Patient Blood Management Guidelines: Module 1

Critical Bleeding Massive Transfusion

Quick Reference Guide

ISBN 978-0-9873687-9-9

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Disclaimer

This document is a general guide to appropriate practice, to be followed subject to the circumstances, clinician's judgement and patient's preferences in each individual case. It is designed to provide information to assist decision making. Recommendations contained herein are based on the best available evidence published up to the dates shown in Appendix D of the Module. The relevance and appropriateness of the information and recommendations in this document depend on the individual circumstances. Moreover, the recommendations and guidelines are subject to change over time.

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Patient Blood Management Guidelines: Module 1 – Critical Bleeding / Massive Transfusion

Development of this module was achieved through clinical input and expertise of representatives from the Colleges and Societies listed below and an independent consumer advocate (see Appendix A in the module).

The National Blood Authority gratefully acknowledges these contributions.

Australasian College for Emergency Medicine
Australian and New Zealand College of Anaesthetists
Australian and New Zealand Intensive Care Society
Australian and New Zealand Society of Blood Transfusion
Australian Orthopaedic Association
Australian Red Cross Blood Service
College of Intensive Care Medicine of Australia and New Zealand
Haematology Society of Australia and New Zealand
Royal Australian and New Zealand College of Obstetricians and Gynaecologists
Royal Australasian College of Physicians
Royal Australasian College of Surgeons
Royal College of Nursing Australia
Royal College of Pathologists of Australasia
Thalassaemia Australia

College and Society endorsement of this Module can be found at www.nba.gov.au

National Blood Authority Australia

Funding, Secretariat and Project Management was provided by the National Blood Authority Australia.
The development of the final recommendations has not been influenced by the views or interests of the funding body.

Abbreviations and acronyms

APTT	activated partial thromboplastin time
ARDS	acute respiratory distress syndrome
ASBT	Australasian Society of Blood Transfusion
CRG	Clinical/Consumer Reference Group
FFP	fresh frozen plasma
INR	international normalised ratio
MTP	massive transfusion protocol
NBA	National Blood Authority
NHMRC	National Health and Medical Research Council
PP	practice point
PT	prothrombin time
R	recommendation
RBC	red blood cell
rFVIIa	recombinant activated factor VII

Contents

Introduction

This document summarises for clinicians the *Patient Blood Management Guidelines: Module 1 – Critical Bleeding/Massive Transfusion*,[1] the first in a series of six modules that focus on evidence-based patient blood management.

Patient blood management aims to improve clinical outcomes by avoiding unnecessary exposure to blood components. It includes the three pillars of:

- optimisation of blood volume and red cell mass
- minimisation of blood loss
- optimisation of the patient's tolerance of anaemia.

These principles apply in the management of any haematological disorder. Patient blood management optimises the use of donor blood and reduces transfusion-associated risk.

If blood components are likely to be indicated, transfusion should not be a default decision. Instead, the decision on whether to transfuse should be carefully considered, taking into account the full range of available therapies, and balancing the evidence for efficacy and improved clinical outcome against the potential risks.

The other five modules in this series are perioperative, medical, critical care, obstetrics and paediatrics/neonates. Together, the six modules replace the 2001 National Health and Medical Research Council/Australasian Society of Blood Transfusion (NHMRC/ASBT) *Clinical practice guidelines on the use of blood components*.[2] Revision of the 2001 guidelines was needed because of:

- increasing evidence of transfusion-related adverse outcomes, leading to the emergence of new practices, including restrictive transfusion strategies and the increased use of alternatives to transfusion in the management of anaemia
- variable (and frequently poor) compliance with the recommendations of the 2001 guidelines, indicated by a high degree of variation in transfusion practices
- failure of the 2001 guidelines to address a range of clinical settings where blood management is commonly required, including critical bleeding and massive transfusion, chronic medical conditions, obstetrics and paediatrics.

This document was developed by a Clinical/Consumer Reference Group (CRG) representing specialist colleges, organisations and societies, with the active participation of the clinical community.

This document includes:

- a summary of the *recommendations* that were developed by the CRG, based on evidence from a systematic review
- a summary of the *practice points* that were developed by the CRG through consensus decision-making
- a *massive transfusion protocol* (MTP)[a] template, which can be adapted to meet local needs.

Details of the systematic review used in the development of this module are given in a two-volume technical report.[3,4]

[a] The use of the word 'protocol' in 'massive transfusion protocol' throughout this report is not strictly prescriptive.

Recommendations

The CRG developed recommendations (given below) where sufficient evidence was available from the systematic review of the literature. The recommendations have been carefully worded to reflect the strength of the body of evidence. Each recommendation has been given a grade, using the following definitions, which were set by the NHMRC:

GRADE A	Body of evidence can be trusted to guide practice
GRADE B	Body of evidence can be trusted to guide practice in most situations
GRADE C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
GRADE D	Body of evidence is weak and recommendations must be applied with caution.

RECOMMENDATION		Relevant section of module
R1 **GRADE C**	It is recommended that institutions develop an MTP that includes the dose, timing and ratio of blood component therapy for use in trauma patients with, or at risk of, critical bleeding requiring massive transfusion (Grade C).[5,6]	4.2
R2 **GRADE B** **GRADE C**	The routine use of rFVIIa in trauma patients with critical bleeding requiring massive transfusion is not recommended because of its lack of effect on mortality (Grade B)[7] and variable effect on morbidity (Grade C).[7]	4.6

MTP, massive transfusion protocol; rFVIIa, recombinant activated factor VII

Summary of practice points

The CRG developed practice points where, as was commonly the case, the systematic review found insufficient high-quality data to produce evidence-based recommendations, but the CRG felt that clinicians require guidance to ensure good clinical practice. These points are based on consensus among the members of the committee.

PRACTICE POINT		Relevant section of module
PP1	In patients with critical bleeding requiring massive transfusion, the following parameters should be measured early and frequently: ▪ temperature ▪ acid–base status ▪ ionised calcium ▪ haemoglobin ▪ platelet count ▪ PT/INR ▪ APTT ▪ fibrinogen level. With successful treatment, values should trend towards normal.	4.1
PP2	Values indicative of critical physiologic derangement include: ▪ temperature < 35°C ▪ pH < 7.2, base excess > –6, lactate > 4 mmol/L ▪ ionised calcium < 1.1 mmol/L ▪ platelet count < 50 × 10^9/L ▪ PT > 1.5 × normal ▪ INR > 1.5 ▪ APTT > 1.5 × normal ▪ fibrinogen level < 1.0 g/L.	4.1

PRACTICE POINT		Relevant section of module
PP3	In critically bleeding patients requiring, or anticipated to require, massive transfusion, an MTP[a] should be used. A template MTP is provided within the module.[b] [a] The use of the word 'protocol' in 'massive transfusion protocol' throughout the module is not strictly prescriptive. [b] The template MTP is intended for local adaptation.	4.2
PP4	In patients with critical bleeding requiring massive transfusion, insufficient evidence was identified to support or refute the use of *specific* ratios of RBCs to blood components.	4.2
PP5	In patients with critical bleeding requiring massive transfusion, haemoglobin concentration should be interpreted in the context of haemodynamic status, organ perfusion and tissue oxygenation.	4.3
PP6	In patients with critical bleeding requiring massive transfusion, the use of RBC and other blood components may be life saving. However, transfusion of increased volumes of RBC and other blood components may be independently associated with increased mortality and ARDS.	4.4
PP7	In patients with critical bleeding requiring massive transfusion, the use of an MTP to facilitate timely and appropriate use of RBC and other blood components may reduce the risk of mortality and ARDS.	4.4
PP8	An MTP should include advice on the administration of rFVIIa when conventional measures – including surgical haemostasis and component therapy – have failed to control critical bleeding. NB: rFVIIa is not licensed for this use. Its use should only be considered in exceptional circumstances where survival is considered a credible outcome (see Template MTP example).	4.6
PP9	When rFVIIa is administered to patients with critical bleeding requiring massive transfusion, an initial dose of 90 µg/kg is reasonable.	4.6

PRACTICE POINT		Relevant section of module
PP10	In patients with critical bleeding requiring massive transfusion, suggested doses of blood components are:[a] ▪ FFP: 15 mL/kg ▪ platelets: 1 adult therapeutic dose ▪ cryoprecipitate: 3–4 g. [a] Or as directed by the haematologist/transfusion specialist in specific clinical situations, such as obstetrics.	4.8

APTT, activated partial thromboplastin time; ARDS, acute respiratory distress syndrome; FFP, fresh frozen plasma; INR, international normalised ratio; MTP, massive transfusion protocol; PT, prothrombin time; RBC, red blood cell; rFVIIa, recombinant activated factor VII

CRASH 2[8]	
In trauma patients with or at risk of significant haemorrhage, tranexamic acid (loading dose 1 g over 10 minutes, followed by infusion of 1 g over 8 hours) should be considered. The CRASH 2 trial was published on 14 June 2010 after the cut-off date of the systematic review.[8] No systematic review was conducted on tranexamic acid in critical bleeding/massive transfusion. The study population was not restricted to critical bleeding requiring massive transfusion.	4.9

Massive transfusion protocol (MTP) template

The MTP template is given below. This section discusses local adaptation of the template MTP, and development of guidelines on activation and cessation of the MTP.

Local adaptation

A multidisciplinary team should adapt the MTP template to:

- incorporate the recommendations and practice points provided in the module
- take into account local resources (e.g. access to blood components)
- provide details of how components will be delivered to the correct patient and location
- include supporting information that explains how the clinical, laboratory and support staff will communicate
- highlight the need for early communication with a haematologist or transfusion specialist.

The MTP template can also be modified for specific populations such as obstetric patients, given the potential for concealed haemorrhage and early development of disseminated intravascular coagulation.

The local facility should also develop materials to accompany the MTP, clarifying the roles and responsibilities of the team members (e.g. task cards).

Activation and cessation

The multidisciplinary team should also develop guidelines for the activation and cessation of the MTP. This will help to ensure that the MTP is used appropriately, and wastage of blood components is minimised.

Activation of the MTP should take into account:

- cause and rate of the haemorrhage
- mechanism of injury (if present)
- current physiological state
- likely requirement for ongoing blood component support.

The MTP template given here includes suggestions on when to activate an MTP. The guidelines on activation and cessation of the MTP should be clearly communicated to all relevant staff.

Use of the MTP should be audited.

Massive transfusion protocol (MTP) template

Senior clinician determines that patient meets criteria for MTP activation

Baseline:

Full blood count, coagulation screen (PT, INR, APTT, fibrinogen), biochemistry, arterial blood gases

Notify transfusion laboratory *(insert contact no.)* **to:**
'Activate MTP'

Laboratory staff

- Notify haematologist/transfusion specialist
- Prepare and issue blood components as requested
- Anticipate repeat testing and blood component requirements
- Minimise test turnaround times
- Consider staff resources

Haematologist/transfusion specialist

- Liaise regularly with laboratory and clinical team
- Assist in interpretation of results, and advise on blood component support

Senior clinician

- **Request:**[a]
  - o 4 units RBC
  - o 2 units FFP
- **Consider:**[a]
  - o 1 adult therapeutic dose platelets
  - o tranexamic acid in trauma patients
- **Include:**[a]
  - o cryoprecipitate if fibrinogen < 1 g/L

[a] Or locally agreed configuration

Bleeding controlled?

YES

NO

Notify transfusion laboratory to:
'Cease MTP'

This information, developed by consensus, broadly covers areas that should be included in a local MTP.

This template can be used to develop an MTP to meet the needs of the local institution's patient population and resources.

OPTIMISE:

- oxygenation
- cardiac output
- tissue perfusion
- metabolic state

MONITOR
(every 30–60 mins):

- full blood count
- coagulation screen
- ionised calcium
- arterial blood gases

AIM FOR:

- temperature > 35^0C
- pH > 7.2
- base excess < – 6
- lactate < 4 mmol/L
- Ca^{2}+ > 1.1 mmol/L
- platelets > 50 x 10^9/L
- PT/APTT < 1.5 x normal
- INR $\leq$ 1.5
- fibrinogen > 1.0 g/L

Suggested criteria for activation of MTP

- **Actual or anticipated 4 units RBC in < 4 hrs, + haemodynamically unstable, +/– anticipated ongoing bleeding**
- **Severe thoracic, abdominal, pelvic or multiple long bone trauma**
- **Major obstetric, gastrointestinal or surgical bleeding**

Initial management of bleeding

- Identify cause
- Initial measures:
  - compression
  - tourniquet
  - packing
- Surgical assessment:
  - early surgery or angiography to stop bleeding

Specific surgical considerations

- If significant physiological derangement, consider damage control surgery or angiography

Cell salvage

- Consider use of cell salvage where appropriate

Dosage

Platelet count < 50 x 10^9/L	1 adult therapeutic dose
INR > 1.5	FFP 15 mL/kg[a]
Fibrinogen < 1.0 g/L	cryoprecipitate 3–4 g[a]
Tranexamic acid	loading dose 1g over 10min, then infusion of 1g over 8 hrs

[a] Local transfusion laboratory to advise on number of units needed to provide this dose

This information, developed by consensus, broadly covers areas that should be included in a local MTP.
This template can be used to develop an MTP to meet the needs of the local institution's patient population and resources.

Initial management of bleeding

- Avoid hypothermia, institute active warming
- Avoid excessive crystalloid
- Tolerate permissive hypotension (BP 80–100 mmHg systolic) until active bleeding controlled
- Do not use haemoglobin alone as a transfusion trigger

Special clinical situations

- Warfarin:
  - add vitamin K, prothrombinex/FFP
- Obstetric haemorrhage:
  - early DIC often present; consider cryoprecipitate
- Head injury:
  - aim for platelet count > 100 x 10^9/L
  - permissive hypotension contraindicated

Considerations for use of rFVIIa[b]

The *routine* use of rFVIIa in trauma patients is not recommended due to its lack of effect on mortality (Grade B) and variable effect on morbidity (Grade C). Institutions may choose to develop a process for the use of rFVIIa where there is:

- uncontrolled haemorrhage in salvageable patient, and
- failed surgical or radiological measures to control bleeding, and
- adequate blood component replacement, and
- pH > 7.2, temperature > 34^0C.

Discuss dose with haematologist/transfusion specialist

[b] rFVIIa is not licensed for use in this situation; all use must be part of practice review.

ABG	arterial blood gas
FFP	fresh frozen plasma
APTT	activated partial thromboplastin time
INR	international normalised ratio
BP	blood pressure
MTP	massive transfusion protocol
DIC	disseminated intravascular coagulation
PT	prothrombin time
FBC	full blood count
RBC	red blood cell
rFVIIa	activated recombinant factor VII

Product Information

Table F.1 Blood component product information and dosage – Australia

Component	Content and characteristics	Volume per bag[a]	Typical adult dose (~ 70 kg)	Number of bags to provide typical dose
FFP	▪ Plasma recovered from a whole blood donation or apheresis collection ▪ Contains all coagulation factors	250–334 mL	10–15 mL/kg	3–4
Platelets: pooled	▪ A pool of platelets derived from the buffy coat of four whole blood donations ▪ Leucodepleted	>160 mL	1 bag	1
Platelets: apheresis	▪ A suspension of platelets prepared from a single apheresis donor ▪ Leucodepleted	100–400 mL	1 bag	1
Cryo-precipitate	▪ Prepared from a single donated whole blood unit ▪ Contains an average of > 0.35 g/bag ▪ Contains high levels of fibrinogen, factor VIII, von Willebrand factor, factor XIII, fibronectin	30–40 mL	3–4 g fibrinogen	8–10
Cryo-precipitate: apheresis	▪ Prepared from FFP obtained from a plasmapheresis donor ▪ Contains an average of > 0.8 g/bag	60 mL (± 10%)	3–4 g fibrinogen	4–5

FFP, fresh frozen plasma

[a] Actual volume indicated on label

Table F.2 Blood component product information and dosage – New Zealand

Component	Content and characteristics	Volume per bag[a]	Typical adult dose (~ 70 kg)	Number of bags to provide typical dose
FFP	▪ Plasma recovered from a whole blood donation or apheresis collection ▪ Contains all coagulation factors ▪ Leucodepleted	180–300 mL	10–15 mL/kg	3–4
Platelet pooled	▪ A pool of platelets derived from the buffy coat of four whole blood donations ▪ Leucodepleted	200–350 mL	NA	1
Platelet apheresis	▪ A suspension of platelets prepared from a single apheresis donor ▪ Leucodepleted	180–400 mL	NA	1
Cryo-precipitate	▪ Prepared from FFP obtained from a plasmapheresis donor with a fibrinogen level > 2.4 g/L ▪ Contains an average of 1.4 g/bag ▪ Contains high levels of factor VIII, von Willebrand factor, factor XIII, fibronectin. ▪ Leucodepleted	80–120 mL	3–4 g	2-3

FFP, fresh frozen plasma; NA, not applicable

[a] Actual volume indicated on label

References

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