5.3: Infectious hazards of transfusion

Historically, transfusion-transmitted infections (TTIs) dominated the transfusion safety agenda but they are now rare in developed countries. However, constant vigilance is required to counter the risk from established and newly emergent pathogens in the era of mass international travel. Novel transfusion-transmissible agents, such as prions, have also emerged to threaten the safety of the blood supply.

5.3.1: Viral infections

With modern donor selection and testing, hepatitis B, hepatitis C and HIV transmission are now very rare in the UK (Table 5.3). The current risk of an infectious donation entering the UK blood supply is now <1 in 1.2 million donations for hepatitis B, <1 in 7 million for HIV and <1 in 28 million for hepatitis C.

With the exception of hepatitis B, conventional screening tests were traditionally based on the detection of viral antibodies in donor blood. There is a small risk of infectious products entering the blood supply if a donation is made during the window period early in the course of infection before a detectable antibody response. These window periods have been much reduced by the addition of antigen testing and nucleic acid testing (NAT). Donations from new donors carry a slightly higher risk of viral positivity than repeat (previously tested) donors. Table 5.4 summarises the 23 confirmed viral transmissions (28 affected recipients) reported to the UK Blood Services between 1996 and 2012.

Table 5.3 Estimated risk per million blood donations of hepatitis B virus, hepatitis C virus and HIV entering the blood supply due to the window period of tests in use, UK 2010–2012 (data and information collected by the NHSBT/Public Health England Epidemiology Unit)
### Table 5.4 Confirmed viral transfusion-transmitted infections, number of infected recipients and outcomes reported to UK Blood Services 1996–2012 (extracted from SHOT Annual Report 2012)

<table>
<thead>
<tr>
<th>Infection</th>
<th>No. of incidents</th>
<th>No. of infected recipients</th>
<th>Deaths related to infection</th>
<th>Major morbidity</th>
<th>Minor morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>11</td>
<td>13</td>
<td>0</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>HIV</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>HTLV</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Parvovirus B19</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

#### 5.3.1.1: Hepatitis A

This is primarily an acute enteric infection spread by the faeco-oral route (contaminated food or water). Transmission by transfusion is very rare as affected individuals are usually unwell and deferred from donation. There is no carrier state and blood donations are not screened for hepatitis A antibody or antigen. As a non-enveloped virus it is resistant to methods of pathogen inactivation such as solvent detergent treatment.

#### 5.3.1.2: Hepatitis B
The hepatitis B virus (HBV) is readily transmitted by infectious blood or body fluids, including sexual intercourse and parenteral drug use, and perinatal transmission is common in endemic areas such as the Far East and China. Most patients recover after the initial episode of acute hepatitis but some develop a chronic carrier state, estimated at 350 million individuals worldwide, with long-term risk of cirrhosis of the liver and hepatocellular cancer. Hepatitis B remains the most commonly reported viral TTI in the UK because of window period transmissions but more sensitive screening tests for blood donations, such as HBV NAT, are increasingly effective.

5.3.1.3: Hepatitis C

There are around 170 million affected individuals worldwide. Initial infection is often symptomless but around 80% of patients develop a chronic carrier state with long-term risk of cirrhosis, liver failure and liver cancer. Hepatitis C was formerly a major cause of TTI, known as ‘non-A non-B hepatitis’, but the risk of transmission by blood transfusion has fallen dramatically since the introduction of antibody screening in 1991 and progressively more sensitive tests for hepatitis C antigen and RNA since 1999.

5.3.1.4: Hepatitis E

Caused by a small non-enveloped RNA virus, hepatitis E was formerly believed to be most prevalent in warmer climates and less developed countries where it is mainly spread by the faeco-oral route. In Western countries, recent studies have indicated large numbers of asymptomatic infections and up to 13% of individuals in England are seropositive for hepatitis E antibodies. Hepatitis E usually produces a self-limiting acute hepatitis but can lead to chronic infection, especially in immunocompromised patients, and may cause cirrhosis of the liver. An increase in the frequency of diagnoses of hepatitis E in patients in the UK has been seen in recent years. Transmission by blood transfusion has been confirmed with single UK cases reported to SHOT in 2004 and 2012. Blood Services are monitoring the situation closely, and working to establish the risk to transfusion recipients.

5.3.1.5: Human immunodeficiency virus (HIV) 1 and 2

Transfusion transmission by both single-donor and pooled blood components was common early in the course of the 1980s epidemic of acquired immunodeficiency syndrome (AIDS). Modern donor selection and screening has made transmission a rare event in the UK. The two incidents identified since SHOT reporting began (1996 and 2003) were both from HIV antibody negative window period donations before the introduction of HIV RNA screening.

5.3.1.6: Cytomegalovirus (CMV)

Cytomegalovirus is a common herpes virus that causes asymptomatic infection or a mild glandular fever-like illness in most healthy individuals. Despite an antibody response (seroconversion), the virus persists in blood monocytes and 50–60% of adults in the UK, including blood donors, are lifelong carriers of the virus. It can be transmitted by transfusion of cellular blood components although this may be difficult to distinguish from reactivation of previous infection. CMV can cause severe, sometimes fatal, infection in fetuses, neonates and immunocompromised adults. There has long been debate about the relative merits of donor CMV antibody screening (CMV negative components) or routine pre-storage leucodepletion in preventing transmission to patients at risk. In 2012, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) produced an evidence-based position statement (http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_133086.pdf). This can be summarised as follows:

- CMV seronegative red cells and platelets should be provided for intrauterine transfusions and neonates (up to 28 days after expected date of delivery).
- CMV seronegative granulocytes should be provided for CMV seronegative recipients.
Transfusion Handbook / 5.3: Infectious hazards of transfusion

- CMV seronegative red cells and platelets should be provided, where possible, for pregnant women.
  In an emergency, such as major haemorrhage, standard leucocyte-depleted components should be
given to avoid delay.
- Standard pre-storage leucodepleted components are suitable for all other transfusion recipients,
  including haemopoietic stem cell transplant patients, organ transplant patients and immune deficient
  patients, including those with HIV.

5.3.1.7: Human T-cell lymphotropic virus types I and II (HTLV I and II)

These T-cell-associated RNA retroviruses are endemic in southwest Japan, the Caribbean Basin, sub-
Saharan Africa and parts of South America, where they affect 15–20 million people. They are transmitted by
sexual contact, breastfeeding, shared needles and blood transfusion. The clinical significance of HTLV II is
uncertain but HTLV I is associated with a 1 to 4% lifetime risk of developing adult T-cell leukaemia
/lymphoma (ATLL) or the chronic neurological disease HTLV I related myelopathy (HAM) many decades
after infection. The combination of donor screening for antibodies to HTLV I and II plus leucodepletion of
cellular blood components has virtually eliminated transmission by transfusion in the UK.

5.3.1.8: Human parvovirus B19 (HPV B19)

Infection with this common, seasonal, non-enveloped DNA virus is often asymptomatic and there is no
chronic carrier state. It causes the childhood illness erythema infectiosum (‘slapped cheek syndrome’).
Transient infection of red cell precursors in the marrow can cause an aplastic crisis in patients with
shortened red cell survival such as sickle cell disease, thalassaemia major and chronic haemolytic
anaemias. Infection of non-immune mothers in the second trimester of pregnancy may cause severe
anaemia (hydrops fetalis) or death of the fetus. The virus can be transmitted by cellular blood components
or frozen plasma and is resistant to pathogen inactivation techniques such as solvent detergent treatment.
Although routine blood donor testing is not performed, only one TTI was reported to SHOT between 1996
and 2012. Products manufactured from large donor plasma pools, such as immunoglobulins and clotting
factor concentrates, are screened for high titres of HPV B19 RNA.

5.3.1.9: West Nile Virus (WNV)

This mosquito-borne flavivirus has spread from its traditional distribution in Africa, western Asia, southern
Europe and Australia in recent years and now produces seasonal epidemics across the United States and
Canada, usually between May and November. Most infections are mild or asymptomatic, but around 0.5%
of patients develop severe encephalitis that may be fatal. Blood donors may transmit the infection during
the 3- to 15-day incubation period; therefore, individuals returning from affected areas are deferred from
donation for 28 days or may be accepted for donation with the added precaution of WNV NAT screening.

5.3.2: Bacterial infections

5.3.2.1: Syphilis

All donations are routinely screened for antibodies to Treponema pallidum. Transmission is now extremely
rare and no cases have been reported since SHOT surveillance began in 1996.

5.3.2.2: Other bacterial infections

Blood components may be contaminated by bacteria, most often derived from the donor arm at the time of
collection, which can proliferate on storage and harm the recipient. Bacteria from the normal skin flora, such
as the coagulase negative staphylococci rarely produce severe infections although febrile reactions may
occur. More pathogenic gram positive bacteria, such as Staphylococcus aureus, and gram negatives, such
as E. coli, Klebsiella spp. and Pseudomonas spp., may produce life-threatening reactions. Between 1996
and 2012, 40 acute transfusion reactions due to confirmed bacterial transmission were reported to SHOT,
affecting 43 recipients, of whom 11 died. Thirty-three of these transmissions were from platelet packs and seven were from red cells.

Bacterial TTIs are more common with platelet components because of their storage at 20–24°C. The risk increases with storage time after donation and is the main reason for the short shelf life of platelet components. Platelet donors often give two or more adult therapeutic doses at a single apheresis session, with the risk of an infected donation affecting multiple recipients. Up to 1 in 2000 platelet packs contain detectable bacteria 5 days after donation and fatal reactions have been reported in 1 in 25 000–80 000 transfusions. By contrast, most pathogenic bacteria grow poorly in refrigerated red cell components although some gram negative organisms, such as Yersinia enterocolitica and Pseudomonas spp., can proliferate in these conditions.

5.3.2.3: Preventing bacterial transmission

Improved techniques for cleaning/decontamination of the donor arm and diversion of the first 20–30 mL of the donation into a side-pouch (this blood is used for donor testing) have produced a marked fall in the reports of bacterial TTIs in the UK. No cases were reported to SHOT between 2009 and 2012. As an additional safety measure, the UK Blood Services have introduced automated culture of all platelet donations and this may allow the safe extension of their shelf life from 5 to 7 days.

Pathogen inactivation (PI) technologies for platelets and red cells, such as the use of light-activated psoralens that kill organisms by damaging their DNA or RNA, are being developed and have the potential to eliminate both bacterial and viral TTIs. At present, the cost-effectiveness of PI is uncertain and early clinical studies of the currently licensed system have raised concerns about its effect on platelet function.

5.3.3: Protozoal infections

5.3.3.1: Malaria

Despite increasing international travel, transfusion-transmitted malaria remains a rare event in the UK. There have been two cases reported to SHOT (both Plasmodium falciparum) since 1996, the last in 2003, one of which was fatal. A policy of taking a travel history at the time of donation combined with deferral and, where indicated, testing for malarial antibodies has proved effective.

5.3.3.2: Chagas disease

This serious multi-system disease, caused by Trypanosoma cruzi, is endemic in Central and South America and may be transmitted by blood transfusion. No transfusion-transmitted cases have been recorded in the UK and precautions centre on donor history of residence/travel and, where appropriate, testing for antibodies to the parasite.