BACKGROUND

All blood transfused in Canada is collected from volunteer donors. To ensure the safety of the blood products, donors are carefully screened against an extended list of eligibility criteria and their donated blood products are tested for transfusion-transmissible diseases. Donor eligibility criteria also reduce potential health risks for the donor. This chapter describes the donor selection process, the pathogen testing done on blood products, and the pathogen inactivation processes that can further reduce the potential risk of transfusion-transmitted diseases.

DONOR SELECTION

Donors are questioned about medical conditions and behaviors to determine if their blood donation would pose an increased risk to their own health or the health of the recipient. Donors must provide identification at registration. Computer records are checked to determine whether a deferral code has been attributed to the donor after previous donations. Donors are asked to read a pamphlet (What you must know to give blood) explaining the donation process, the 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, and informs donors that testing may fail to identify individuals who are in the early stages of infection.

After reading the pamphlet, the donor’s medical history is assessed with a standard electronic questionnaire. Donors may fill out the questionnaire at home on the day of donation, or in the clinic. Donors are asked about illness in major organ systems that may put them at increased risk of an adverse reaction to donation. They are also asked 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, at the present time, the questionnaire is the only means of excluding donors with a risk of Creutzfeldt-Jakob disease (CJD), variant CJD, malaria, zika virus, babesiosis or leishmaniasis. Testing is not performed for these agents and other unknown agents.

Selective testing is performed for Chagas disease, on donors identified as being at risk based on the questionnaire. Selective testing is also performed for West Nile Virus (WNV) during the winter months on donors identified as being at risk based on the questionnaire. Donors are also asked about travel outside of Canada, the continental US and Europe, and deferred for three weeks after their return to reduce the risk of transmission of Zica virus. In addition, individuals taking teratogenic medications are identified and excluded from donation. Depending on the magnitude of the risk, donors may be deferred temporarily or indefinitely. For example, at the present time, people who have taken illegal drugs by injection are indefinitely deferred, while travellers to a region where malaria is considered endemic are deferred from donation of cellular blood components for one year.

Donors must be at least 17 years old (18 in Quebec) and meet certain height and weight requirements. For younger donors, more stringent height and weight criteria may apply. Approximately 15% of donors are determined to be ineligible; most of these are temporary deferrals. It is estimated that less than four in 100 people eligible to donate in Canada actually donate blood each year. The average donor donates approximately twice a year.

Over one-third of deferrals are due to inadequate hemoglobin levels. Based on studies of iron deficiency in our
BLOOD COLLECTION PROCESS

Whole Blood Donations

Prior to donation, the donor’s blood pressure and temperature are taken and must be within an acceptable range. In addition, a measure of their hemoglobin level is done on a capillary blood sample. Both arms are examined for signs of injection intravenous drug use. The donor’s skin is disinfected using a swab stick containing 2% chlorhexidine gluconate and 70% isopropyl alcohol. An alternative disinfection protocol is used for donors allergic to chlorhexidine.

Phlebotomy is performed using a sterile single-use kit that contains an anticoagulant nutritive solution. The time for phlebotomy varies from 10 to 15 minutes. Approximately 480 ml of blood are collected per donation. The first few millilitres of blood are directed to a diversion pouch before filling the main collection bag. The diversion pouch has been shown to decrease the contamination of the collection bag with bacterial skin flora. The blood in the diversion pouch is used for the serological and infectious disease testing performed on each unit of blood collected.

Apheresis Donations

The process for screening apheresis donations is very similar to the one for whole blood donation. Several additional criteria are present to ensure the safety of the donor and the quality of the blood product.

Plateletpheresis donors must have a platelet count of 150 x 10^9 per litre prior to undergoing each procedure. Plateletpheresis may be performed every 14 days for a maximum of 24 donations in a calendar year. Depending on donor characteristics, such as initial platelet count and blood volume, each plateletpheresis donation may yield a single or multiple platelet units, or both platelet and plasma products.

Plasmapheresis donors must have a total serum protein of over 60 g/l at each donation and a normal serum protein composition, verified periodically. Donors may make weekly plasmapheresis donations. The maximum quantity of plasma that may be collected per donation and during a twelve month period is dependent on the donor’s weight.

SCREENING TESTS PERFORMED ON BLOOD DONATIONS

Transfusion-Transmissible Disease Testing

Multiple screening tests are performed on each donation to detect the presence of transfusion-transmissible infectious agents. The screening tests performed may detect antigens, antibodies or nucleic acids of the infectious agents. Table 1 provides the screening and confirmatory tests performed at Canadian Blood Services.

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.

NAT for HIV, HCV and HBV are performed on all blood donations throughout the year. Testing for WNV is performed based on potential risk. During the WNV season, from June 1st to November 30th, all donations are tested for WNV due to the increased risk. However, during the winter months, from December 1st to May 31st, WNV testing is performed only on donors who are identified as being at-risk on the donor questionnaire because of travel outside of Canada in the eight weeks prior to their current donation.

Testing for antibodies to Trypanosoma cruzi (Chagas disease) is performed on donors identified as being at-risk on the donor questionnaire. Donors are designated as at-risk if they, their mother or their maternal grandmother was born in Mexico, Central America or South America or if the donor has resided in these at-risk countries for a significant period of time.\(^7,^8\)

Testing for antibodies to cytomegalovirus (CMV) is performed on a small subset of donations to provide CMV-negative products only for fetuses receiving intrauterine transfusions.\(^9\) Since CMV is a cell-associated virus and all cellular components are leukoreduced in Canada, the risk of CMV infection related to blood products is extremely low.

Table 1: Transfusion-transmissible disease testing at Canadian Blood Services.

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Screen Tests</th>
<th>Confirmatory/Supplemental Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV 1/2 (human immunodeficiency virus, types 1 and 2)</strong></td>
<td>• Anti-HIV-1/2 HIV NAT</td>
<td>• HIV-1/2 confirmatory testing</td>
</tr>
<tr>
<td><strong>HBV (hepatitis B virus)</strong></td>
<td>• Hepatitis B surface antigen (HBsAg)</td>
<td>• HBsAg confirmatory testing</td>
</tr>
<tr>
<td></td>
<td>• Antibody to hepatitis B core antigen (HBcore)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• HBV NAT</td>
<td></td>
</tr>
<tr>
<td><strong>HCV (hepatitis C virus)</strong></td>
<td>• Anti-HCV</td>
<td>• HCV confirmatory testing</td>
</tr>
<tr>
<td></td>
<td>• HCV NAT</td>
<td></td>
</tr>
<tr>
<td><strong>HTLV-I/II (human T-cell lymphotrophic viruses, types I and II)</strong></td>
<td>• Anti-HTLV I/II</td>
<td>• HTLV confirmatory testing</td>
</tr>
<tr>
<td><strong>Treponema pallidum (pathogen for syphilis)</strong></td>
<td>• Micro-hemagglutination assay for <em>Treponema pallidum</em> (MHATP)</td>
<td>• Fluorescent treponema antibody absorption (FTA-ABS)</td>
</tr>
<tr>
<td><strong>WNV (West Nile virus)</strong>*</td>
<td>• WNV NAT</td>
<td>• None</td>
</tr>
<tr>
<td><strong>Trypanosoma cruzi (pathogen for Chagas)</strong>*</td>
<td>• Anti-Trypanosoma cruzi chemiluminescent assay</td>
<td>• ELISA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Immunoblot</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Polymerase chain reaction (PCR)</td>
</tr>
<tr>
<td><strong>CMV (cytomegalovirus)</strong>†</td>
<td>• Anti-CMV particle agglutination assay</td>
<td>• None available</td>
</tr>
</tbody>
</table>

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Pathogens | Screen Tests | Confirmatory/Supplemental Tests
--- | --- | ---
*performed on at-risk donors. | †performed on a subset of donors for components required for IUT.

Donors who have initially reactive results on antigen or antibody testing have repeat testing performed twice on the same sample. If one of these two repeats is reactive, the donation is discarded and additional testing is performed to determine the true status of the donor for donor notification and counselling and for donor re-entry 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.

**Nucleic Acid Amplification Testing (NAT)**

For NAT multiplex screen testing, a reactive pool is resolved to an individual reactive specimen and the viral target that it is reactive for (HIV RNA, HCV RNA or HBV DNA). For WNV the reactive pool is resolved to the individual reactive specimen. Donors reactive on the multiplex screen test are indefinitely deferred, whereas donors reactive on the WNV screen test are deferred for 56 days.

**Bacterial Testing**

Because platelets are stored at room temperature, they are the blood product most likely to support bacterial growth. All platelet units are tested for bacterial contamination using an automated blood culture system incubated for up to six days. Platelets are issued as “negative to date”, and will be recalled, along with other blood products from the same donation, if the culture subsequently becomes positive.

**Blood Group Determination and Antibody Detection**

ABO and Rh grouping are performed using an automated hemagglutination assay. Confirmatory typing is done for first-time donors found to be Rh negative, and donors are tested for the presence of Rh D and weak D antigens. Testing is also performed for unexpected red blood cell antibodies. The methods used may be less sensitive than those required in pre-transfusion antibody detection. In recipient testing, a low level of antibody may be of clinical importance, since an anamnestic response may occur. In donor testing, only a small amount of passive antibody transfusion will occur.

Phenotyping for RhC/c, RhE/e, Kell, Duffy, Kidd and S/s is routinely performed on a subset of repeat donor samples using an automated, algorithmic approach. This has led to a substantial inventory of red blood cell units end-labeled as negative for those antigens. The number of donors tested depends on the antigen; for some antigens, such as Kell, up to 60% of active donors have been phenotype tested. Red blood cell antigen genotyping is also performed on some donors. This testing allows for identification of certain rare phenotypes and confirms variable serologic reactivity for some antigens. Genotype testing may also be performed when serologic reagents are not readily available to define a particular red blood cell antigen type or when family members of rare donors are investigated as part of the Canadian Blood Services rare donor program. Negative phenotypes defined by serologic or genotyping methods are reported on the end label.

**PATHOGEN INACTIVATION SYSTEMS**

Current pathogen inactivation (PI) technologies are based on chemical or photochemical principles. They have been shown to prevent alloimmunization and significantly terminate the growth of pathogens such as bacteria, viruses and protozoa. Certain PI technologies are marketed for the treatment of single transfusion doses of plasma or platelet products in some jurisdictions. Applications of these technologies for the treatment of red
Chapter 6: Donor Selection, Transmissible Disease Testing and Pathogen Reduction

Blood cell products and for units of whole blood are under development.\textsuperscript{11,12}

PI methods for plasma products include solvent-detergent treatment of plasma in pools and methylene blue followed by ultraviolet (UV) A illumination for single unit plasma.\textsuperscript{14,15} Both these methods are in use in several European and other non-North American jurisdictions.\textsuperscript{17,18}

PI methods for both plasma and platelets include amotosalen (S59, apsoralen) plus UVA illumination, riboflavin plus UVA/B light illumination, and UVC illumination alone.\textsuperscript{11,19} All three methods are in use for plasma or both plasma and platelets products in some European jurisdictions. Amotosalen plus UVA illumination was approved for apheresis platelets in the United States in 2015. Riboflavin plus UVA/B light illumination is the subject of a recently completed international clinical trial in which Canada was a participant.\textsuperscript{20}

At this time, platelet and red blood cell units that have undergone PI are not yet licensed for use in Canada. A pooled plasma product that has undergone PI using solvent-detergent is licensed and is available with some restrictions.

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REFERENCES


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