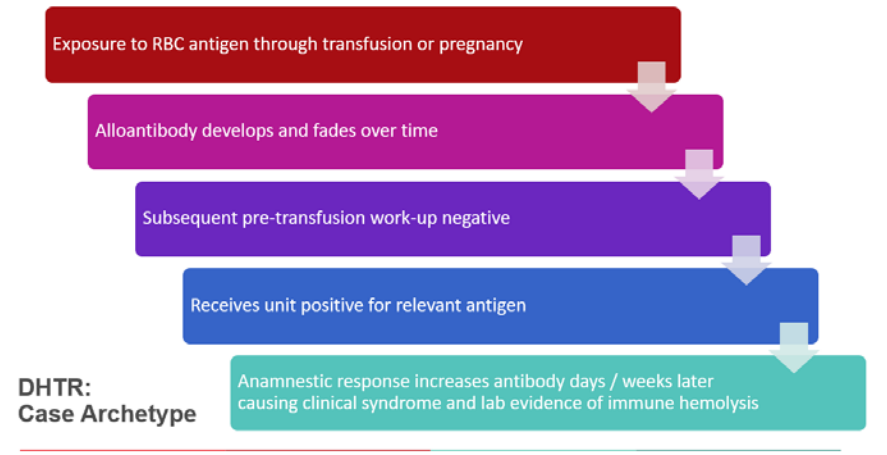
Testing on all donations occurs for HIV-1/2, anti-HBV, anti-HCV, syphilis and anti-human T-cell lymphotropic viruses-I/II (HLTV-I/II). Testing for antibodies to *Trypanosoma cruzi* (Chagas disease) is performed on at-risk donors based on the donor questionnaire. Testing for antibodies to cytomegalovirus (CMV) is performed on a small subset of donations to provide CMV-negative products for fetuses receiving intrauterine transfusions.

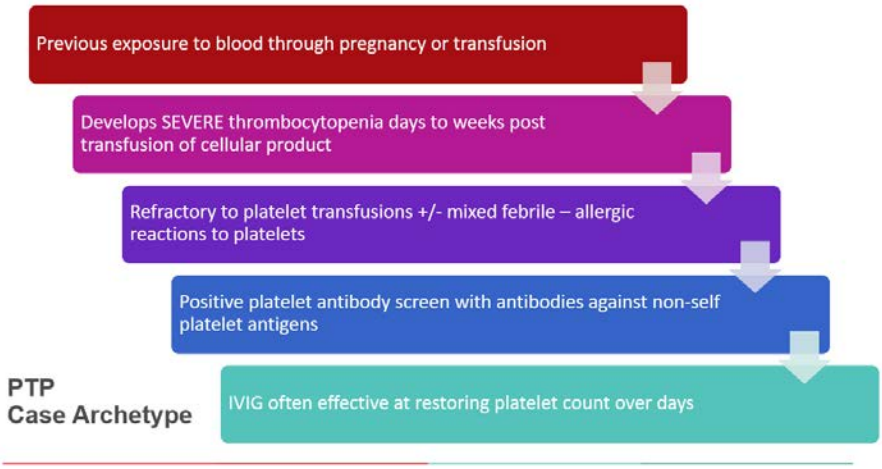
Platelets manufactured from buffy coat or collected by apheresis can be stored at room temperature with gentle agitation for up to seven days prior to transfusion. This storage requirement makes platelet units the blood component most likely to be associated with bacterial growth.
These platelet units are tested for bacterial contamination using an automated blood culture system incubated for up to seven days after inoculation.
Canadian blood services maintain 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, infectious disease surveillance internet reports, non-peer reviewed scientific information, news media, information from scientific meetings and teleconferences, and person-to-person discussions with peers. The scanning activities include assessing the risk to blood components, source plasma and hematopoietic stem cell products.

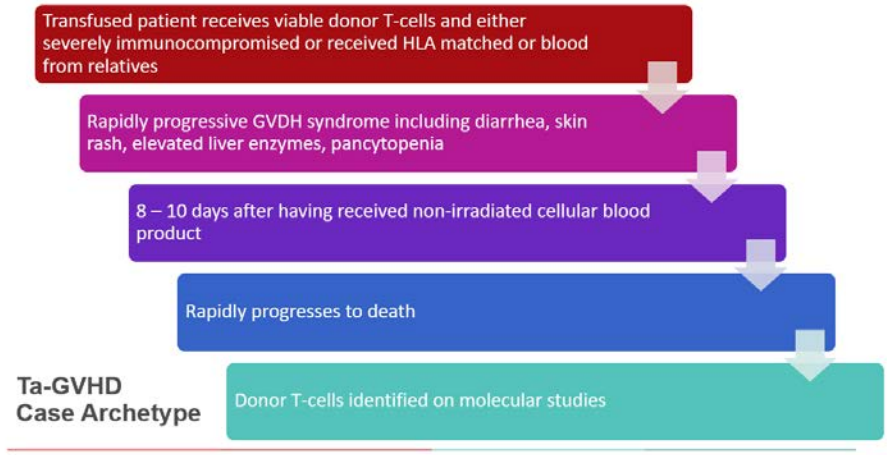
Canadian Blood Services also undertakes surveillance projects for agents such as *Babesia* and Hepatitis E virus. Information generated in these surveillance exercises is used for risk analysis and risk-based decision-making approaches for blood safety.

Dr. Waseem Anani, Delayed Non-Infectious Reactions

Review of delayed hemolytic transfusion reaction, post-transfusion purpura, and transfusion associated graft vs. host disease.







Dr. Katerina Pavenski, Informed Consent

Key points

- Studies show that there is room to improve the informed consent process for transfusion
- Consent for transfusion is required because of
  - Ethical obligation: respects patient's autonomy, involves patient in his/her care, allows patient to "own" treatment decision
  - Legal obligation: Informed consent is legislated nationally and, in some provinces, provincially (although does not specifically address consent for transfusion)
  - Standards: consent is required by the Canadian Society for Transfusion Medicine and Canadian Standards Association

- Who should obtain consent? Obtaining informed consent is the responsibility of the *physician or a nurse practitioner* who orders the transfusion
- Process: to obtain informed consent, follow this process:
  - Determine the person's **capacity to decide** (if deemed incapable, locate a substitute decision-maker)
  - Obtain **consent** or **refusal**
  - **Document** in chart informed consent/refusal
  - **Communicate** your patient's decision to the other members of the healthcare team

- Elements of Informed Consent: Inform patient of:
  - the nature of treatment
  - What component is to be transfused? Why?
  - risks of transfusion – most common; uncommon but severe; and material to your patient
  - expected benefits
  - possible alternatives and their risks
  - the likely consequences of not having the treatment
  - right to refuse transfusion
- Obtaining consent is about giving information and receiving feedback from a patient
- Reference ORBCON informed consent pocket card: https://transfusionontario.org/wp-content/uploads/2020/06/InformedConsent2017.pdf

Dr. Nadine Shehata, Alloimmunization & Anemia in Pregnancy

Alloimmunization (the development of an antibody to a foreign red cell antigen) occurs in women who are exposed to foreign paternal antigens during pregnancy or to foreign red cell antigens from red cell transfusion as alloantibody development occurs when an individual does not have the antigen of which she is exposed. If the alloantibody is an IgG alloantibody, it can traverse the placenta (IgM antibodies do not traverse the placenta), bind to the cognate antigen on the red cells of the fetus causing destruction of red cells and thus fetal anemia (hemolytic disease of the fetus (HDF). Anemia can extend to the neonatal period (hemolytic disease of the newborn (HDN)).

The risk of development of an alloantibody is not only dependent on exposure but also on the immunogenicity of the red cell antigen, the volume of red cell antigen exposed (higher volumes of red cell antigen exposure is associated with higher the risk of developing alloantibodies during pregnancy), the gestational age when the antigen develops in utero (earlier in gestation is associated with increases the risk of developing alloantibodies during pregnancy) and the ability for the mother to develop a cytotoxic antibody.

Because of these factors, not all mothers develop an alloantibody that is capable of causing HDFN. Once a woman develops an alloantibody however, there is a risk of severe HDFN e.g. fetal anemia although some women do not have HDFN. The D, K and c antigen are associated with more severe HDFN.

Preventing alloantibody development prevents the risk of HDFN particularly severe disease. Prevention of alloimmunization is achieved by reducing exposure to paternal antigens and/or red cell antigens vua red cell transfusion. The only paternal red cell antigen exposure that can be prevented/reduced is exposure to paternal D antigen by administering Rh immune globulin (RhIG) to the mother prophylactically or when there is fetal maternal hemorrhage (entry of fetal blood into the maternal circulation) as occurs during normal pregnancy or risk of fetal maternal hemorrhage (as occurs with trauma during pregnancy).

RhIG is a plasma derived product from donors with high anti-D antibodies. It is administered prophylactically at 28 weeks gestation to D negative mothers and after delivery if the neonate is D+. The prophylactic dose at 28 weeks gestation administered to a D negative mother assumes the father is D+. RhIG is also given within 72 hours of a sensitizing event (from fetal maternal hemorrhage) but may be given up 10 days after such an event.

Reduction of exposure of red cell antigens from red cell transfusion is achieved by red cell transfusion avoidance unless necessary (e.g. bleeding or symptomatic anemia) or if red cell transfusion is required, by administering K antigen negative red blood cells (which can be requested from the blood bank) to women of child bearing age to prevent alloimmunization to the K antigen.

Red blood cell transfusion is often prescribed according to hemoglobin concentrations. During pregnancy the hemoglobin concentration decreases because of hemodilution (increased blood volume relative to red cell mass). As such, hemoglobin concentrations decrease in pregnancy to a maximum of approximately 15g/L by the third trimester. As there are no trials of hemoglobin transfusion thresholds for red cell transfusion during pregnancy, transfusion is administered with anemia in pregnancy if the mother is symptomatic or bleeding or if the fetus is symptomatic (e.g. fetal tachycardia). Nonetheless the most common cause of anemia in pregnancy is iron deficiency so that ensuring mothers are iron replete by using prenatal vitamins and checking CBCs at the end of the first trimester to ensure a mother is not becoming anemic potentially results in a reduction of anemia and need for transfusion. Iron deficiency anemia can be treated with iron salts during the entire pregnancy and iv iron (iron sucrose) in the second and third trimester.

Dr. Yulia Lin, Pre-operative Patient Blood Management

What is patient blood management?

- Evidence-based, multidisciplinary approach to optimizing care of patients who might need transfusion, often described with 3 main pillars
    1. Treat Anemia
    2. Minimize blood loss
    3. Appropriate use of blood

Why is treating preoperative anemia so important?

1. Preop anemia is associated with increased mortality
2. Preop anemia is potentially modifiable (both as a risk factor and a treatable condition)
3. Preop anemia is common ~ 1/3 of pts going for surgery have anemia!
4. Preop anemia is associated with transfusion
5. Transfusion is a bad outcome
6. The donor supply is precious resource

How to treat preoperative anemia?

- Autologous blood
    - Only to be used for patients with very rare blood type, for whom blood donors cannot be easily found
- Diagnose iron deficiency anemia
    - Check the CBC 4-6 weeks preop.
    - For high blood loss major surgery, the target is preop Hb if 130 g/L in both males and females
    - Iron deficiency anemia is defined as:
        - Ferritin < 30 mcg/L; or
        - Ferritin < 100 mcg/L AND transferrin saturation < 20%
    - Low iron stores defined as:
        - Ferritin < 100 mcg/L
- Treat iron deficiency anemia
    - Always remember to identify the cause (Bleeding is the most common source)
    - Start with oral iron salts when possible
    - Consider iv iron when
        - Oral iron is not tolerated or ineffective
        - Short time to surgery < 4-6 weeks
        - Severe anemia, e.g. Hb < 100 g/L
        - Active bleeding
- Consider the role of erythropoiesis stimulating agents in
    - Patients with religious objections to blood
    - Patients with multiple alloantibodies where it is difficult to find blood
    - Patients with high blood loss surgery (although cost-effectiveness less clear here)