Massive Transfusion Protocol

Will Davies

May 2014
Massive Transfusion Protocol

Massive transfusion protocol (MTP) template

1. 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 to: ‘Activate MTP’

   Laboratory staff
   - Notify haematologist/transfusion
   - 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:
     - 4 units RBC
     - 2 units FFP
   - Consider:
     - 1 adult therapeutic dose platelets
     - Tranexamic acid in trauma patients
   - Include:
     - Cryoprecipitate if fibrinogen < 1 g/L

   AIM FOR:
   - Temperature > 35°C
   - 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 ≤ 1.5
   - Fibrinogen > 1.0 g/L

   Bleeding controlled?
   - YES
   - NO

   Notify transfusion laboratory to: ‘Cease MTP’

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
- Fibrinogen < 1.0 g/L: cryoprecipitate 3–4 g
- Tranexamic acid:
  - loading dose 1 g over 10 min, then infusion of 1 g over 8 hrs
- Local transfusion laboratory to advise on number of units needed to provide this dose

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

Resuscitation
- 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 fVIIa
The routine use of fVIIa 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 fVIIa 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°C
- Discuss dose with haematologist/transfusion specialist

fVIIa is not licensed for use in this situation, all use must be part of practice review.
Based Entirely Upon

National Blood Authority NMHRC 2011
The Guideline has been Endorsed by:

- 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
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**Baseline:**
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- Request:
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  - 2 units FFP
- Consider:
  - 1 adult therapeutic dose platelets
  - Tranexamic acid in trauma patients
- Include:
  - Cryoprecipitate if fibrinogen < 1 g/L

**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°C
- pH > 7.2
- Base excess < –6
- Lactate < 4 mmol/L
- Ca²⁺ > 1.1 mmol/L
- Platelets > 50 × 10⁹/L
- PT/APTT < 1.5 × normal
- INR ≤ 1.5
- Fibrinogen > 1.0 g/L

Bleeding controlled?
- YES
- NO

Notify transfusion laboratory to: ‘Cease MTP’
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,
- failed surgical or radiological measures to control bleeding,
- adequate blood component replacement,
- pH > 7.2, temperature > 34°C.

Discuss dose with haematologist/transfusion specialist.

### Special clinical situations

- Warfarin:
  - add vitamin K, prothrombinex/FFP
- Obstetric haemorrhage:
  - early DIC often present; consider cryoprecipitate
- Head injury:
  - aim for platelet count > 100 × 10⁹/L
  - permissive hypotension contraindicated

### Considerations for use of rFVIIa

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:

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- adequate blood component replacement, and
- pH > 7.2, temperature > 34°C.

Discuss dose with haematologist/transfusion specialist.

### Dosage

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dose/Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet count &lt; 50 × 10⁹/L</td>
<td>1 adult therapeutic dose</td>
</tr>
<tr>
<td>INR &gt; 1.5</td>
<td>FFP 15 mL/kg⁸</td>
</tr>
<tr>
<td>Fibrinogen &lt; 1.0 g/L</td>
<td>cryoprecipitate 3–4 g⁹</td>
</tr>
<tr>
<td>Tranexamic acid</td>
<td>loading dose 1 g over 10 min, then infusion of 1 g over 8 hrs</td>
</tr>
</tbody>
</table>

Local transfusion laboratory to advise on number of units needed to provide this dose.

**Key Terms**

- **ABG**: arterial blood gas
- **INR**: international normalised ratio
- **DIC**: disseminated intravascular coagulation
- **RBC**: red blood cell
- **FFP**: fresh frozen plasma
- **BP**: blood pressure
- **PT**: prothrombin time
- **rFVIIa**: activated recombinant factor VII
- **APTT**: activated partial thromboplastin time
- **MTP**: massive transfusion protocol
- **FBC**: full blood count
<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Body of evidence can be trusted to guide practice</td>
</tr>
<tr>
<td>B</td>
<td>Body of evidence can be trusted to guide practice in most situations</td>
</tr>
<tr>
<td>C</td>
<td>Body of evidence provides some support for recommendation(s) but care should be taken in its application</td>
</tr>
<tr>
<td>D</td>
<td>Body of evidence is weak and recommendations must be applied with caution</td>
</tr>
</tbody>
</table>

National Health and Medical Research Council (NHMRC) (2009). *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines*, NHMRC, Canberra, Australia
**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 to:**
‘Activate MTP’

---

**EVIDENCE?**

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**Laboratory**
- 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

---

**Consider:**
- 4 units RBC
- 2 units FFP
- 1 adult therapeutic dose platelets
- tranexamic acid in trauma patients

**Include:**
- cryoprecipitate if fibrinogen < 1 g/L

---

**Bleeding controlled?**

**YES**

**NO**

---

**Notify transfusion laboratory to:**
‘Cease MTP’

---

**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°C
- pH > 7.2
- base excess < –6
- lactate < 4 mmol/L
- Ca^{2+} > 1.1 mmol/L
- platelets > 50 \times 10^9/L
- PT/APTT < 1.5 \times normal
- INR ≤ 1.5
- fibrinogen > 1.0 g/L
What Criteria Should be Used?

- **In adults**, ‘massive transfusion’ may be defined as a transfusion of half of one blood volume in 4 hours, or more than one blood volume in 24 hours or blood loss of more than 150 mL per minute. (Adult blood volume is approximately 70 mL/kg). (1)

- **In children**, ‘massive transfusion’ may be defined as a transfusion of more than 40 mL blood/kg. (The normal blood volume of a child is approximately 80 mL/kg.)

## Classes of Shock

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood Loss (ml)</strong></td>
<td>&lt;750</td>
<td>750-1500</td>
<td>1500-2000</td>
<td>&gt;2000</td>
</tr>
<tr>
<td><strong>Blood Loss (% blood vol)</strong></td>
<td>&lt;15</td>
<td>15-30</td>
<td>30-40</td>
<td>&gt;40</td>
</tr>
<tr>
<td><strong>Pulse (/min)</strong></td>
<td>&lt;100</td>
<td>100-120</td>
<td>120-140</td>
<td>&gt;140</td>
</tr>
<tr>
<td><strong>BP</strong></td>
<td>Normal</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>Pulse Pressure</strong></td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>RR (/min)</strong></td>
<td>14-20</td>
<td>20-30</td>
<td>30-40</td>
<td>&gt;35</td>
</tr>
<tr>
<td><strong>Urine Output (ml/hr)</strong></td>
<td>&gt;30</td>
<td>20-30</td>
<td>15-20</td>
<td>Negligible</td>
</tr>
<tr>
<td><strong>Mental State</strong></td>
<td>Slightly Anxious</td>
<td>Anxious</td>
<td>Confused</td>
<td>Confused/Lethargic</td>
</tr>
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Note: Values are estimated for a 70 kg male

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- Assist in interpretation of results, and advise on blood component support

**Optimise:**
- oxygenation
- cardiac output
- tissue perfusion
- metabolic state

**Monitor**
(every 30–60 mins):
- full blood count
- coagulation screen
- ionised calcium
- arterial blood gases

**Evidence?**

**Consider:**
- 4 units RBC
- 2 units FFP
- 1 adult therapeutic dose platelets
- Tranexamic acid in trauma patients

**Include:**
- Cryoprecipitate if fibrinogen < 1 g/L

**Bleeding controlled?**

**Yes**

Notify transfusion laboratory to: ‘Cease MTP’

**No**

**AIM FOR:**
- Temperature > 35°C
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In patients with critical bleeding requiring massive transfusion, what is the effect of variation of physiologic, biochemical and metabolic (including temperature) parameters on morbidity, mortality and transfusion rate?

- 10 studies, comprising 8 retrospective and 2 prospective analyses of registry data, medical records or charts.
- Most of the studies of critically bleeding and transfused patients found that reduced core body temperature, lower pH or higher base deficit, coagulopathy and thrombocytopenia were associated with increased mortality.
- BUT the evidence was not conclusive once odds ratios were calculated.
Individual Variables were Hard to Extrapolate

• The only statistically significant factor in increased mortality was an increase in INR which had a mortality odds ratio of 1.62; 95%CI: 1.18, 2.24; p< 0.01 (1)

• Studies were found to provide an evidence statement on the effects of hypothermia, metabolic acidosis, thrombocytopenia and coagulopathy on morbidity or transfusion rate.

• Mortality was found to be highest where acidosis and hypothermia occurred with coagulopathy. This combination has become known as the ‘lethal triad’ or ‘bloody vicious cycle’.

Recommendation:

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.

LEVEL OF EVIDENCE FOR THIS RECOMMENDATION?

Body of evidence is weak and recommendations must be applied with caution.
Values Indicative of Critical Physiologic Derangement

- 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
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Bleeding controlled?

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**OPTIMISE:**
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Is Early use of FFP and Plts of Benefit?

LEVEL OF EVIDENCE FOR THIS RECOMMENDATION?


Body of evidence is weak and recommendations must be applied with caution.
In trauma patients with critical bleeding requiring massive transfusion, a ratio of ≤ 2:1:1 of red blood cells:fresh frozen plasma:platelets is associated with reduced mortality. 

However, due to the possibility of survivor bias, it is not possible to recommend a target ratio of RBC:FFP:platelets.

1. Improved survival following massive transfusion in patients who have undergone trauma. Cinat ME et al. Archives of Surgery.134(9):964–968.
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:

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### Resuscitation

- Avoid hypothermia, institute active warming.
- Avoid excessive crystalloid.
- Tolerate permissive hypotension (BP 80–100 mmHg systolic) until active bleeding controlled.
- Consider transfusion trigger for ongoing bleeding.
- Add vitamin K, prothrombinex/FFP.
- Obstetric haemorrhage:
  - early DIC often present; consider cryoprecipitate.
- Head injury:
  - aim for platelet count > 100 x 10⁹/L.
  - permissive hypotension contraindicated.

### Specific surgical considerations

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

### Cell salvage

- Consider use of cell salvage where appropriate.

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- FFP: fresh frozen plasma
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- PT: prothrombin time
- rFVIIa: activated recombinant factor VII
- APTT: activated partial thromboplastin time
- MTP: massive transfusion protocol
- FBC: full blood count
Recombinant Factor VIIa

LEVEL OF EVIDENCE FOR THIS RECOMMENDATION?

requiring massive transfusion, administration of rFVIIa has no effect on 48-hour or 30-day mortality. (1)

Summary

• Most of the guidelines are based on consensus opinion rather than strong evidence.
• BUT this is the consensus opinion of a lot of experts, probably better than my opinion!
• Local areas have their own MTP based on the structure outlined here.
• Stick with one you are happy with.
IPad “Massive Transfusion Protocol” App is available at:
Further Reading