

LEUCOCYTE DEPLETION OF BLOOD COMPONENTS - POLICY RECOMMENDATION OF BLOOD TRANSFUSION SERVICES OF SOUTH AFRICA

Leucocytes in blood components are responsible for a number of adverse effects associated with blood transfusion. The pathogenesis has not been precisely elucidated in many instances but it is likely that it is immunologically mediated. Potential mechanisms include clonal deletion or anergy, induction of suppressor cells, production of anti-idiotypic antibody, suppression of NK cell activity and several others.¹ As a consequence a number of clinicians prefer to use leucocyte depleted components.

The clinical indications advanced for depleting blood components of leucocytes (leucodepletion) are as follows:

- Avoidance of febrile - non haemolytic transfusion reactions (FNHTR's)
- Reduction in incidence of refractoriness to platelet transfusions (as a result of HLA alloimmunisation)
- Prevention of cytomegalovirus (CMV) infection by blood components
- Reduction in incidence of post operative infections
- Reduction in incidence of cancer recurrence (specifically colo-rectal cancer)
- Reduction in post-operative mortality
- Avoidance of reactivation of viral infections such as HIV and CMV
- Avoidance of sensitisation to transplantation antigens
- Avoidance of prion transmission [i.e. avoidance of agent for variant Creutzfeldt-Jakob disease (vCJD)]

Accordingly, filters capable of reducing leucocytes by several orders of magnitude have been developed and can effectively reduce the number of white cells in, for example, a red cell concentrate to $< 1 \times 10^6$. A less efficient but much more economical process for depleting components of leucocytes involves removing the buffy coat from red cell components. The buffy coat refers to the ± 0.5 cm layer that sits on top of the red cells following centrifugation of the donated blood unit and consists largely of young red cells (reticulocytes), platelets and leucocytes. The removed buffy coats can be pooled, admixed with plasma and, by means of differential centrifugation, used for the preparation of platelet concentrates. This ultimately results in red cell concentrates with residual leucocytes intermediate in number between leucocyte depleted components and those with the buffy coat retained. Buffy coat derived platelet concentrates have also been shown to have fewer leucocytes than other technologies using platelet rich plasma as starting material. It is important to note that single donor platelet concentrates collected by apheresis are leucocyte depleted as part of the process of collection.

A number of countries (about 20 in all and almost exclusively first world) have adopted a policy of routinely leucocyte depleting all red cell and platelet components by including pre-storage leucodepletion filtration in the component manufacturing process - so-called *universal* leucocyte reduction (ULR). Others have adopted a policy of *selective* leucodepletion of components (e.g. USA, Australia). The costs associated with ULR are considerable e.g. in the USA it would amount to $> \$400$ m per annum and in South Africa, ULR would add approximately 24% to the total transfusion budget. Given the competing health priorities in South Africa,

there should therefore be convincing evidence that such an intervention is clinically beneficial and cost effective².

The Transfusion Services in South Africa have reviewed the medical literature and conclude the following:

- There is good evidence to support the avoidance of FNHTR's by leucodepletion^{3,4}
- Leucodepletion of platelet concentrates will reduce the incidence of platelet refractoriness to platelet transfusions⁵
- Leucodepletion significantly reduces the risk of transfusion-transmitted CMV infection in susceptible individuals⁶
- The evidence for reduction in post-operative infection is not consistent⁷⁻¹⁰
- The evidence for reduction in cancer recurrence is not consistent¹¹
- Although meta-analyses do not provide convincing evidence of an overall reduction in post-operative mortality for leucodepleted products, sub group analyses suggest a benefit for seriously ill and cardiac surgery patients^{8,10}
- An association with reactivation of viral infections (HIV and CMV) and non-leucodepleted components has not been demonstrated¹²
- Sensitisation to transplant antigens can be ameliorated by leucodepletion where HLA allo-immunisation is important¹³
- Leucodepletion may reduce prions in blood components but there is as yet no evidence that leucodepletion will avoid transmission of vCJD by blood components¹⁴

RECOMMENDATIONS

A policy of *selective* leucodepletion of blood components is therefore recommended as follows:

- All standard red cell concentrates will be buffy coat depleted
- Random donor platelet concentrates will be prepared from buffy coats
- Single donor platelet concentrates collected by apheresis must incorporate a leucocyte depletion process
- Patients on chronic transfusion regimens should receive leucodepleted products
- Patients at risk for CMV infection should receive leucocyte depleted products
- Organ and stem cell transplant patients should receive leucocyte depleted products
- Infants < 1 year old should receive leucodepleted products
- Cardiac surgery, and critically ill patients should receive leucocyte depleted products
- Pre-storage (< 48 hours after donation) leucodepletion in blood processing laboratories is recommended since there is better quality control of the finished product and there is some evidence to suggest that cytokines may accumulate with storage.¹³ If this product is unobtainable it is recommended that the freshest units available be filtered in the blood bank for immediate use. Bedside leucodepletion filters should only be utilised when neither of the former two options are available. It is also important to note that the standard blood giving administration set with an in line 170µm filter should be still be used to administer leucodepleted

components. Furthermore, once blood has been filtered in the blood bank there is no justification for using a bedside leucodepletion filter i.e. blood must not be leucodepleted twice.

We emphasise that the above should be regarded only as guidelines. If individual clinicians wish to use leucocyte-depleted products for indications that fall outside these guidelines they should request accordingly and the Blood Services will provide the product if available.

It must be borne in mind that all leucodepletion filters are imported and that the cost of a leucocyte depleted blood component is considerably greater than a standard component.

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