Guideline for the generic transfusion management of adult massive haemorrhage

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Date written	Nov 2016
Review date	Nov 2019
Summary	For adult patients with massive haemorrhage better outcomes are achieved by the use of early intensive plasma replacement to prevent/reverse coagulopathy
Aims	To provide recommendations for the haematological management of massive haemorrhage in any clinical situation (apart from obstetrics). This includes the use of blood components and transfusion alternatives.
Objectives	To ensure appropriate assessment and management of massive transfusion during massive haemorrhage. To optimise the use of blood components in this population and to minimise wastage.
Clinical condition	Massive haemorrhage
Target Patient Group	Patients with massive blood loss that leads to a heart rate more than 110 beats/minute and/or systolic blood pressure less than 90 mmHg. Or, the loss of one blood volume within a 24 hr period, or 50% blood volume loss within 3 hours, or a rate of loss of 150ml per minute.
Target Professional Group	All staff involved in managing massive haemorrhage
Adapted from	BCSH (2015). A Practical Guideline for the Management of those with, or at risk of Major Haemorrhage British Journal of Haematology. Volume 170, Issue 6, pages 788–803, September 2015 http://onlinelibrary.wiley.com/doi/10.1111/bjh.13580/epdf BCSH (2004), 'Guidelines for the use of Fresh Frozen Plasma, Cryoprecipitate and Cryosupernatant', British Society of Haematology; 126: 11-28 http://www.bcshguidelines.com/pdf/freshfrozen_280604.pdf Addendum to BCSH Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. May 2016 http://www.bcshguidelines.com/documents/Addendum_FFP_Apr_2016.pdf BCSH (2016), 'Guidelines for the use of Platelet Transfusions', British Society of Haematology; http://www.bcshguidelines.com/documents/BCSH_platelet_guideline_08_08_16_v2.pdf CRASH-2 Collaborators (June 2010) Effects of tranexamic acid on death, vascular occlusive events and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Norfolk D (2013) Handbook of Transfusion Medicine 5th edition. The Stationery Office: http://www.transfusionguidelines.org.uk/index.asp?Publication=HTM A H Rose, A Kotze, D Doolan, D R Norfolk,M C Bellamy (2009) Massive Transfusion - Evaluation of Current Clinical Practice and Outcome in Two Large Teaching Hospitals Trusts in Northern England. Vox Sanguinis 97, 247-253 NICE Guidelines (2016): Major trauma: assessment and initial Management. https://www.nice.org.uk/guidance/ng39/resources/major-trauma-assessment-and-initial-management-1837400761285 British Committee for Standards in Haematology (2013) Guidelines on the management of anaemia and red cell transfusion in adult critically ill patients. British Journal of Haematology. Volume 160, Issue 4, pages 445–464, February 2013
Recommendations	All clinical areas with the potential for massive haemorrhage situations should keep a copy of this guideline and flowcharts for easy access
Clinical algorithms	Appendix 1: Treatment Algorithm
Reviewed by	Consultant doctors and anaesthetists at SJUH & LGI and pharmacy leads
Authorised by	Signature/date

Location of master copies	Signature	Date
1		
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Intranet version available at:		

Review date	Reviewed by	Changes Y/N	Signature
Sept 2013	HTT	Yes	
Sept 2016	HTT & Key Stakeholders	Yes	

To view the Transfusion Management of Massive Haemorrhage in Obstetrics Guideline, see: http://nww.lhp.leedsth.nhs.uk/common/guidelines/detail.aspx?ID=2146
To view the Transfusion Management of Massive Haemorrhage in Neonates & Paediatrics Guideline, see:
http://nww.lhp.leedsth.nhs.uk/common/guidelines/detail.aspx?ID=2412

Appendices

***Patients in the outlying hospitals at Seacroft, Chapel Allerton and Wharfedale, who experience massive haemorrhage must be transferred to either LGI or SJUH as soon as possible*.**

1. Introduction

Complications of major blood loss and massive transfusion may jeopardise the survival of patients from many different specialities, and challenge haematological and blood transfusion resources.

To improve confidence and maintain best practice when managing massive haemorrhage clinical teams are required to hold regular (at least annually) 'dry-runs' / 'drills' to practice individual team member roles in a massive haemorrhage scenario to ensure a cohesive team approach in managing patient care.

The purpose of this generic Guideline is to provide recommendations for the haematological and transfusion management of adult massive haemorrhage in any clinical situation. This includes the use of blood components and transfusion alternatives. Any specialty specific massive haemorrhage treatment required extra to this generic transfusion management must be covered by local SOPs.

NB: LTHT specialties with specific massive haemorrhage management include; obstetrics

2. Background

This guideline assumes that all necessary measures to identify and control bleeding sites are on-going. Furthermore, effort must be directed at preventing hypothermia.

While there are arbitrary definitions of massive blood loss e.g. the loss of one blood volume within a 24 hour period, 50% blood volume loss within 3 hours or a rate of loss of 150ml per minute, these may be difficult to apply in the acute situation. BCSH (2015) consider,

- the massive haemorrhage protocol should be initiated when bleeding leads to a heart rate more than 110 beats/minute and/or systolic blood pressure less than 90 mmHg **AND**
- a senior doctor (Registrar or above) authorises its use to ensure that scarce blood component resources are used appropriately

A successful outcome requires prompt action and good communication between senior clinical specialities, diagnostic laboratories, blood bank staff and the local blood centre. **Correctly labelled blood samples** and early expert involvement e.g. vascular, surgeons, anaesthetists, endoscopists, interventional radiologists or others with specific expertise are key to patient survival.

EVERY PATIENT MUST WEAR AN I.D. WRISTBAND, AND THERE MUST BE A ROBUST SYSTEM IN PLACE FOR IDENTIFICATION OF UNKNOWN UNCONSCIOUS PATIENTS, INCLUDING SUBSEQUENT MERGING OF CLINICAL AND LABORATORY RECORDS.

3. Communication

If admission or transfer of a patient is expected who is, or is at risk of, massive bleeding, contacting the key personnel outlined in section 5.1 including the Blood Transfusion Laboratory as part of an 'early warning system' may enable them to anticipate the patient's requirements in readiness and therefore minimise delay.

When communicating with blood transfusion laboratories (at the earliest possible opportunity), it is vital to use appropriate wording when ordering blood and its components. If products are required immediately (without delay) the person speaking to the blood transfusion laboratory giving the patient details **MUST say they're "initiating the massive haemorrhage protocol" and then give their details and the patient's details.** That is, they should be ready to communicate the **type of situation, the urgency of the situation, the patient's name, date of birth (if available) and I.D. number** so that the request can be prioritised and components be made available without delay.

Early notification of the Transfusion Laboratory allows staff to check stock and reschedule non-urgent work. Upon this request, Lab staff will begin to prepare the requested transfusion pack and will send components to the requesting area as soon as they are available.

A member of the clinical team should be nominated to act as co-ordinator responsible for overall organisation, liaison, communication with the Blood Bank and documentation. This is a critical role for a designated member of the permanent clinical staff.

4. Documentation

N.B. It is imperative to document within the patient's case notes both the indication for transfusion and details of each blood component and its donation number. Blood Safety & Quality Regulations 2005 (U.K. law) state: **the fate of every unit of blood or blood component MUST be documented**. This can be achieved by using the Autofate system on ward / theatre PCs or Blood Track Kiosk or failing that, by signing and returning the manila tag attached to the blood product bag to the issuing Transfusion Laboratory.

Details of the patients receiving any emergency O negative Red Blood Cells (RBC) used must be communicated to Blood Bank as soon as possible. This will also inform them of the need to replace O negative units as necessary.

The following steps should happen simultaneously or in very close succession

5. First Steps in Resuscitation

Hypothermia increases the risk of coagulopathy and may be prevented by keeping the patient warm. During uncontrolled haemorrhage, avoid clear fluids for volume resuscitation unless there is profound hypotension and no imminent availability of blood components.

6. Recommended Transfusion Management Plan

- NB: in the very early stages of severe haemorrhage the haemoglobin will not accurately reflect the blood loss. Transfusion is rarely indicated when the haemoglobin concentration is >80g/l **unless haemorrhage is continuing**.

Determination of whether intermediate haemoglobin concentrations justify red cell transfusion should be based on the patient's risk factors for complications of inadequate oxygenation, such as rate of blood loss, cardiorespiratory reserve, oxygen consumption, and atherosclerotic disease. Measured cardiological variables such as heart rate and blood pressure in combination with arterial blood gases may assist the decision making process, but it should be emphasised that silent ischaemia may occur in the presence of stable vital signs.

It is strongly recommended to appoint a single communicator and/or scribe to ensure prompt communication with all key stakeholders.

6.1 Contact Key Personnel - if not already present:

- Duty Consultant of the team caring for the patient
- Duty Anaesthetist and on-call Consultant Anaesthetist if appropriate
- Duty and on-call Interventional Radiologist if appropriate
- Duty and on-call Endoscopist if appropriate
- Blood Bank & use the trigger phrase: "this is a massive haemorrhage" and request "Initiate the massive haemorrhage protocol", give details of the patient's full name, DOB and ID (NHS) number and ward. Telephone ext: 23398 (LGI), 65559 (SJUH)
- **Duty Consultant Haematologist if clotting is a concern including if the patient is on oral anticoagulation other than warfarin e.g. novel anticoagulants** (for management advice see): http://nww.lhp.leedsth.nhs.uk/common/guidelines/detail.aspx?ID=4536.
- **Ensure porters are contacted immediately***

*__SJUH__: Clinical staff must contact porters and arrange urgent collection and delivery of blood components via the CARPS electronic requesting system or, tel. 65000 then select option 1

__LGI__: Blood Bank will arrange for porters to collect and deliver blood components.

However, appointing a dedicated 'runner' from your team may help speed up collection and delivery of blood components.

6.2 Investigations to Guide Blood Component Requirements and Treatment

Developing hypothermia, acidosis and hypocalcaemia will further worsen coagulopathy. It is important to monitor haemostatic changes to guide the use of blood components after initial resuscitation, with coagulation and platelet testing performed after every 4 units red cells and 4 units FFP depending on the severity of blood loss, until bleeding ceases. Alternatively coagulation can be monitored by thromboelastography (TEG). Where available, staff trained to use near-patient testing devices such as TEG can monitor clot strength and subsequent fibrinolysis after each round of 4 units FFP and/or platelets can offer rapid reliable data to guide component therapy but needs expert interpretation.

Blood samples should be sent to the laboratory at the earliest possible opportunity as results may be affected by crystalloid / colloid infusion. **IT IS ESSENTIAL TO ENSURE THAT HANDWRITTEN PATIENT DETAILS (first and last name, DOB, ID (NHS) No.) ARE FULLY AND CORRECTLY ENTERED ON TRANSFUSION SAMPLE TUBES,** this will prevent re-bleeding the patient and any delay in the provision of blood and its components.

Table 1: recommended baseline blood samples

Test required	Sample type & size	Send to:
Full Blood Count	EDTA 4mls (lavender)	Haematology Laboratory
Group & Crossmatch	EDTA 6mls (pink)	Transfusion Laboratory ***-hand deliver***
Coagulation screen (including fibrinogen estimation)	Coagulation tube 3.5mls (blue) ***full tube critical***	Haematology Laboratory
Biochemistry (U&E, LFT, Calcium)	Serum 5mls (gold)	Clinical Biochemistry Laboratory
Blood gas analysis	Heparin syringe 1ml	Take to nearest blood gas analyser

N.B: It is strongly advised to hand deliver any blood samples to the appropriate laboratory to ensure they are labelled correctly and for speedy processing.

Arterial blood gas analysis should also be part of the monitoring process as worsening acidosis (pH<7.35) indicates poor tissue perfusion. However, the Hb reading from the blood gas analyser **should not** be used to guide clinical decisions on transfusion as the result can be highly misleading and numerous serious incidents have been reported to the SHOT (Serious Hazards of Transfusion) haemovigilence scheme.

Be aware that slow turnaround time in haematological testing may mean that the results do not reflect the dynamic clinical situation during on-going haemorrhage.

It is recommended after transfusion of 4 units each of red cells/FFP to check all baseline parameters including calcium at least 4 hourly. Further component therapy should be guided by these laboratory and/or TEG results as well as clinical response.

Further advice if necessary, can be sought from the Consultant in Transfusion Medicine (contact via switchboard) regarding appropriate investigations, their interpretation and optimum corrective therapy.

6.3 Transfusion Support in Massive Haemorrhage

Red cell transfusion is usually necessary if 30-40% blood volume is lost and rapid loss of >40% is immediately life threatening.

Plasma fibrinogen predictably falls to sub-haemostatic levels (<1.5g/l) after 1 to 1.5 blood volume replacement, earlier in the presence of coagulopathy and hyperfibrinolysis.

Coagulation is also impaired by hypothermia, acidosis and reduced ionised calcium concentration (which can be measured on many blood gas analysers). Ionised hypocalcaemia may be caused by rapid transfusion of blood components containing citrate coagulant, although this is uncommon in the presence of normal liver function.

The platelet count usually remains above $50x10^9$/L until 1.5 to 2.5 blood volumes have been replaced.

From national and international research evidence, current BCSH Guidance on management of ADULT massive haemorrhage recommends maintaining a transfusion ratio of 1:1, that is 1 dose (4 units) of red cells to every 1 dose (4 units) of Fresh Frozen Plasma (FFP).

When the patient meets the definition of massive haemorrhage defined in section 2:

Contact Blood Bank and state: "this is a massive haemorrhage on ward X and give the patient's full name, DOB, ID (NHS) number" and request**: "Initiate the Massive Transfusion Protocol"** where the relevant blood components will be sent as soon as they are available.

6.3.1 **The Massive Transfusion Protocol** contains: 4 units red cells, 4 units FFP

- In an extreme situation it may be necessary to use Emergency Group O negative red cells if the blood group is unknown or whilst waiting for a transfusion sample to be processed. If this is the case the number of units of O negative red cells must count towards the total number of red cells given in the first instance to maintain the 1:1 ratio e.g. if 2 units of O negative red cells are used, the total number of first dose group specific or crossmatched red cells must also be 2 units

- Group specific red cells should be given at the earliest possible opportunity as Group O negative blood is a scarce resource

- Fully crossmatched red cells should be given when available

- Once the decision has been made to activate the massive haemorrhage protocol, avoid using additional crystalloid or colloid solution

6.3.2 Tranexamic Acid

Alongside changes in the use of blood components in managing massive haemorrhage, the importance of antifibrinolytics has been demonstrated in the CRASH-2 study it is recommended to give concomitant tranexamic acid. This should be as soon as possible or at least within 3 hours of the start of the haemorrhage. In patients with massive haemorrhage secondary to trauma the CRASH-2 study (June 2010) showed a decreased mortality in patients given tranexamic acid v's placebo. CRASH-2 used a loading dose of **1gram intravenous tranexamic acid over 10 minutes followed by 1gram tranexamic acid intravenous infusion in 100ml sodium chloride 0.9% or glucose 5% over 8 hours.** Do not add directly to blood or administer via the same line as penicillin.

The results of the CRASH-2 trial applied only to patients with trauma. Patients with other causes of bleeding, such as gastrointestinal are usually older than trauma patients with different co-morbidities and it is unclear whether the results of CRASH-2 should be extrapolated from trauma to GI bleeding. The use of tranexamic acid in surgical patients has been reviewed and found it reduced the probability of receiving blood transfusion by a third. It is suggested there is no increased risk of vascular occlusive events in this group of patients (BCSH, 2015).

6.3.3 **If bleeding continues** despite administering the above blood components contact Blood Bank and state: "this is a continuing massive haemorrhage on ward X and give the patient's full name, DOB, ID (NHS) number" and request:

- Red cells and FFP in a 1:1 ratio
- If required, also request 1 adult dose of platelets (which consists of 4 pooled donor units and contains >240x10^9 platelets per transfusion). See 6.3.7 below for further information on use of platelets.

NB: Evidence suggests using a 1:1 ratio improves patient outcome by controlling / limiting the development of coagulopathy. The Red Cells and FFP should be administered as soon as they are available BEFORE THE RESULTS OF LABORATORY CLOTTING TESTS ARE AVAILABLE. In the presence of continuing haemorrhage, aim for minimum platelets to red cell to FFP ratio of 1:1:1, guided by sequential laboratory coagulation tests or TEG. Once the initial blood components have transfused and bleeding continues, consider the use of cryoprecipitate if clinically indicated and/or depending on blood test results.

If the patient is being closely monitored the rate of infusion can be over minutes, depending on the clinical picture.

NB: Blood and FFP should ideally be given via separate I.V. access but if this is not possible then the giving set must be changed when changing from one type of component to another i.e. FFP to RBC or vice versa.

6.3.4 Red Cells:

Where available, the use of a specifically designed blood warming device is recommended to prevent hypothermia during administration of red cells (but not FFP or platelets - see below) at high infusion rates.

- Group specific blood is the same blood group as the patient but not crossmatched for antibodies, this can take up to 30 minutes to be available after receipt of a correctly labelled sample, it is the safest to use until the antibody check is finished
- Fully crossmatched blood is the same blood group as the patient AND has been fully checked for any antibodies. This process can take up to 40 minutes to complete and crossmatched blood will be sent as soon as it is available

NB: Although red cell transfusion can be lifesaving, there are potential risks such as increased morbidity and mortality due to organ failure and transfusion-related acute lung injury and so the exposure to red cells should be minimized. This restrictive red cell transfusion policy is associated with a reduced risk of health care associated infections. BCSH guidelines for red cell use in critical care (2013) recommend that anaemic critically ill patients with stable angina should have their Hb maintained >70 g/l, but transfusion to a Hb 100 g/l has uncertain benefit; and in patients suffering from acute coronary syndrome, the Hb should be maintained at >80 g/l.

6.3.5 Fresh Frozen Plasma:

- Four units of pre-thawed donor FFP (which may be group A) is available on standby within Blood Bank for massive haemorrhage use only
- Further doses of FFP must be thawed in Blood Bank before use: a process which takes up to 40 minutes

For your information during the pre-administration bedside check, see below compatibilities of FFP

Recipient Group	O	A	B	AB
1st choice donor group	O	A	B	AB
2nd choice donor group	A	AB	AB	A*
3rd choice donor group	B	B*	A*	B*
4th choice donor group	AB	-	-	-

**only suitable for emergency use.*

6.3.6 octaplasLG®

- All patients born after 1/1/1996 should receive octaplasLG® instead of fresh frozen plasma. octaplasLG® is solvent detergent treated virally inactivated blood group specific pooled product and sourced from vCJD free countries and is used as a vCJD control measure for those not exposed to environmental factors related to vCJD.
- octaplasLG® is used and administered in the same way as FFP but should be prescribed as octaplasLG®
- **NB:** *pre-thawed* octaplasLG® is not stored in Blood Bank. It is a clinical decision whether or not the massive haemorrhage situation requires instant FFP or if can wait up to 30 minutes for octaplasLG® to be thawed.
  octaplasLG® is obtained from Blood Bank by telephone detailing the patient's name, date of birth and ID number.

  To help with the decision whether to use FFP or wait for octaplasLG;
  - octaplasLG and FFP have similar constituents/properties
  - octaplasLG is virally inactivated and has a lower risk than FFP of transfusion reactions such as TRALI
  - In the UK there is no risk ratio for developing vCJD from transfusion. Since the outbreak of vCJD there have been 177 cases of vCJD in UK, 4 of which were confirmed as transfusion transmitted

  Δ see below for further information

NB: Both FFP and octaplasLG® once thawed must not be warmed further so must not be given via a Level One or Belmont infuser or other fluid warming device.

6.3.7 Platelets (1 adult dose)

BCSH state thrombocytopenia is considered a late event in massive haemorrhage, typically seen only after a loss of at least 1.5 blood volumes (Counts et al, 1979; Hiippala, 1998). Outside trauma and in major haemorrhage other than after cardiopulmonary bypass, there is little evidence to inform optimal use of platelet transfusion. Increasing numbers of patients are on anti-platelet medications, and there is the uncertain contributory role of platelet function defects in patients with major bleeding.

LTHT Guidelines on management of bleeding in patients on novel anti-coagulants state: If the patient is also on antiplatelet therapy give one adult dose of platelets irrespective of the platelet count and consider further platelet transfusion if bleeding is continuing as per usual haemorrhage guidelines.
For further information see:
http://nww.lhp.leedsth.nhs.uk/common/guidelines/detail.aspx?ID=4536

- Aim to give platelets after 4 units of RBC and 4 units FFP if the clinical picture suggests on-going blood loss. If clinical bleeding has been stopped, platelets should be given based on the platelet count or TEG results
- **One dose of universal donor group A platelets is kept for use in emergency massive haemorrhage in each Blood Bank** and will be sent on request. Further units will be ordered from the National Blood Service (NBS) centre as required

- Be aware, delivery from NBS (Seacroft) to clinical areas can be delayed in heavy traffic, therefore it is recommended to request platelets when the platelet count has fallen below $100x10^9$/l to help maintain the level $>50x10^9$/l during massive haemorrhage.

6.3.8 Cryoprecipitate (2 pooled packs for an average adult)

If fibrinogen falls to <1.5g/L and/or abnormalities in laboratory tests or abnormal TEG results, it may be necessary to consider the use of cryoprecipitate.

- Cryoprecipitate must be thawed in Blood Bank before use: a process which takes up to 40 minutes
- Cryoprecipitate is available in pooled doses. One bag of pooled cryo' contains 5 single units. Pooled units are intended for adults with 2 pooled packs for an average adult
- 1 adult dose of cryoprecipitate will contain between 3-6g fibrinogen which will typically raise the plasma fibrinogen level by approx. 1 g/l
- It is important to re-test coagulation screen post-infusion

ALL blood components must be given via a giving set with a 200 micron filter

FURTHER TRANSFUSION REQUESTS SHOULD DEPEND ON TEG READINGS / HAEMATOLOGY RESULTS & CLINICAL PICTURE

BUT: IF THERE IS ON-GOING SIGNIFICANT HAEMORRHAGE THE BASIC PRINCIPLE OF 1 UNIT OF RBC TO 1 UNIT OF FFP TO 1 UNIT OF PLATELETS SHOULD CONTINUE

Any unused blood components MUST be returned to Blood Bank immediately

Δ For Information: The currently imported FFP by the National Blood Service is a "single donor" blood component produced from US male donors. It is treated with methylene blue and light as a viral inactivation method and is primarily intended for use in patients born since Jan 1st 1996
Sixteen of the Member States of Council of Europe employ Pathogen Reduced technologies for plasma while seven have introduced a universal pathogen plasma inactivation practice. The most frequently used PR technology is the Solvent Detergent (SD) treatment.
In SHOT report 2011, the estimated risk of acute reaction to octaplas was 1 to 24,809 while that of severe reactions was 1 in 86.832. The rate of acute reaction to octaplas was significantly lower to standard FFP (p=0.006), while the rate of severe reactions was also lower but did not reach statistical significant.

6.3.9 Further Coagulation Level Guide:

Transfusion Trigger	Component / Dose
PT and/or APTT >1.5 times normal	FFP dose: 12-15ml/kg
Fibrinogen <1.5 g/l	Cryo' dose: 2 pooled packs = between 3-6g fibrinogen
Platelets $<50x10^9$/l	Platelet dose: 1 adult dose

After completion of massive haemorrhage treatment or at least every hour, haemostatic tests and FBC should be repeated at least every hour if bleeding is on-going, so that trends may be observed and adequacy of replacement therapy documented. Widespread microvascular oozing is a clinical marker of haemostatic failure irrespective of blood tests and should be treated aggressively.

6.3.10 Intraoperative Cell Salvage (ICS):

BCSH (2015) and NICE (2015) recommend the use of ICS as it may be of great value in reducing requirements for allogeneic donor blood and can be accessed from areas where it is in routine use.

ICS can produce a rapid supply of red cells with 250ml of washed salvaged red cells being equivalent to one unit of allogeneic donor red cells. Cell salvage can be particularly useful in managing haemorrhage associated with ruptured aortic repair, splenic and liver trauma, pelvic and femoral fractures, abdominal and thoracic trauma. It is important to remember that FFP will need to be administered in conjunction with the salvaged red cells in the same 1:1 ratio.

6.3.11 Prothrombin Complex Concentrate

While the use of prothrombin complex concentrate (PCC) is recommended in the urgent reversal of the effect of vitamin K antagonists, currently there is no good evidence to support the use of PCC in the management of Massive haemorrhage, BCSH (2015).

6.3.12 Massive Haemorrhage Stand Down

Blood Bank must be informed to '**STAND DOWN'** as soon as it is apparent the massive haemorrhage protocol is no longer needed. This will help to conserve resources.

7. Disseminated Intravascular Coagulation (DIC)

This is one of the serious early complications of massive haemorrhage. Contributory factors to and evidence of DIC include:

- Hypothermia
- Prolonged hypovolaemia and hypoxia
- Acidosis
- Low levels of coagulation factors including Factors V, VIII and fibrinogen
- Thrombocytopenia

Haematological evidence of prolonged PT, APTT with thrombocytopenia and fibrinogen levels < 1 g/l are highly suggestive of impending DIC. Frequent estimation of platelet count, fibrinogen, PT and APTT is strongly recommended and measurement of D-dimer may also be useful in providing an early warning. Laboratory evidence of DIC should be sought before microvascular bleeding becomes evident so that action can be taken to address the underlying cause.

Treatment consists of platelets, FFP and cryoprecipitate given 'sooner rather than later' in sufficient dosage but avoiding circulatory overload. The clinical outcome of DIC depends on the ability to reverse the underlying cause.

8. Risks of massive transfusion

Clinicians should be aware that there are risks associated with massive transfusion and blood component therapy; including:

- Incorrect Blood Component Transfused (IBCT)
- Transfusion Related Acute Lung Injury (TRALI)
- Immune complications and acute reactions
- Hyperkalaemia due to high extracellular potassium in stored red cell units *and* ionised hypocalcaemia due to citrate toxicity especially if there is liver synthetic dysfunction. This may interfere with coagulation and have other adverse metabolic consequences**. Ionised calcium and potassium levels may need to be measured as often as every 15 minutes depending on the rate of blood component administration.** Ionised calcium levels may be corrected by slow intravenous bolus of calcium chloride. A dose of 10mL calcium chloride 10% over 10 minutes has been recommended, followed by repeat of the assay. For ease of use, a Min-I-Jet or pre-filled syringe is available in the Trust standard blue crash box. **Aim to maintain calcium levels ≥1.0 mmo/L.**

All suspected transfusion reactions MUST be reported to the Hospital Transfusion Team immediately in order to comply with MHRA investigation and reporting requirements.

9. De-briefing

To ensure effective massive haemorrhage management systems are in place clinical areas should organise a 'de-brief' after each massive haemorrhage case to establish any learning points and/or if any changes in practice are required in response to any recurrent issues to improve the outcome in future massive haemorrhage situations.
The de-brief group should consist of all key stakeholders including representation from the Hospital Transfusion Team and Transfusion lab to enable a full and robust analysis of the approach to the massive haemorrhage case.

10. Managing Established Bleeding in Different Patient Subgroups

10.1 Gastro-intestinal (GI) bleeding is a common indication for transfusion of blood components. BCSH (2015) state the publication of a single centre RCT (with defined inclusion/exclusion criteria) comparing liberal and restrictive policies for red cell transfusion in patients with non-massive acute upper GI bleeding showed a higher 6-week survival and lower re-bleeding rate in patients allocated to a restrictive threshold for red cell transfusion at 70 g/l (post-transfusion target 70–90 g/l) (Villanueva et al, 2013). Portal pressures were reported to be significantly increased in the liberal transfusion group. Although there are no comparable studies addressing changes in coagulopathy or thrombocytopenia, it seems sensible to follow a restrictive approach to the use of FFP and platelets in patients with acute upper GI bleeding unless there is massive life-threatening haemorrhage or evidence of severe derangements in laboratory tests.

In early signs of hypovolaemic shock, tachycardia may not occur early in patients who take beta-blockers. Blood pressure may not fall until about 20% blood is lost. Older people with high blood pressure or atherosclerosis may be in the stage of decompensated shock even if their blood pressure is at 120 mm Hg or above

Late signs of hypovolaemic shock include: Increase of tachycardia, or bradycardia, arrhythmia, tachypnoea: >30/min or bradypnoea: <12/min, capillary refill time (CRT) >5 seconds or absent, hypothermia and low, "narrow" blood pressure i.e. systolic pressure falls earlier than diastolic, because it is more dependent on blood volume; systolic blood pressure may not fall until 30% blood is lost.

In the case of gastrointestinal haemorrhage it is can be difficult to determine if bleeding is on-going without an endoscopy.

It is a NICE quality statement that patients with severe acute upper gastrointestinal bleeding should be offered an emergency endoscopy, usually undertaken in the operating theatre to protect the airway and maintain optimal perfusion within 2 hours of initial resuscitation".

To arrange the emergency endoscopy, please contact the on-call gastroenterologist and to arrange the theatre slot, please liaise directly with acute theatres and the emergency anaesthetist.

During uncontrolled haemorrhage BCSH and NICE recommend avoiding clear fluids for volume replacement, however in some situations e.g. upper GI haemorrhage it may be necessary to restore circulating volume using pre-warmed crystalloid or colloid as appropriate whilst waiting for blood components to be available, attention should be paid to avoiding dilutional coagulopathy and to be aware colloid solution may adversely affect coagulation results.

Gastroenterology may find the Baskett index useful in providing a bed-side estimation of blood loss.

	Class I	Class II	Class III	Class IV
Blood loss, volume (ml)	<750	750-1500	1500-2000	>2000
Blood loss (% of circulating blood)	0-15	15-30	30-40	>40
Systolic blood pressure	No change	Normal	Reduced	Very reduced
Diastolic blood pressure	No change	Raised	Reduced	Very reduced/ unrecordable
Pulse (beats per minute)	Slight tachycardia	100-120	120 (thready)	>120 (very thready)
Respiratory rate	Normal	Normal	Raised (>20/min)	Raised (>20/min)
Mental state	Alert, thirsty	Anxious or aggressive	Anxious, aggressive or drowsy	Drowsy, confused or unconscious

Adapted from Baskett, PJF. ABC of major trauma. Management of Hypovolaemic Shock. BMJ 1990; 300: 1453-1457.

NB: The role of tranexamic acid in GI haemorrhage has not been proven; its role is being addressed in a large pragmatic RCT, the HALT-IT study (http://haltit.lshtm.ac.uk/ProtocolSummary.pdf)
For further advice on upper GI bleeding, see:
http://nww.lhp.leedsth.nhs.uk/common/guidelines/detail.aspx?id=3263

10.2 Trauma: BCSH (2015) state, the recent PROPPR trial (Holcomb et al, 2015) reported that in patients who have or are at risk of massive blood loss, initial infusion with plasma, platelets and red blood cells in a 1:1:1 ratio compared to 1:1:2 ratio did not improve overall survival. However in additional analyses more patients in the 1:1:1 group were reported to achieve 'anatomic' haemostasis and fewer may have experienced death due to exsanguination by 24h. The relative contribution of platelets or plasma to the resuscitation outcomes could not be defined in this study. We recommend that plasma: red blood cells are given initially in a 1:1 ratio, but when bleeding is under control, laboratory testing should guide blood component therapy. We suggest consideration of early use of platelets.

10.3 Obstetrics: have a dedicated massive haemorrhage protocol; including 1:1:1 transfusion management, see Leeds Health Pathways:
http://nww.lhp.leedsth.nhs.uk/common/guidelines/detail.aspx?ID=2146

10.4: Neonates & Paediatrics have a dedicated massive transfusion guideline, see Leeds Health Pathways: http://nww.lhp.leedsth.nhs.uk/common/guidelines/detail.aspx?ID=2412

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NICE guideline (2015) Blood Transfusion. https://www.nice.org.uk/guidance/ng24

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See also: http://www.transfusionguidelines.org.uk/index.asp?Publication=HTM

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http://www.sign.ac.uk/pdf/sign105.pdf

Algorithm for the Generic Transfusion Management of Adult Massive Haemorrhage

-Adapted from BCSH Guidelines (2015): A Practical Guideline for the Management of those with, or at risk of Major Haemorrhage

Recognise blood loss and trigger massive haemorrhage protocol

- When bleeding leads to a heart rate more than 110 beats/minute and/or systolic blood pressure less than 90 mmHg
- And/or the loss of one blood volume within a 24 hour period, 50% blood volume loss within 3 hours or a rate of loss of 150ml per minute

Contact Key Personnel as appropriate e.g. Duty or On-Call Consultant caring for the patient, Anaesthetist, Interventional Radiologist, Endoscopist, Haematologist (if clotting is a concern)

Team Leader to co-ordinate further management and appoint 1 person to liaise with Blood Bank LGI: 23398 (24h) or 22413 (9-5pm), SJUH: 65559 (24h) or 67513 (9-5pm).
State: **"initiate the massive haemorrhage protocol"** and give the patient's name, date of birth and ID Number and to where you want the blood components issuing

- Use group-specific RBC as soon as possible

NB: SJUH: on CARPS make an 'urgent' request for blood collection, LGI: blood will be delivered

Take baseline blood samples prior to transfusion for:

- Full blood count, Crossmatch, Clotting screen including Clauss Fibrinogen, U&E, LFT, Calcium, ABG

Administer RBC:FFP in a ratio of 1:1

(NB: Include any O negative used in the initial total ratio & inform Blood Bank when used)

NB: octaplasLG® should be used for patients born after 1/1/1996 but is NOT stored pre-thawed, it is a clinical decision whether or not to wait for thawing - see section 6.3.6

Prevent hypothermia: use fluid warming device / keep the patient warm

Consider Administering Tranexamic Acid 1gram bolus over 10 minutes followed by I.V. infusion of 1gram over 8 hours - within 3 hours of haemorrhage

IF BLEEDING CONTINUES

Give Red Cells and FFP in a 1:1 ratio:
4 units red cells
4 units FFP

- Consider 1 adult dose of platelets if clinically indicated and/or depending on Lab/TEG results
- Consider cryoprecipitate if clinically indicated +/- fibrinogen<1.5g/L or as guided by TEG

When laboratory results are available:

IF:	GIVE:
Falling Hb	Red cells
APPT and/or PT ratio>1.5 g/l	FFP 12-15 ml/kg
Fibrinogen <1.5 g/l	Cryoprecipitate 2 packs
Platelet count <50x10^9/l	Platelets 1 adult dose (order when <100x10^9/l)

Stand Down:

Inform Blood Bank
Return unused blood components
Fate blood units

Continue cycle of monitoring and giving appropriate blood components depending on laboratory results until bleeding stops

Aims for Therapy:

Hb 80-100g/L	**Fibrinogen** >1.5g/L
Platelets >50 x 10^9 /L	**Ca** $^{2+}$ >1 mmol/L
PT ratio < 1.5	**pH** > 7.35 (on ABG)
APTT ratio <1.5	**Temp** >36°C

Monitor for hyperkalaemia

Glossary

Activated Partial Thromboplastin Time (APTT) - a laboratory test that measures the activity of clotting factors in the Intrinsic pathway of coagulation. It is commonly prolonged in DIC and following dilution of normal clotting factors by massive red cell transfusion.

Disseminated intravascular coagulation (DIC) occurs when there is generalised activation of the coagulation and fibrinolytic pathways with consumption of multiple clotting factors and platelets. Common causes include sepsis and traumatic tissue injury. The laboratory profile typically includes prolongation of both the Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT), reduced plasma fibrinogen level and elevation of D-dimer (a breakdown product of fibrin clots). There is often thrombocytopenia due to consumption of platelets and evidence of red cell fragmentation on the blood film. Decompensated DIC may be associated with clinical signs of both bleeding and thrombosis in the same patient.

FFP - Fresh Frozen Plasma - obtained from normal blood donors and used as a therapeutic source of clotting factors.

Prothrombin Time (PT) - a laboratory test that measures the activity of clotting factors in the extrinsic pathway of coagulation. It is commonly used to monitor warfarin therapy and is often prolonged in liver disease and DIC and following dilution of normal clotting factors by massive red cell transfusion..

Prothrombin Time Ratio (PT Ratio) - the ratio of the patient's PT to the PT of normal plasma. It provides a measure of the degree of clotting abnormality.

SHOT - Serious Hazards of Transfusion - the UK Haemovigilence network. SHOT is a voluntary reporting system for serious transfusion errors and reactions and complements the mandatory reporting system for Serious Adverse Events in transfusion mandated by the Medicines and Healthcare Products Regulatory Agency (MHRA). SHOT produces recommendations for the NHS and Blood Transfusion Services to increase patient safety.

TEG (Thromboelastography) - a global test of coagulation and fibrinolysis that can be used in the clinical area (point of care test). It can identify abnormalities in clotting factors, platelets and fibrinolytic activity and may be used to target appropriate blood component therapy.

Thrombocytopenia - a reduction in the peripheral blood platelet count (normally 150-400x10^9/l). A level of 50x10^9/l is adequate for most surgery and is the minimum target for patients requiring massive transfusion or bleeding from DIC. If necessary, requests for platelet transfusion therapy are initiated at 100x10^9/l in patients with massive bleeding (predictable when 2 blood volumes have been replaced by red cells and plasma transfusion) as platelets have to be ordered from the National Blood Service centre.