

AUSTRALASIAN SOCIETY OF BLOOD TRANSFUSION INC.

Topics in

Transfusion

Medicine

SPECIAL EDITION:

GUIDELINES

- 1. IRRADIATED BLOOD PRODUCTS**
- 2. LEUCOCYTE DEPLETION OF BLOOD AND BLOOD COMPONENTS**

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**GUIDELINES
FOR**

- 1. Irradiated Blood Products**
- 2. Leucocyte Depletion of Blood and
Blood Components**

1996

**Prepared by
The Scientific Subcommittee of
The Australasian Society of Blood Transfusion Inc.**

**145 Macquarie Street
Sydney NSW 2000**

INTRODUCTION

On behalf of the Society's Scientific Subcommittee it is a great pleasure to introduce two further sets of guidelines; "Irradiated Blood Products" and "Leucocyte Depletion of Blood and Blood Components". Both are the culmination of many hours of work and discussion by members of the Scientific Subcommittee, plus consultations with a variety of other experienced ASBT members.

The Society has now developed quite a significant track record and expertise in the production and publication of such practice and management guidelines. "Guidelines for Pretransfusion Testing" and "Guidelines for Pre-operative Autologous Blood Collection" have and are gaining widespread national recognition and acceptance.

These endeavours are not only significant but timely. Practice management guidelines and evidence-based medicine are currently a major focus of the National Health and Medical Research Council to whom the ASBT's guidelines will be submitted.

Stepping aside from my role as a co-opted member of the Scientific Subcommittee, I think that the committee deserves to be acknowledged for all of their hard work and I wish them continuing success in their future activities.

John Gibson
Editor

Scientific Subcommittee Membership 1996

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Members:	Dr G Davey	Victoria
	Dr J Gibson	New South Wales
	Mrs J James	Victoria
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These guidelines are the considered opinion of the Scientific Subcommittee and the Council of the Australasian Society of Blood Transfusion. They are not intended as proscriptive statements but best practice guides. All correspondence should be directed to the Chairman of the Scientific Subcommittee.

IRRADIATED BLOOD PRODUCTS

Introduction

Cellular blood products are irradiated to reduce the risk of graft versus host disease (GVHD) following transfusion of these products to patients who are usually immunosuppressed. Transfusion associated GVHD is a rare complication and is due to survival and engraftment of viable donor lymphocytes. Clinical features include erythematous skin rash, fever, gastrointestinal and hepatic dysfunction.

Currently, product irradiation is the only readily available method of preventing transfusion associated GVHD. Third generation leucocyte depletion filters in use at present are not 100% effective, especially for blood donations which have a higher than normal white cell count.

Irradiation of Products

Gamma radiation is the most common form of radiation used to inactivate all potentially proliferative cells and sources available include Cobalt 60 and Caesium 137 isotopes. Specially designed blood bank irradiators or radio-therapy machines calibrated to deliver the equivalent dose are used to carry out the irradiation of blood and blood products.

Dose requirements

The current FDA (USA) guidelines recommend that "the dose delivered shall be a minimum of 25 Gray (Gy) (2500 Rads) targeted to the central position of the container. A minimum dose of 15 Gy shall be delivered to all other parts of a component". A dose of 30 Gy is preferable.

Quality Assurance

To ensure that the products irradiated have received the minimum dose, radiation sensitive film that gives visual indication of dose received should be used at each irradiation procedure.

Products that have been irradiated should be permanently labelled to indicate that they have been irradiated.

The irradiators must have at least an annual dosimetry calibration performed to ensure correct dosage of radiation delivered.

Products to be irradiated

The following products are known to contain viable lymphocytes and therefore should be irradiated, when indicated.

- Whole Blood
- Red Cell Concentrates
- Platelets
- Buffy Coat Preparations

The following products have NOT been associated with GVHD

- Fresh Frozen Plasma
- Cryoprecipitate

Product Shelf-life

Irradiated red cells should have an expiry date that is either the originally assigned post collection expiry, or 28 days (Baxter packs), 21 days (Tuta packs) from the date of irradiation, whichever occurs first. The effect of hyperkalaemia should be considered when transfusing irradiated blood for intrauterine transfusions or neonatal exchange transfusions. In these cases, blood that has been irradiated less than 24 hours previously should be used. For neonatal top-up transfusions or transfusions for paediatric patients, red cells should be transfused within 96 hours of irradiation. Irradiated platelet expiry can remain at 5-7 days post collection.

Risks associated with irradiated products

At the recommended dose of irradiation, mild hyperkalaemia due to accelerated potassium leakage from red cells is the only side effect worthy of consideration for risks associated with irradiated blood products. This effect is of little consequence to adult recipients or recipients of platelets only.

Irradiation at the recommended dose will not affect viral transmission and is not a substitute for CMV negative or leucodepleted products. Irradiated products have the same risk in causing febrile reactions and HLA alloimmunisation as any other non-leucodepleted blood products.

Clinical indications for irradiated cellular products

A) Absolute - definite evidence associated with GVHD

- 1) Allogeneic and Autologous Bone Marrow/PBSC Transplant recipients
- 2) Aplastic anaemia (patients receiving immunosuppressive therapy)
- 3) Hodgkin's Disease
- 4) Dedicated Donations (from first or second degree relatives)
- 5) Intrauterine and all subsequent transfusions and neonatal exchange transfusions
- 6) Premature/Very Low Birth Weight infants (<1500g)
- 7) Congenital Cellular Immunodeficiency Disorders
- 8) HLA matched single donor platelets.
- 9) Patients receiving purine analogues with associated immunosuppression.
- 10) Granulocyte transfusions.

B) Possible indications - cases have been reported but no controlled studies available

Lymphoid malignancies

- 1) T Cell malignancies
- 2) Patients with B cell malignancy who receive chemotherapy and/or radiotherapy leading to lymphopenia $<0.5 \times 10^9/L$.

Non lymphoid malignancies

- 1) Acute Myeloid Leukaemia
- 2) Chronic Myeloid Leukaemia
- 3) Any patient who received high doses of chemotherapy and/or irradiation sufficient to cause lymphopenia $<0.5 \times 10^9/L$.
- 4) Patients receiving long term or high dose steroids as therapy for their malignancies.

C) No indication - no cases reported

- 1) AIDS (where none of the above apply)
- 2) Congenital humoral deficiency disorder
- 3) Term infants (where none of the above apply)
- 4) Thalassaemias
- 5) Haemophilia

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LEUCOCYTE DEPLETION OF BLOOD AND BLOOD COMPONENTS

INTRODUCTION

The presence of leucocytes in blood products has been shown to be detrimental to the quality of the product and responsible for many of the adverse side effects of transfusion. Established events attributable to the presence of leucocytes in transfused blood components and which warrant consideration in patient treatment include:

- viral transmission (HIV, CMV, HTLV1)
- non haemolytic transfusion reactions
- initiation of immune response

Leucocyte reduction of red cells can be achieved by (in order of increasing cost):

a) *Removing the buffy coat from red cells at source.*

This results in approximately a one log removal of leucocytes and may be sufficient to prevent most febrile nonhaemolytic transfusion reactions in patients who, have previously experienced these reactions. These units retain a normal shelf life. This product may not be available at some centres. If reactions persist the use of leucocyte depletion filters is indicated.

b) *Filtering red cells and platelets*

Leucocyte depletion filters (LDF) effect a 3-4 log reduction of leucocytes when used correctly. Filtering is best accomplished at source (ie. by the transfusion service) as soon as possible after collection. It is well established that this approach provides consistent leucodepletion and reduces the release of cytokines during storage. Filtering can also be conducted by placing a LDF in the transfusion line at the bedside or performed in the laboratory prior to the commencement of transfusion. Filtered components have a normal shelf life provided the procedure has been conducted in a closed system ie. using a sterile docking device. Due to the risk of bacterial contamination, the shelf life of components filtered in an open system must be reduced to no more than 24 hours from the time of filtering.

c) *Washing red cells*

This will achieve a 1.5 - 2 log removal, provided the buffy coat is removed before or during the washing procedure. Washed cells are prepared in an open system and therefore have only a 24 hour shelf life after washing. This product is generally not recommended as it is more expensive and less effective than LDF.

d). *Freezing and deglycerolising red cells*

The level of leucocyte depletion approximates that of LDF. A 24 hour shelf life applies as for washed red cells. This process is very expensive and is not recommended for the routine preparation of a leucocyte depleted product. Use of this product should be reserved for patients for whom long term storage is required either because they have a rare blood type or have multiple antibodies.

LDF are most commonly used for leucocyte depletion because of their convenience and the fact that a satisfactory level of leucocyte depletion is achieved to meet most clinical requirements.

There are many different brands and types of LDF. Specific filters are designed for either red cell or platelet concentrate filtration and are not interchangeable. LDF for platelet concentrates also achieve a 3-4 log removal of leucocytes.

The number of units of red cells or platelet concentrates which can be filtered through one filter also varies. Leucocyte depletion does not prevent Graft vs Host Disease in susceptible patients and is therefore not a substitute for irradiation.

The following guidelines for the application of leucocyte depletion consider the cost effectiveness of using leucocyte depletion filters (LDF) as these are expensive. "Established indications" are those for which there is clear evidence of clinical benefit. "Possible indications" include applications for which clinical benefit is unproven.

ESTABLISHED INDICATIONS

1) *Non Haemolytic Febrile Reactions to Red Cell Transfusion (NHFTRr)*

Patients experiencing repeated NHFTRr (> 2) may be uneventfully transfused with leucocyte depleted red cells. Initially, "Buffy coat removed" red cells should be used if available. If reactions persist with this product then the routine use of LDF is indicated.

2) *Aplastic Anaemia for Possible Marrow Transplant.*

There is clear evidence that alloimmunisation due to pretransplant transfusions significantly increase the incidence of allograft rejection in this setting (1). It is therefore recommended that all cellular products should be transfused through LDF for these patients.

3) *Intrauterine Transfusion*

The use of LDF is recommended on theoretical grounds because of the possible risks of maternal alloimmunisation to white cells and viral transmission adversely affecting the fetus. LDF should be used in addition to irradiation of blood products for this procedure.

4) *Prevention of CMV Transmission*

Reduction of contaminating leucocytes to $< 5 \times 10^6$ in cellular products using LDF has been shown to be as effective in preventing CMV transmission as selection of CMV antibody negative products (based on the currently available tests for CMV antibody) (2,3). LDF should only be used in this setting when CMV antibody negative products are unavailable for patients who are immunosuppressed and either untested or CMV antibody negative.

POSSIBLE INDICATIONS

1) *Febrile Reactions to Platelet Transfusions (NHFTRp)*

The relative role of HLA alloimmunisation in NHFTRp is unclear. Recent studies reveal a significant role for cytokines as mediators of febrile reactions (4). Consequently the use of LDF does not always prevent NHFTRp (5). There would seem to be no clear indication for using LDF for prevention of NHFTRp unless HLA or neutrophil antibodies are demonstrable.

2) *Prevention of Alloimmunisation in Patients on Regular Platelet Support*

Although the use of LDF has convincingly been shown to markedly reduce the incidence of HLA alloimmunisation, it is unclear whether the routine use of LDF is cost effective for patients on regular platelet support. The reasons are:

- a) Non immune causes of refractoriness are common.
- b) Some HLA antibodies are transient.
- c) Alloimmunised patients may be managed with HLA matched or crossmatched platelets.

3) *Prevention of Transfusion Induced Immunosuppression*

The established immunosuppressive effects of transfusion have been said to be associated with increased incidence of cancer recurrence following curative surgery, especially for colon cancer, and also with increased incidence of post surgical infections. The role of transfusion in these events however has not been clearly established because of other confounding factors influencing the outcome of surgery (6,7). There is no conclusive evidence that leucocyte depletion may alleviate these effects. It is therefore not recommended that LDF be used for this purpose.

QUALITY ASSURANCE OF LEUCOCYTE FILTERED PRODUCTS:

There are several variables that govern the effectiveness of leucocyte filtration:

a) *The number of leucocytes in the product.*

With very high levels of leucocytes the filter may become saturated and untrapped leucocytes pass through the filter.

b) *The number of units of product passed through the filter.*

An excessive number of units of product passed through one filter will also lead to a leucocyte overload and reduced efficiency. The filter manufacturer's instructions for use should be strictly followed.

c) *The storage time of the product*

Cell fragments accumulate in red cell units during storage. These may pass through LDF and may retain alloimmunising capability. Blood units used for leucodepletion should therefore be the freshest available.

d) *The rate of filtration.*

There is evidence that leucocyte depletion with some filters is more efficient when a fast flow rate is used (maximum flow under normal gravity) (8). This is achieved by laboratory based filtration procedures but bedside filtration is usually conducted over a period at least 1-2 hours.

For bedside filtration it is recommended that filters that are efficient at slower flow rates be used or that transfusion be conducted as quickly as practicable.

e) *The temperature of blood units when filtered.*

The temperature of the product when filtered has been found to influence the effectiveness of leucocyte removal by LDF (9). The efficiency of leucodepletion is reduced as the temperature of refrigerated bag of blood warms to room temperature. Blood units, once issued to a clinical area for leucocyte filtration at the bedside, should therefore be transfused as quickly as practicable.

Bedside vs Transfusion Service filtration.

It has been well established that filtration of blood and components at source results in more consistent leucodepletion to the required 5×10^6 level (10). Filtration at source enables better control of most of the variables cited above. However, as a significant amount of bedside filtration is practised, and monitoring of residual leucocyte numbers cannot be accurately achieved in this setting, the following guidelines will assist in achieving efficient leucocyte removal.

- 1) Stored blood for leucocyte filtration should be as fresh as possible.
- 2) Filter manufacturer's instructions for use should be strictly adhered to, especially instructions concerning priming (or not priming), ensuring removal of air from the filter, transfusing no more than the recommended number of red cell or platelet units through one filter and adherence to instructions regarding flushing or otherwise of the filter.
- 3) **Blood should not be forced through the filter under pressure.** Transfusion should take place as quickly as practicable under normal gravity.
- 4) A standard procedure for these transfusions should be documented within each institution and be readily available to relevant staff.
- 5) Staff responsible for setting up these transfusions should be trained for this function.

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