NHS
Blood and Transplant

Information for clinicians

Cytomegalovirus (CMV) Negative Blood Components

Guidance on the indications for CMV IgG negative blood components.

What is CMV?

CMV is a type of herpes virus. Primary infection is usually asymptomatic but may cause a flu or glandular fever-like illness, leading to a lifelong infection in all age groups. The virus can reactivate from its latent state and it is commonly shed asymptomatically in various bodily secretions, such as nasopharyngeal secretions and urine. More severe disease may occur in individuals with impaired immunity such as fetuses, neonates and patients, of any age, who have been immuno-suppressed by disease or treatment.

How are people exposed to CMV?

Infection frequently occurs in childhood and, in the UK, it is estimated that 50-60% of adults are CMV positive. As CMV is very common, most adults will have been infected earlier in life and will have developed an immune response to the virus in the form of immunoglobulin (IgG) i.e. they will be CMV IgG positive.

A person can become infected with CMV in several ways, most commonly via person-to-person contact, through exposure to body fluids. A mother can infect her unborn baby in utero or her newborn baby via breastfeeding. Most disease in immuno-compromised patients occurs through these routes or from reactivation of a previous CMV infection.

CMV is less commonly transmitted by receiving donated blood or organs from a donor who is carrying CMV, or who has an acute CMV infection but is CMV IgG negative i.e. they have not yet formed an immune response but have the virus circulating in their blood. Transmission of CMV present in blood components can give rise to a primary infection in CMV negative patients or reinfection in previously infected patients.

Why is CMV important?

CMV can cause a potentially life-threatening infection in patients who cannot form an effective immune response, particularly following HSCT and in the perinatal period.

There are certain groups at particular risk of severe disease:

- **Fetuses and neonates:** CMV is the most common congenital infection in the developed world, affecting 1-2% of infants worldwide (Luck and Sharland, 2009) and 0.3-0.4% in the UK (Griffiths et al, 1991). CMV is estimated to cause up to 12% of all sensorineural hearing loss (Peckham et al, 1987) and 10% of cerebral palsy. Primary infection is more likely to cause symptomatic congenital CMV and may increase the risk of spontaneous abortion, stillbirth and fetal hydrops. Ophthalmic complications including chorioretinitis, cataract and blindness occur in 10-20% of congenital cases presenting in the neonatal period. Mortality from symptomatic neonatal CMV infection is 10-30%, but much higher if the baby is premature.
- **Immuno-compromised patients:** Immuno-compromised patients who have not been infected with CMV (CMV negative) are also at risk from transfusion-transmitted CMV infection, person-to-person contact, and stem cell or solid organ transplants. The Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) undertook a literature review and risk assessment and concluded that leucodepletion (i.e. the blood component is filtered to reduce white cells) is as effective as CMV IgG negative blood components. These patients should therefore receive leucodepleted blood; CMV IgG negative donations are not required. This approach has also been adopted in other developed countries. However, granulocyte components cannot be leucodepleted and therefore CMV negative granulocyte components are required for CMV negative patients.

Who needs to receive CMV IgG negative blood components?

In March 2012, SaBTO released a position statement containing the following indications for the provision of CMV IgG negative blood components:

- Intra-uterine transfusions
- Neonates up to 28 days post expected date of delivery
- Pregnancy:
    - Elective transfusions during pregnancy (not during labour or delivery)
    - If in an emergency situation it is not possible to provide CMV negative blood components, leucodepleted components may be used
- CMV negative patients requiring granulocyte transfusion.

Organ transplant patients do not require CMV IgG negative blood components. CMV IgG negative red cells and platelets may be replaced with leucodepleted blood components for adults and children post HSCT for all patient groups, including negative donors and recipients. However, individual transplant centres should have a policy of CMV monitoring by PCR for HSCT and some groups of transplant patients. This practice allows the distinction between early detection of any possible CMV infection (whether transfusion-transmitted, acquired or reactivated) or passive acquirement of CMV IgG antibody (multiple transfusions, transfusion of plasma or immunoglobulins) .

What is a CMV negative blood component?

CMV negative blood components are those collected from donors who have been tested and found negative for CMV IgG antibodies. A proportion of donations are screened by the blood services for CMV IgG antibodies to provide a ‘CMV negative’ inventory for red cells and platelets, which are provided to hospitals on request.

Depending on age group, 25-40% of UK blood donors are CMV IgG antibody positive (this is a smaller number than that stated above for ‘adults’, as the prevalence of CMV IgG positivity increases with age and donor populations are younger than screened adult populations).

How is the risk of CMV transmission through blood components reduced?

The virus can be transmitted through white cells contained in blood componentsI i.e. units of red cells and platelets. In the UK, blood components (except white cell components) are leucodepleted to reduce the transmission risk of variant Creutzfeldt Jakob Disease (vCJD). However, it cannot be guaranteed that the risk of transmitting CMV is eliminated (Vamvakas, 2005), in the same way that CMV IgG testing is not a guarantee.

Frozen components, including fresh frozen plasma (FFP) and cryoprecipitate, have not been shown to transmit CMV so the CMV status is not shown on the label of these components.

Granulocyte components should be provided as CMV negative for all CMV negative patients. A medical decision may be made to transfuse units which are not CMV tested, or which are known to be CMV IgG positive, into a CMV negative patient if the urgency to treat a non-responsive bacterial or fungal infection outweighs the risks of potentially developing CMV infection at a later stage. For further information contact your transfusion practitioner, consultant haematologist or transfusion laboratory.

References:

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