In Canada and other countries, many steps are taken to minimize the risk of infection through the transfusion of blood or blood products (1). However, the infection risk can never be zero because these are biological products taken from living donors who are never ‘germ free’ (2). This is in contrast to drugs that can be manufactured de novo under sterile conditions in a laboratory. The present note provides an update on transfusion infection risks in Canada. It replaces the 2003 note (3), and may be helpful to practitioners in discussions with patients and parents toward obtaining informed consent before blood or blood product administration.

While any infectious agent that has a blood phase has the potential to be transmitted by transfusion of blood or blood products, the probability of infection in the recipient depends on a number of factors, including (4):

- the prevalence of the agent in the blood of the donor population;
- the tolerance of the agent to blood handling, storage and manufacturing procedures;
- the infectivity and pathogenicity of the agent;
- the recipient’s health status; and
- the effectiveness of donor screening or donor testing for the agent.

The importance of these factors is well illustrated by the tale of West Nile virus (WNV). WNV has only recently been introduced into the North American bird population and, through secondary transmission via mosquitoes, to humans (5,6). Not surprisingly, given the blood phase of infection, WNV was shown in 2002 to be transmissible by blood (7), with an estimated mean risk of 2/10,000 to 5/10,000 (maximum 21/10,000) in outbreak regions in the United States (8). This resulted in rapid efforts to develop a screening test to detect WNV infection in blood donors (9). Both the Canadian Blood Services and Héma-Québec started testing for WNV infection in June 2003, using a new test that has an estimated sensitivity of 75% to 90% to detect infected donors during the WNV season. The seasonal variation in the transmission of WNV from mosquitoes to humans means that the prevalence of WNV in unscreened blood is predicted to change over the next few years as the bird population becomes immune, resulting in decreased transmission from the avian population to mosquitoes and to people. With WNV donor screening testing now in place, the risk of contamination in blood collected from donors during a WNV outbreak is now estimated to be 1/100,000 to 3/100,000. This measure reflects the sensitivity of the test and the prevalence of infection among donors in a given region.

This past season, the blood donor WNV screening program has had the added benefit of providing public health authorities with a marker for infection rates among local and regional populations. Public health authorities in most jurisdictions now provide regular updates concerning the penetration of WNV in birds, animals and humans in Canada during the mosquito season. In the same way that Canadians monitor the Weather Channel, health care practitioners need to monitor the ‘Web-based public health channels’ through their local public health unit, a provincial or territorial health Web site or via Health Canada’s West Nile Monitor (10), to gain a sense of the background risk for WNV in their region.

In Canada, the infectious disease risks of transfusion are minimized through multiple steps, including: blood collection from volunteer unpaid donors, donor interview and selection procedures, donor screening by serological and other tests (Table 1), and viral inactivation procedures included in the manufacturing processes of blood products (1).

TABLE 1

<table>
<thead>
<tr>
<th>HIV-type 1/2/3 group</th>
<th>Antibody/NAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>Hbs Ag, Anti-HBc</td>
</tr>
<tr>
<td>HTLV type VIII</td>
<td>Antibody</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Nonvenereal test – Treponemal test/PK-TP</td>
</tr>
<tr>
<td>HCV</td>
<td>Antibody/NAT</td>
</tr>
<tr>
<td>WNV</td>
<td>NAT</td>
</tr>
<tr>
<td>Other†</td>
<td>CMV antibody on selected units only</td>
</tr>
</tbody>
</table>

*Personal communications: Dr Gilles Delage, Héma-Québec; Dr Heather Hume, CBS. Héma-Québec and CBS are developing bacterial culture testing for thrombopharesis platelets; †While the newer PRISM human immunodeficiency virus (HIV) antibody test does detect HIV group O, donors are still asked questions related to travel to parts of the world where HIV-O infection is prevalent, until a change in practice is approved; ‡Antibody to hepatitis B core antigen (Anti-HBc) testing has been introduced by Héma-Québec in 2003 and will be introduced by CBS in late 2004; §Héma-Québec and CBS are developing bacterial culture testing for thrombopharesis platelets. CMV Cytomegalovirus, Hbs Ag Hepatitis B surface antigen, HBV Hepatitis B virus, HCV Hepatitis C virus, HTLV Human T-lymphotropic viruses, NAT Nucleic acid testing, WNV West Nile Virus.
As noted in Table 2, solvent/detergent procedures dissolve the lipid envelope of the human immunodeficiency virus, WNV, hepatitis B virus and hepatitis C virus, but are not effective against nonlipid enveloped viruses such as hepatitis A virus or parvovirus B19. Heat inactivation is effective against a wide range of viruses, including WNV, hepatitis A virus and parvovirus (14). The leukocyte reduction technique that is used by Canadian Blood Services and Héma-Québec to further improve the safety of the blood supply also reduces the infection transmission risk, particularly for cytomegalovirus (CMV) (13).

Table 3 identifies specific inactivation steps in the manufacture of different plasma-derived products that decrease viral infection risks.

Unfortunately, the solvent/detergent and heat inactivation procedures noted in Table 2 cannot be used on red blood cells or platelets, because neither can withstand these vigorous viral inactivation processes. Pathogen reduction techniques suitable for these labile blood components are in development and, in some cases, being tested in clinical trials.

Almost all reported acute infectious complications arising from blood product transfusion are associated with bacterial pathogens (15, 16) (Table 4). While the use of closed multi-component plastic blood pack collection systems has helped to decrease the problem, contamination of platelet concentrates is still a concern (16). The risk of bacterial contamination of frozen components such as fresh frozen plasma and cryoprecipitates is now very low, because the usual microbes (Table 4) are killed by freezing and other storage conditions. Where plasma has been found to be the source of infection, this was usually due to contamination of the water bath used to thaw the product (17). The use of microwave techniques specifically designed for this purpose minimizes this risk.
The estimated per unit risks of contamination in blood, blood products and manufactured plasma-derived products in Canada for a number of viral, bacterial, parasitic, prion and tick borne agents are presented in Tables 5 and 6. Where Canadian data are not available, data from the United States and other countries have been included (4,12,18-20). As the data in Tables 5 and 6 show, the risks in Canada of transmitting infectious agents by blood, and especially by plasma manufactured products, are extremely low. For context, a 1/3,000,000 risk is similar to that of being hit by lightning.

The risk estimates for transmission of CMV remain complex (21). Although 40% to 70% of donors are CMV-positive, the risk of disease in nonimmunocompromised recipients is very low, while the risk of disease in immunocompromised patients is significant. For CMV seronegative recipients, the risk of CMV infection in solid organ transplant recipients and in bone marrow transplant recipients is 2% to 3% and 20% to 30%, respectively. This risk can be decreased with selection for seronegative donors and/or the use of leukocyte depletion filters, eg, the estimated risk for a bone marrow transplant recipient is only 2.4% using a leukocyte depletion filter (13).

Although the risk of transmission of infectious agents through blood and plasma products is very low, the possibility of risk with a new or previously unrecognized agent is always present. Hence, a reassessment of the potential transfusion risk of a new or previously unrecognized agent is always necessary. Therefore, it is important to make sure that transfused patients are aware that they received blood, blood products or manufactured plasma-derived products, and that the discharge or outpatient note adequately documents these transfusions and records the label code numbers for the specific products used.

Recently, a pilot project aimed at improving surveillance for adverse events with transfusion of blood and blood products (Transfusion Transmitted Injuries Surveillance System) was carried out by Health Canada and four provinces (British
This pilot has demonstrated the benefits of standardized case definitions, report forms, and the added value of electronic reporting for ease and timeliness of data analysis. The Transfusion Transmitted Injuries Surveillance System program has now been extended to four other provinces and is expected to be applied nationwide by 2006. When fully implemented, this program is expected to improve the quality and timeliness of risk estimates for blood related infectious diseases and injuries.

REFERENCES


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The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate. This article also appears in Paediatr Child Health 2004;9(3).