SOUTHAMPTON Children's Hospital

Wessex Paediatric Oncology Supportive Care Guidelines: Transfusion & Coagulation.

Scope
This guideline applies to all Paediatric Oncology patients in the region. It does not apply to neonates on neonatal units.

Purpose
Children receiving treatment at the Southampton Paediatric Oncology Principal Treatment Centre (PTC) have open access to the designated Paediatric Oncology Ward at either the PTC or their Paediatric Oncology Shared Care Unit (POSCU) Hospital. Their parents/carers will be in possession of contact details for these wards and have been instructed to contact them for any medical problems that arise while they are receiving treatment. These Guidelines are intended for the use of the medical teams at the PTC or POSCU. If one of the Paediatric Oncology patients presents to a medical service outside of the PTC or POSCU, please contact the medical teams at the PTC or POSCU for advice.

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Contents

Patients/parents who have no previous experience of transfusion, will be concerned about safety. Information should be given to the family prior to transfusion and informed consent should be obtained. Leaflets are available to order or download from NHS Blood and Transplant (NHSBT) service. Remember to document the reason for transfusion & response in the notes. See local hospital blood transfusion policy.

Useful leaflets which can be downloaded include:

- A parents guide for children needing a blood transfusion (This leaflet pack contains a parents guide, a comic for older children and a sticker book for younger children).
- Information for patients needing a platelet transfusion
- Information for parents of children needing fresh frozen plasma
- Information for patients needing irradiated blood products (This leaflet contains a sticker for the front of the child's notes and a card that should be completed and handed to the parents).

To download:
http://hospital.blood.co.uk/patient-services/patient-blood-management/patient-information-leaflets

1.1 Leucocyte-depletion

Improved safety measures were introduced to reduce the risk of transfusion transmitted infections including variant Creutzfeldt Jacob disease (vCJD). All blood products have been routinely leuco-depleted (< 5 WC x 106/unit) since 1999.

1.2 Cytomegalovirus (CMV) negative blood components

The department of Health Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) released a position statement on CMV testing of blood components. It concluded that leuco-depletion offers sufficient protection against the risk of CMV transmission and that CMV negative products should not be considered necessary for CMV negative patients receiving chemo/radiotherapy or requiring a stem cell transplant. (www.dh.gov.uk/health/2012/03/sabto)

SaBTO concluded that CMV negative blood components **should** be provided for the following:-

- Intra-uterine transfusions
- Neonates
- Planned transfusion during pregnancy
- Granulocyte transfusions to patients who are CMV IgG negative and receiving or planned to receive an allogeneic stem cell transplant from a CMV IgG negative donor.

1.3 Hepatitis E negative products

While the risk of HEV to the general population is negligible, SaBTO has now recommended that certain patient groups who are immune-compromised/immune-suppressed should receive HEV negative blood components. Unlike screening for cytomegalovirus (CMV), this recommendation is being applied to both cellular components (i.e. red cells, platelets and granulocytes) and plasma components (fresh frozen plasma and cryoprecipitate). **For advice and further information see attached SabTo flowchart which can be found at www.hospital.blood.co.uk/products/hepatitis-e-screening/**

1.4 Irradiated blood products

Although all cellular blood components have been leuco-depleted since 1999, residual lymphocytes can cause fatal transfusion associated graft-v-host disease (TA-GVHD) in severely immune-compromised patients. Irradiation with 25Gy inactivates the lymphocytes, thus preventing the problem.

Table 1: These groups of patients must always receive irradiated red cells and platelets

Type of patient	**Length of requirement for irradiated red cells and platelets**
All patients with Hodgkins lymphoma	Lifelong
All patients receiving treatment with purine containing analogues: fludarabine, cladribine, clofarabine, nelarabine, deoxycoformycin & bendamustine	Continue indefinitely
All recipients of allogeneic stem cell transplant (SCT) start from initiation of conditioning chemo-radiotherapy	Continue indefinitely
All recipients of autologous bone marrow (BM) or peripheral blood stem cell transplant (PBSCT)	From initiation of conditioning therapy then continue for 3 months post transplant or 6 months if total body irradiation (TBI) given as part of conditioning.
All donors of bone marrow or peripheral blood stem cells	From 1 days prior to and during harvesting (BM or PBSC) (to prevent the collection of viable allogeneic T lymphocytes which could withstand cryopreservation).
All patients undergoing BM or PBSC harvest for future autologous re-infusion	From 7 days prior to and during harvest
All cases where there may be a shared haplotype between the donor and recipient	i.e. HLA matched platelets donations from first or second degree relatives
All severe T lymphocyte immunodeficiency syndromes • Combined immunodeficiency (CID) • Severe combined immunodeficiency (SCID) • 22q11 deletion (Di George / Velo-Cardio-Facial syndrome) • Wiskott-Aldrich syndrome	Lifelong
All patients treated with anti-thymocyte globulin	Continue indefinitely
All patients treated with alemtuzumab (Campath)	Continue indefinitely
Neonates who have received an Intrauterine transfusion (IUT)	Continue for 12 months post date of birth (local Southampton policy) (nationally this is 6 months post **expected** date of delivery, but to avoid errors easier to use 12 months after the date of birth).

- **Granulocyte transfusions should always be irradiated and transfused with minimum delay**
- **Fresh frozen plasma and cryoprecipitate do not need to be irradiated**
- Gamma irradiation dose not affect the expiry date of platelets. Red cells for top-up transfusion should be transfused within 14 days of irradiation.

The requirement for irradiated blood components must be clearly documented in the notes & parent held records. Shared care centres and the local transfusion laboratory must be informed

about patients receiving irradiated blood products. The patient/parent should be issued with the NHS BT card which they keep for future reference. A form indicating the reason for irradiation should be completed and faxed to the blood transfusion laboratory at UHS.

1.5 Anaemia

Symptoms of anaemia will be dependent upon the child's age and the rate of fall in haemoglobin. Consider transfusion if patient is symptomatic but do not routinely react to numbers alone. Consider also the stage of treatment; hold off transfusion where it seems likely the child's count is about to recover, whereas more likely to transfuse if count is falling**.**

In general, consider transfusing packed cells if Hb < 70 g/l dependent on symptoms. Always check the protocol and consider additional factors such as need to maintain Hb if undergoing concurrent radiotherapy, thresholds vary. If patient very anaemic, transfuse slowly: do not attempt to attain a normal Hb in first transfusion, but aim for a safe level. In patients with aplastic anaemia minimise the use of transfusion to reduce the risk of allo-sensitisation which could compromise the success of future bone marrow transplantation. However, with leuco-depletion the risk of allo-sensitisation in aplastic anaemia is much less than previously.

A standard pack of red cells has a volume of ≈ 180- 350 mls. Red cells must be compatible and ideally of the same blood group.

Transfusion should **commence within 30 minutes of blood being removed from fridge, & must be completed within 4 hours** (UHS NHS FT policy).

For top up transfusions transfuse at 5 ml/kg/hr – usually 15 ml/kg over 3 hours.
This allows transfusion to be started slowly for first 15 minutes, & completed well within specified 4 hours of removal from fridge.

Dose: Calculate the desired rise in haemoglobin Hb: 3ml/kg will raise the Hb by 10g/l

Dose of Red Cells for transfusion		
Volume required (ml packed cells)	=	Weight (kg) x rise in Hb required **(g/l)** x 0.3

If volume calculated is <200mls: order in mls (add enough volume to prime the line, approx 30mls) prescribe at a maximum rate of 5mls/kg/hr. Paedi-packs (6packs taken from 1 adult unit) are available for smaller transfusions so reducing wastage and donor exposure.

If volume >200mls: can be rounded to nearest adult unit and run at 5mls/kg/hr. For children need to specify volume to be transfused as units vary in volume (180-350 ml). Try to avoid wasting part units where possible.

Avoid transfusion in newly diagnosed leukaemia patient with WCC > $50x10^9$/l because of leukostasis, unless absolutely necessary, until WCC reduced to a safe level.

- **discuss with PTC consultant**
- **if required do not give more than 5ml/kg over 4 hours**
- **rarely need to raise the Hb >60g/l**

Initial G&S sample will be kept for up to 1 days for cross match.

- If patient transfused within last 28 days, new X-match sample required within 12 hours of transfusion.
- If patient transfused more than 28 days ago, new X-match sample required within 1 week of transfusion.
- **New patients require 2 separate blood group samples taken at different times prior to the initial transfusion.**

1.6 Thrombocytopenia

Indications for giving platelet transfusion: -

- Platelet count < 10 x 10^9/l

- Platelet count < 20 x 10^9/l **and** 1 or more of the following
  - child needing an LP (assuming competent operator in still child)
  - coagulopathy or heparin therapy
  - severe mucositis
  - risk of bleeding due to a local tumour infiltration
  - platelets likely to fall below 10 x 10^9/l before next evaluation & if any delay in obtaining platelets eg particular blood type, remote location –if patient stable in hospital & count only just < 20 x 10^9/l, need to consider the whole clinical picture including timing of expected count recovery
    Not needed for BMA or asparaginase or minor bleeding

- Platelet count 20 – 40 x 10^9/l and 1 or more of the following
  - DIC in association with induction therapy for leukaemia
  - Hyperleucocytosis WBC >50 x10^9/l

- Platelet count < 30 x 10^9/l and child receiving chemotherapy for CNS tumour which has been incompletely resected. In cases with completely resected CNS tumours, it is feasible to let the platelet count fall to 10x10^9/l before transfusion.

- Platelet count < 50 x 10^9/l and central line insertion insertion

- If major bleed (haematemesis, melena, haematuria, haemoptysis) or minor bleed (epistaxis/vaginal/soft tissue) but enough to require transfusion of red cells, transfuse to a count of 50 x 10^9/l.

- Life-threatening bleed, bleeding at critical sites (lungs/CNS/eyes), transfuse to 100 x10^9/l

Platelets must be compatible for blood group, but ideally of the same group. If same blood group not available, then components lacking high titre anti-A or anti-B should be transfused to Group A or B recipients. (See table below)

When giving to cover invasive procedures, give immediately prior to procedure, as the highest increment will be within the first hour of transfusion. If however, patient not known to increment well, need to repeat FBC 1 hour post transfusion to ensure patient has achieved a satisfactory platelet count.

Amount of Platelets to transfuse
< 15 kg: 15 ml/kg (can give up to 20ml/kg if desired)
> 15 kg: 1 adult therapeutic unit.

Transfuse over 30-60 minutes

Platelets for anyone < 16 years should be an apheresis unit to reduce donor exposure.
It may not always be possible to have an irradiated apheresis unit of blood group identical platelets when required & then a clinical judgement should be made as to what takes priority in the time constraints.

If a satisfactory increment is not achieved amounts transfused may need to be doubled - discuss with haematologist. Poor increments may be seen if bleeding, infection, DIC, splenomegaly or HLA class 1 antibodies.

Document 1hr and 24hr platelet increment post transfusion, if concern about suboptimal response.

Poor incremental recovery defined as:

- Failure to rise >20-30x10^9/l at 1 hr or 10-20x10^9/l at 24hrs post transfuision.
- Check for non-immune causes and treat appropriately
- If no cause identified, send samples to NHSBT to test for HLA antibodies (discuss with haematologist)
- If HLA antibodies present, request HLA matched platelets (NHSBT to call up specific donors so forward planning required)

In the latter there may be a need for giving HLA matched platelets, but this still may not eliminate the problem of poor increments.

Ordering platelets at University Hospital Southampton need to give 2 hours notice before next routine delivery. Currently deliveries are at 9.30, 13.30 &16.30.

1.7 Coagulation

Acquired coagulopathy could be due to vitamin K deficiency, DIC, liver disease or anti-coagulation. Should be treated with vitamin K in first instance. Other products reserved for **symptomatic** coagulopathy not responsive to vitamin K treatment; or if coagulopathy & urgent surgical intervention needed. Cryoprecipitate reserved for coagulopathy associated with low fibrinogen (<1 g/L), as has a higher concentration of fibrinogen than FFP. See UHS transfusion protocol.

1.7.1 Vitamin K deficiency:

Systemic Vit K will act within 30 – 120 minutes. Measure response by checking the pro-thrombin time (PT) or INR. Remember unwell patients may become vitamin K deficient.

Dose of Vitamin K see table 3.

1.7.2 Fresh Frozen Plasma (FFP)

Indications for FFP:

- DIC / severe sepsis
- severe liver disease
- major haemorrhage
- Vit K deficiency with significant bleeding
- Coagulation factor deficiency if specific concentrate not available

Prepared form plasma sourced from outside UK for preparation and treated to reduce risk of viral transmission: either methylene blue treated FFP from single donor **or pooled solvent-detergent treated plasma from multiple donors** (**octoplas**). **Octoplas** will be first choice in UHS NHS FT – each unit is exactly 200mls.

Dose of FFP/Octoplas see table 3.

Need to re-check coagulation following transfusion to assess response.

1.7.3 Cryoprecipitate:

Indications for Cryoprecipitate:

Correction of a low fibrinogen level due to

- DIC / severe sepsis
- Severe liver disease
- Major haemorrhage
- Congenital hypo – or afibrinogenaemia (if Fibrinogen concentrate not available)

Usually given to correct a low fibrinogen if a child is bleeding or requires a surgical procedure.

Need to check coagulation post transfusion to assess response. Sourced from donors outside UK and now methylene blue treated for patients born in or after 1996. Each unit is 10-40mls in volume.

Dose of Cryoprecipitate: see table 3.

1.8 Transfusion Reactions

Refer to local blood transfusion policy & action plan. In Southampton see reaction poster for investigation & treatment.

1.8.1 Acute haemolytic transfusion reactions

Signs and symptoms (agitation, flushing, pain in abdomen, flank, chest or at site of infusion, fever, hypotension, generalised oozing, dark urine - haemoglobinuria) may occur after 5-10 ml blood. Stop transfusion. Investigate possible causes and treat. (Ref below.)

1.8.2 Non-haemolytic febrile transfusion reactions (NHFTR)

NHFTR (shivering, pyrexia) are much less common now with the use of leuco-depleted products (see above) and bacterial contamination needs to be excluded.
NHFTR are treated with paracetamol and piriton. If symptoms are not severe & do not progress after 30 minutes, transfusion of red cells may be continued at a slower rate. Absorption of piriton when given orally is very variable in terms of speed of onset of action and amount absorbed; therefore use piriton intravenously for treating or preventing transfusion reactions. Duration of action is approximately 4-6 hours in adults and has been reported to be less in children. Give 1 hour before as prophylaxis.

If temperature > 1.5°C above baseline, or patient unwell with hypotension & tachycardia, must assume bacterial contamination & treat accordingly. This applies particularly with platelets as these are stored at 22°C & so bacterial contamination more likely, whereas blood is stored at 4°C. Coagulase negative staphylococcus is the most likely culprit, contamination occurring at the time of collection, but other organisms possible. Infusion of the blood product should be discontinued, the blood product returned immediately to blood bank and haematology staff notified (the blood product will be cultured). The patient should be cultured and commenced on piperacillin/tazobactam & teicoplanin.

1.8.3 Allergic reactions/anaphylaxis

Severe allergic reactions may be associated with antibodies against IgA: special arrangements will need to be made for future transfusions in these patients. Treat allergic reactions with chlorpheniramine & hydrocortisone. Anaphylaxis is treated in the usual way with adrenaline, oxygen, and fluids: 20 ml/kg 0.9% saline. Hydrocortisone & chlorpheniramine can be given after immediate resuscitation. Send appropriate samples for investigation including IgA levels unless already known.

1.8.4 Transfusion related acute lung injury (TRALI)

Acute respiratory distress caused by donor plasma containing antibodies against patient's leucocytes. Chills, fever, non-productive cough and breathlessness follow transfusion. X-ray shows perihilar nodules with infiltration of lower lung fields. Treat with oxygen, ventilate if necessary. Investigate appropriately.

1.9 Table 2. Doses of drugs required in transfusion reactions and vitamin K deficiency

Drug	Route	Age	Dose	Comments
Vitamin K deficiency				
Phytomenadione	Oral	< 12 years	300micrograms/kg (max. 10mg)	
	Oral	12 – 17 years	10mg	
	IV		250-300micrograms/kg (max. 10mg)	Diluted with 5% dextrose. Give over 5-10 minutes Systemic Vit K will act within 30-120mins. Measure response by checking the pro-thrombin time (PT) or INR
Transfusion reactions				
Paracetamol		See BNFC		
Chlorphenamine	IV	1 month- 5months	250microgram/kg (max. 2.5mg)	IV: must be diluted and given slowly over at least 1 minute, repeat up to 4 times/24hrs
	IV	6 months – 5 years	2.5mg	
	IV	6-11 years	5mg	
	IV	12-17 years	10mg	
Hydrocortisone	IV	1 month- 5months	25mg	
	IV	6 months – 5 years	50mg	
	IV	6-11 years	100mg	
	IV	12-17 years	200mg	
Adrenaline	IM	1 month- 5 years	150micrograms	0.15ml of 1:1000
	IM	6-11 years	300micrograms	0.3ml of 1:1000
	IM	12-17 years	500micrograms	0.5ml of 1:1000

For full prescribing information consult BNFC https://www.medicinescomplete.com/mc/bnfc/current/PHP78111-antihistamines-allergen-immunotherapy-and-allergic-emergencies.htm?q=anaphylaxis&t=search&ss=text&tot=178&p=2#

1.10 Table 3. Blood Product doses and transfusion instructions: Order Hep E negative components where possible			
Blood Products			
Blood (RCC)	IV	**For top up transfusions transfuse at 5 ml/kg/hr – usually 15 ml/kg over 3 hours.** Transfusion should **commence within 30 minutes of blood being removed from fridge, and must be completed within 4 hours** (UHS NHS FT policy).	Volume required (ml packed cells)=Weight (kg) x rise in Hb required **(g/l)** x 0.3. If volume calculated is <200mls: order in mls (add enough volume to prime the line, approx 30mls) prescribe at a maximum rate of 5mls/kg/hr. Paedi-packs (6packs taken from 1 adult unit) are available for smaller transfusions to reduce wastage and donor exposure. If volume >200mls: can be rounded to nearest adult unit and run at 5mls/kg/hr. For children, need to specify volume to be transfused as units vary in volume (180-350 ml). Try to avoid wasting part units where possible.
Platelets	IV	< 15 kg: 15 ml/kg (can give up to 20ml/kg if desired) > 15 kg: 1 adult therapeutic unit.	Transfuse over 30-60 minutes
FFP/Octoplas	IV	10 ml/kg at 10 ml/kg/hr	**Octoplas** will be first choice in UHS NHS FT – each unit is exactly 200mls.
Cryoprecipitate	IV	5 ml/kg over 30 minutes but young children may require 10ml/kg	Each unit is 10-40mls in volume.
Buffy Coat	IV	10mls/kg	Administer through standard red cell giving set & infuse over 1-2 hours, normal blood transfusion observations. Febrile reaction likely.

1.11 Table 4. Blood product compatibilities

Recipient/patient ABO blood group	Compatible donor group* (in order of preference)			
	Red cells	Platelets	FFP	Cryoprecipitate**
A	A, O	A, (B, O)	A, AB	A
B	B, O	B, (A, O)	B, AB	A
O	O	O, A, B	O, A, B, AB	O, A
AB	AB, A, B or O	(A, B, O)	AB	A

*For red cells ideally give products of the same group; but if not, must be compatible group as shown & high-titre negative ('NEG-HT').
*For platelets ideally give products of the same group, but where this is not possible, product must be 'NEG-HT'.
Products are given in preferred order ie gp A recipient, first choice platelets would be A, second choice B etc.
Anti-AB in plasma of group O patients often more potent antibody (than in A or B)
AB platelets not produced.

1.12 Granulocyte/Buffy Coat Transfusions

Specialist product for use in severe infection, only available on discussion with BTS.
Will only be administered in the PTC on recommendation of the consultant and after MDT discussion.

Refer to **Clinical Guidelines for the use of granulocyte transfusions**
INF/MED/MA/006/02 prepared by the Granulocyte Working Group

Copy kept at back of ward guidelines, for indications, procedures etc.

Request
Need to discuss with National Blood Transfusion Consultant (they will authorise if appropriate) and local blood bank who need to order from hospital services (Filton in Bristol) in usual way.

Contact NHSBT consultant of week on **01119 594666.**

CMV neg products given if patient CMV neg – sample will be automatically irradiated

Samples
Need baseline sample for HLA typing (if enough lymphocytes) & HLA antibodies class I & II – see document for further testing if needed eg reactions/refractory

Local blood bank require sample for cross matching (as for any red cell transfusion)

Dose
Dose buffy coat in children = 10 ml/kg (also has haematocrit & contains WC & platelets so patients will need fewer red cell transfusions than usual)

Administration
Administer through standard red cell giving set & infuse over 1-2 hours, normal blood transfusion observations. Febrile reaction likely.

Remember to update NBS & blood bank on any change – eg no longer need for buffy coats or if further buffy coat required.

Follow up information will be required by the National Blood Transfusion Service.

1.13 References & Further reading:

- *Handbook of Transfusion Medicine, 4th Edition 2001, HMSO Ed B McClelland www.transfusionguidelines.org.uk*
- *Guidelines on the use of irradiated blood components 2010. www.bcshguidelines.com*
- *Addendum to guidelines on the use of irradiated blood components 2012 www.bcshguidelines.com*
- *Blood reviews (1998) 12, 234-238. Consensus conference on platelet transfusion,*
- *UHS NHS FT Blood Policy on UHS NHS FT Extranet*
- *Transfusion Guidelines for Neonates & Older Children 2003 available on web www.bbts.org.uk or www.bcshguidelines.com see update 2001*
- *Guideline on the administration of blood components 2009 www.bcshguidelines.com*
- *Guideline on the investigation, management and prevention of venous thrombosis in children 2010 www.bcshguidelines.com*
- SaBTO (2015) HEV SCT Clinician Letter draft v0.3i http://hospital.blood.co.uk/media/27890/sabto-hev-clinician-letter-sct-12_08_15.pdf (accessed 25.01.2016)