

POLICY FOR COLLECTION AND TRANSFUSION OF GRANULOCYTES

REASON FOR ISSUE: Removal of ventilation exclusion, removal of aim to provide CMV negative and HLA compatible donors, introduction of lifetime limit on the number of granulocyte donations, change of units of measurement to be consistent with analyser results.

INTRODUCTION

Granulocyte transfusions as a means of treating patients with severe neutropenia and infections have been in clinical practice since the 1970s. However, it was not until research provided guidelines on the minimum number of granulocytes needed and until methods for achieving that number were available, that granulocyte transfusions became a viable therapeutic modality.

SCOPE

NZBS Collection Centres that provide therapeutic apheresis services to District Health Boards.

INDICATIONS

1. Therapeutic Granulocyte Transfusions

The literature has shown granulocyte transfusions may be beneficial and even life-saving in severely neutropenic patients with systemic bacterial or invasive fungal infections. The following criteria will be used in deciding whether to collect granulocytes:

- Persistent neutropenia with a neutrophil count $< 0.2 \times 10^9/L$ and likely to remain neutropenic for more than 5 days
- and**
- The disorder underlying the neutropenia (eg aplastic anaemia) has a good long-term prognosis in this patient
- and**
- A suitable donor is available from whom it is anticipated that a granulocyte collection of $> 10 \times 10^9$ or, in the case of a paediatric patient, $> 0.2 \times 10^9/kg$ granulocytes is attainable
- and**
- either**
- Septicaemia or life-threatening local infection not responding to 72 hours of appropriate antibiotics with significant risk of mortality or permanent morbidity
- or**
- Proven or probable invasive fungal or yeast infection refractory to appropriate anti-fungal therapy.

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2. Prophylactic Granulocyte Transfusions

The limited literature available on prophylactic granulocyte transfusions does offer some support for high-dose cross-match compatible granulocyte transfusions. It is noted that Council of Europe does not currently include prophylaxis as an indication for granulocyte transfusions. Accordingly, all requests for prophylactic granulocyte transfusion will require discussion between NZBS and the clinician involved before commencing collection. The following criteria are the minimum requirements:

- Persistent neutropenia with a neutrophil count $< 0.2 \times 10^9/L$, likely to remain neutropenic for more than 5 days
- and**
- The disorder underlying the neutropenia (eg aplastic anaemia) has a good long-term prognosis in this patient
- and**
- A suitable donor is available from whom it is anticipated that it a granulocyte collection of $> 10 \times 10^9$ or, in the case of a paediatric patient, $> 0.2 \times 10^9/kg$ granulocytes is attainable
- and**
- The patient is at high-risk of developing a serious bacterial or fungal infection.

CONTRA-INDICATIONS

Granulocyte transfusions will be considered to be contra-indicated if:

- The patient's underlying disorder has a poor long-term prognosis
- Alloimmunisation to HLA antigens is known to be present (relative contra-indication)

DONORS

Donors will be obtained from the patient's family, from NZBS's donors and from the New Zealand Bone Marrow Registry.

- The donors must meet the requirements of the current edition of the NZBS Collection Standards
- The donor must be ABO and Rh(D) compatible with the recipient.
- Where the recipient is CMV negative, consideration must be given to sourcing CMV negative granulocyte donations.
- If allogeneic stem cell transplantation is being considered, family members are relatively contra-indicated because of the risk of HLA alloimmunisation.
- The potential risk for thrombotic events should be considered when evaluating potential donors.
- An NZBS Medical Officer must evaluate all donors.
- Granulocytes are mobilized with dexamethasone and/or G-CSF.
- In an effort to minimize donor risk, donors have a lifetime limit of three doses of dexamethasone and G-CSF for granulocyte donations.

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As part of the consent process, donors must be advised of the risks associated with the donation.

- Recognised side effects of dexamethasone include: headaches, insomnia, hunger, and mood changes. Conflicting evidence surrounds whether donors are at risk of posterior subcapsular cataracts later in life following a single dose of steroids.
- Recognised side effects of G-CSF include bone pain, fatigue, and thrombotic complications secondary to thrombocytosis. Donors must also be advised of the theoretical leukaemogenicity risk.
- Recognised side effects of HES include: pruritis and, rarely, anaphylaxis. Coagulation disturbances and renal risks may be mentioned but are not considered real risks in view of the donor's healthy state and the small dose of HES administered.

MOBILISATION

A dose of 5-10µg/kg of G-CSF subcutaneously and/or 8mg dexamethasone orally will be used to mobilise the granulocytes. G-CSF is the preferred option as granulocyte collections after G-CSF can be expected to significantly exceed the minimum of 10×10^9 per unit or $> 0.2 \times 10^9$ /kg for paediatric collections.

COLLECTION

Collection will take place under the supervision of an NZBS Medical Officer using a suitable apheresis collection machine. With the donor's consent, a sedimenting agent, Hydroxyethyl starch (HES) anticoagulated with trisodium citrate, will be used to enhance the collection .

TRANSFUSION

Granulocyte collections must not be leucodepleted, as this will remove the granulocytes. It is noted that the granulocyte collection will contain a large number of lymphocytes and that HLA alloimmunisation is a recognised complication of granulocyte transfusions. For the same reason all granulocyte collections must be irradiated prior to administration.

The granulocyte collection will be collected for and issued to a single named recipient. The collection should be transfused as soon as possible to the patient. If this is not possible, the granulocytes may be stored for up to 24 hours from the time of collection at 20 – 24°C. The storage period must not exceed 24 hours. Do not agitate during storage.

Transport temperature of this component must be kept as close as possible to the recommended storage temperature and the system must be validated to ensure the transport temperature does not vary significantly from the recommended temperature.

The granulocytes must be transfused through a standard blood giving set with a 170-200µm filter. The administration of granulocytes and Amphotericin B infusion must be separated by several hours.

TECHNICAL SPECIFICATIONS

As per Granulocyte Apheresis Standards (112S022)