Criteria for the Use of CMV Seronegative Blood

Cytomegalovirus (CMV) is one of the herpes family of viruses with a very high worldwide prevalence of human infection. Most people are asymptomatic. CMV is a frequent cause of congenital or perinatal viral disease. In some underdeveloped countries the prevalence of the disease approaches 100%. In developed nations approximately 50% of the population are seropositive for CMV.

CMV is a latent virus which may become active for reasons which are not fully understood. The great majority of infected people have no symptoms, however serious disease can develop in some predisposed groups. These include low birthweight neonates born to CMV seronegative women, transplant recipients and other immunocompromised persons.

CMV is shed even in individuals with adequate levels of neutralizing antibodies. Therefore any seropositive donor may have latent or active CMV virus. If the virus is present it can induce CMV infection in the recipient. The frequency of CMV acquisition among recipients of blood products is estimated to be 9.0%[4].
Approximately 15% of seropositive blood donors have been estimated to be potential transmitters of CMV infection[4]. If one third to half of blood donors are seropositive, then 5-7.5% of all donors can transmit CMV infection. Although the risk does not appear great, these donors cannot be identified.

At present, complete prevention of transmitting CMV by blood product transfusion requires the use of seronegative donors only. Since there are not sufficient seronegative blood products available for all the transfusions given, criteria must be established for providing this product to those with the greatest need, i.e. those at the greatest risk of adverse effects from CMV infection. The efficacy of leuko-poor and washed cells, which have reduced numbers of white cells which harbor CMV virus, is being investigated.

**Premature Infants of Low Birth Weight**

The exact criteria for "low birth weight", although varying from institution to institution, are actually quite similar. Dr Adler[2] (Medical College of Virginia) uses a cutoff of 1500 grams but would give CMV seronegative products to neonates over this limit if they would require multiple transfusions. Dr Pety[5] (UCLA) sets the limit at 1300 grams. Chan and Vyas[4] use the criterion of 1,250 grams and require the infant to be seronegative for CMV.
A study by Yeager[8] reviewed the risk of transfusing seropositive blood products. In the study, Yeager showed that among 40 infants born to seronegative mothers and given seronegative blood, no CMV related infections were noted. However when children of seronegative mothers were given seropositive blood, out of 74 infants, ten (13.5%) CMV infections were noted, of which 4 were fatal. When 32 babies of seropositive mothers were given seropositive blood, none developed CMV infection. All the infants who developed severe CMV infection weighed 1,200 grams or less. Infants whose birth weights were greater than 1,200 grams or were full term, regardless of their CMV serologic status, did not appear to be at significant risk. Only low birth weight infants of seronegative mothers, who were transfused with seropositive blood, were at risk for CMV infection. These results were verified by Adler[1].

Therefore, CMV seronegative blood should be used for transfusions given to low birth weight infants (conservatively under 1500 grams) born to seronegative mothers. Since full term infants have not been shown to be at risk, regardless of the serotype of the blood, CMV seronegative products need not be specified in this group. It may be logistically easier and more cost-effective to give seronegative blood to all neonates, than to give seronegative blood only to infants in whom the medical benefit is clear (i.e. seronegative infants with low birth weights). (?)
Intrauterine Transfusions

CMV infections among small newborns are more frequent and more serious if the mother is infected during pregnancy. Therefore all intrauterine transfusions given to seronegative mothers should be seronegative for CMV. Pregnant women and women breast feeding premature infants would also be included in the group requiring CMV seronegative blood transfusions.

Transplant Recipients

The immunosuppressive therapy given to prevent rejection can render the patient highly susceptible to CMV infections. In patients who are seropositive, CMV can develop by reactivation of latent virus. However patients who are seronegative and develop active CMV infection have acquired the virus from either a seropositive organ donor or a seropositive blood donor.

In a study by Bowden[3], it was shown that CMV infections were significantly less common when seronegative bone marrow recipients were given seronegative blood products, only one infection was found among 32 patients. In contrast, 8 out of 25 seronegative patients developed CMV infections when they were given standard
blood products (unscreened blood products from random donors, in whom approximately 50% may be assumed to have been negative for CMV.)

In a study by Rakela[6] involving 26 patients undergoing liver transplantation, twelve CMV associated infections were noted after transplantation. Seven (54%) occurred in 13 patients who were seropositive prior to transplantation and 5 (38%) in seronegative patients. All 5 patients in the seronegative group who became infected had received an organ from a seropositive donor. None of the patients who were seronegative and received an organ from a seronegative donor became infected. However, only CMV seronegative blood was used in seronegative patients and therefore no evaluation of the risk of seropositive products could be inferred in this group.

Five of the seven patients, who were seronegative prior to liver transplantation, received a liver from a seropositive donor and CMV unscreened blood products, developed multiorgan involvement of CMV disease. Although it would be reasonable to assume that the CMV infection stemmed from the donor organ, these patients were treated with unscreened blood products and the effects, if any, of the blood products used in this group were not studied. This study, however, supports the concept of "protective matching"; giving a seronegative recipient an organ from a seronegative donor and using CMV negative blood products, if possible.
Acquired Immune Deficiency Syndrome (AIDS)

Since the majority of patients with AIDS are CMV seropositive, the need for seronegative blood products would be restricted to the few seronegative patients. Patients with AIDS have numerous immunologic abnormalities and are highly susceptible to multiple infections, therefore the use of seronegative products may be justified in those few who prove to be CMV seronegative.

Conclusion

The criteria for patients at high risk for CMV infection has been reviewed. The actual number of patients identified by these criteria will vary with hospital. Although there is not enough donated CMV seronegative blood to fill all required transfusions, approximately 50% of the blood supply is seronegative and we should be able to supply these high risk patients.

Many patients will receive products which are untested for CMV and therefore the effect of these transfusions will be difficult, if not impossible to evaluate. To make it more difficult, the status of these patients as regards their CMV status prior to transfusion is not always studied. We already know that significant numbers of seronegative patients seroconvert after transfusion (approximately 300,000 patients per year in the United
States[4]). What long term effects this will have is difficult to say and remains to be further evaluated.
REFERENCES


2. Adler, SP, personal communication.


5. Pety, personal communication.


7. Stayno, S, Poss, RF, Dworsky, ME, et. al.: Congenital Cytomegalovirus Infection: The Relative Importance of