Blood Management and Protocol Use in Active Bleeding

John A. Norton, DO
Assistant Professor – Clinical
Department of Anesthesiology
The Ohio State University Wexner Medical Center

Acknowledgements

- Stephanie Barringer (Manager, UHE Blood Bank/Laboratory)
- Dr. Scott Scrape (OSU Hematology, Medical Director, Blood Bank)
- Dr. Antolin Flores (OSU CV Anesthesiology)

Objectives

- The participant will understand the concept of patient blood management and why it is important to both patients and providers.
- The participant will have an improved understanding of the impact blood transfusion therapy has on both patients and the hospital.
- The participant will gain an understanding of the practicality of protocol use for routine and emergency blood management scenarios.
- The participant will understand the rationale behind mass transfusion protocol development and its use in different hospital settings.

No Disclosures
Discussion Outline

- Blood management? What and why?
- Evidence for conservative transfusion management?
- Adjuncts/Alternatives to transfusion
- The Mass Transfusion Protocol (MTP)
- MTP readiness in your hospital

Blood products in the US....

- Every two seconds someone in the U.S. needs blood.
- Approximately 36,000 units of red blood cells are needed every day in the U.S.
- Nearly 7,000 units of platelets and 10,000 units of plasma are needed daily in the U.S.
- Nearly 21 million blood components are transfused each year in the U.S.


Patient Blood Management: What?

- Patient blood management (PBM) is an evidence-based, multidisciplinary approach to optimizing the care of patients who might need transfusion.

American Association of Blood Banks
Patient Blood Management (PBM)

- Multi-disciplinary approach
- Blood Bank
- Lab
- Nursing
- Hematology
- Surgery
- Anesthesia
- Medicine
- Critical Care

Mass Transfusion Protocols (MTP)

Mass transfusion Scenario

Non-Massive Transfusion Scenario

Transfusion

Blood product availability

Anemia

Damage Control

Guidelines

Pharmacologic management

Broader perspective than transfusion alone
- Earlier treatment of coagulopathy
- Vigilant monitoring
- Communication

Spahn DR. Alternatives to blood transfusion. Lancet, 2013; 381:1855-65

- Optimise erythropoiesis
  - Identify, assess, and treat anaemia
  - Consider preoperative autologous blood donation
  - Consider erythropoiesis-stimulating agents if minimal anaemia is ruled out
  - Evaluate further assessment if responsive
  - Considered anaemia (haemoglobin in women <120 g/L, haemoglobin in men <130 g/L): transfusion in settings if <10 g/L is a contraindication for elective surgery

- Minimise blood loss
  - Identify and manage bleeding risk (past medical history)
  - Review medications (antiplatelet, anticoagulation treatment)
  - Minimise iatrogenic blood loss
  - Procedure planning and rehearsal
  - Minimise iatrogenic blood loss

- Manage anaemia
  - Unmanaged anaemia (haemoglobin in women <120 g/L, haemoglobin in men <130 g/L) is a contraindication for elective surgery
  - Identify and manage bleeding risk (past and family history)
  - Review medications (antiplatelet, anticoagulation treatment)
  - Minimise iatrogenic blood loss
  - Procedure planning and rehearsal
  - Minimise iatrogenic blood loss

- Time surgery with optimisation of red blood cell mass
  - Meticulous haemostasis and surgical techniques
  - Blood-sparing surgical techniques
  - Acute normovolaemic haemodilution
  - Cell salvage and reinfusion
  - Pharmacological and haemostatic agents
  - Avoid coagulopathy

- Optimise cardiac output
  - Optimise ventilation and oxygenation

- Avoid and treat infections promptly

- Evidence-based transfusion strategies

- Manage nutritional or correctable anaemia
  - Avoid folate deficiency, iron-restricted erythropoiesis
  - Treatment with erythropoiesis-stimulating agents
  - Be aware of drugs that induce or increase anaemia (e.g., ACE inhibitors)

- Optimise cardiac output
  - Optimise ventilation and oxygenation
  - Avoid and treat infections promptly

- Evidence-based transfusion strategies

- Minimise oxygen delivery
  - Minimise oxygen consumption
  - Avoid and treat infections promptly

- Evidence-based transfusion strategies

Preoperative

Intraoperative

Postoperative
Optimise erythropoiesis
• Consider preoperative autologous blood donation
• Consider erythropoiesis-stimulating agents (if blood loss is expected)
• Refer for further assessment if nutritional anaemia is ruled out

Minimise blood loss
• Identify and manage bleeding risk (past and family history)
• Review medications (antiplatelet, anticoagulation treatment)
• Minimise iatrogenic blood loss
• Procedure planning and rehearsal

Manage anaemia
• Manage nutritional or correctable anaemia (eg, avoid folate deficiency, iron-restricted erythropoiesis)
• Treatment with erythropoiesis-stimulating agents if appropriate

Early management of coagulopathy
• Mass transfusion

Spahn DR. Alternatives to blood transfusion. Lancet, 2013; 381:1855-65

PATIENT SAFETY SERIES
Comprehensive maternal hemorrhage protocols reduce the use of blood products and improve patient safety
Laurence E. Shields, MD, Suzanne Wiener, BSN, Janet Falcon, RN, PHD, Barbara Pellegrino, RN

Am J Obstet Gynecol 2011;205(4):368e1-8

2 year observational study, large community health system

Substantial reduction in transfusion rate (16.7 to 6.3/month, p<0.01)

Reduced coagulopathy in PPH patients (DIC reduced by 64%, p<0.01)

Patient Monitoring
• Clinical suspicion
• Physiologic parameters (ex. Ca$_2^+$, acid/base balance, temperature)
• Lab based / Point-of-care testing
• Transfusion thresholds (?)
Patient Blood Management: Why?

Contributing to patient safety...

Communication

Blood product availability

Mass transfusion Scenario

Damage Control

Mass Transfusion Protocols (MTP)

Transfusion

Anemia

Non-Massive Transfusion Scenario

Guidelines

Pharmacologic management

Improve patient safety, outcomes, and process efficiency while reducing waste and care-related cost
ACS-NSQIP (American College of Surgeons – National Surgical Quality Improvement Program) data

- Increased risk of 30 day morbidity and mortality in general surgery patient receiving 1 unit of PRBCs
- Transfusion of 2 intraoperative units further increased risk of surgical site infection in these patients

Transfusion: Risk vs Benefit

**Risks**
- TRALI (#1 mortality)
- TACO (#2 mortality)
- Infection
- Immunomodulation
- Transfusion rxns

**Benefits**
- Improved O2 carrying capacity
- Improved coagulation
- Hemodynamic stability

Fatalities reported to the FDA: Annual summary for fiscal year 2014. fda.gov

Efficiency of product delivery…

- Emergency and mass transfusion protocol development

Massive Transfusion Protocols:
The Role of Aggressive Resuscitation Versus Product Ratio in Mortality Reduction

- Level 1 trauma center, introduced MTP, 4 year review
- Mortality deceased with implementation of a MTP without change in transfusion ratio
- “Our data underscore the importance of expeditious product availability…”
A continued need for waste reduction in blood management?

- International multi-disciplinary panel
- 450 stable inpatient scenarios
- 11% RBC transfusion considered appropriate
- 29% uncertain

59% Inappropriate

One unit… or two?

Opportunity for cost savings?

What do products cost?

• At our institution,
  – RBC base unit, $215
  – Plasma (FFP), $42
  – Platelets, $600-800
  – Cryoprecipitate, $750-800

Annual transfusion cost between $1.6 and $6 million per hospital largely dependent on transfusion rate

RBC purchase cost represented only 21-28% of total transfusion cost (range $726 to $11,835 / unit)

“Implementation of a new blood use initiative…”

“Health First saved $1.44 million dollars by changing transfusion practices to conform to national guidelines”

Patient Blood Management: Why?

Improve patient safety, outcomes, and process efficiency while reducing waste and care-related cost
Is there evidence to support a conservative approach in PBM?

• Generally, yes...
• Evidence over the past 20 years supports a more conservative approach to transfusion practice in most patient populations
• Outcomes using a conservative strategy no worse than liberal strategy in most cases
• Reduced blood product administration

Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion

Transfusion Requirements After Cardiac Surgery: The TRACS Randomized Controlled Trial

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery

A Multicenter, Randomized, Controlled Clinical Trial of Transfusion Requirements in Critical Care

• American Association of Blood Banks
• American Society of Anesthesiologists
• American Society of Hematology
• Society of Critical Care Medicine
• Society of Hospital Medicine
In general:

- Restrictive trigger for RBC transfusion typically defined as a Hgb < 7-8 g/dl (or Hct < 25%)

- In the actively bleeding / symptomatic patient, there is no arbitrary threshold

- The decision to transfuse is a medical decision that must be individualized to each patient


“Thinking” conservatively...

Ensure that patients who need blood get every drop they need, and not a drop more

Transfusion Therapy: Indications for Ordering

The Ohio State University Wexner Medical Center

- These practice guidelines have been developed by a cross-functional group of physicians, management, and staff to advance the safety and quality of care for the patients receiving blood transfusions.
- When applying these guidelines, providers must use their training, experience, judgment, and a patient's specific clinical information to make optimal decisions on the patient’s behalf.
- These guidelines cannot substitute for clinical judgment or the need for flexibility in practice and should not be considered a mandate to transfuse or not to transfuse.

Multi-disciplinary transfusion committee developed evidence-based hospital guideline for transfusion therapy

Flexibility to allow for important clinical decision making based on situation

Red Blood Cells

Active Bleeding

- Hemorrhagic shock
- No Hgb threshold
- MTP

Bleeding Risk

- Non-life threat
- Hgb<8
- If expect large, life threat intraop bleeding and Hgb<10
- If expect small, non-life threat intraop bleeding, and Hgb<8

Anemia

- Asymptomatic
- Hgb<7
- Symptomatic
- Hgb<8 with CV disease

Transfusion Therapy: Indications for Ordering -
The Ohio State University Wexner Medical Center
Plasma and Platelets

- Historically suggested thresholds typically used to guide therapy
- No real evidence basis
- Standard lab based testing used to establish baseline if given time

Plasma

Active Bleeding
- INR ≥ 1.5
- *Hemorrhage with PTT > 60s
- Hemorrhage with severe liver disease
- Hemorrhage with DIC or Vitamin K depletion

Bleeding Risk
- FBG < 100 mg/dl
- MTP
- Invasive procedure with INR ≥ 1.5

*excluding heparin or lupus anticoagulant effect

MTP

Transfusion Therapy: Indications for Ordering - The Ohio State University Wexner Medical Center

Platelets

Acute mass hemorrhage, Neurosurgery, LVAD

DIC, hemorrhage, LP, major surgery

Count <100,000/μL

Count <50,000/μL

Count <20,000/μL

Platelet function d/o > 100,000/μL

Chronic stable thrombocytopenia

BMT, Acute leukemia, solid tumors

Count <5,000/μL

Count <10,000/μL

Count <20,000/μL

Transfusion Therapy: Indications for Ordering - The Ohio State University Wexner Medical Center

Streamlining the process for standard transfusion: examples of protocol use
Liver Transplant Transfusion Algorithm: Ohio State

- H: Hemoglobin
- Cr: Creatinine
- C: Creatinine
- Cl: Chloride
- T: Temperature
- P: Pressure
- A: Arterial
- S: Serum

Suggested testing times:
1. Baseline
2. Anhepatic
3. Neohpatic: reperfusion
4. Prior to transport to ICU

Obtaining Blood Products Checklist

For any issues or concerns, please contact the Attending Apheresis Pathologist from the "Pathology/Clinical Lab" on call schedule search on WebXchange

- **Order**
  - Physician order placed to include the number of units requested (multiple units can be requested)

- **Blood Product Release White Paper Slip**
  - Must be taken/sent to lab in order for Blood Bank to release blood product
  - Slip should include the following:
    - Patient label
    - Amount and name of blood product to be immediately released (up to 2 units of PRBC's or 2 FFP's will be released at one time)

- **Blood Transport Cooler**
  - For 2 units, the Blood Bank will release blood products in a cooler
  - Blood products should remain in the cooler until transfused or returned to lab
  - All unused product must be sent back to lab within 3.5 hours
  - The Cooler must remain closed unless retrieving blood products
  - Cool gel packs and a reminder timer will accompany the cooler

Adjuncts / Alternatives to standard product transfusion?
<table>
<thead>
<tr>
<th>Adjuncts/Alternatives to standard product transfusion…</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Crystalloids (isotonic saline, lactated ringers)</td>
</tr>
<tr>
<td>• Colloids (albumin, hetastarch, hypertonic saline-dextran)</td>
</tr>
<tr>
<td>• Red cell recovery (cell-saver) ✓</td>
</tr>
<tr>
<td>• Autologous donation X</td>
</tr>
<tr>
<td>• Epoetin alfa $</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjuncts/Alternatives to standard product transfusion…</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Vitamin K</td>
</tr>
<tr>
<td>• Factor concentrates (ex. PCC, fibrinogen) $</td>
</tr>
<tr>
<td>• Anti-fibrinolytics (ex. Tranexamic acid) ✓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mass Transfusion Protocols</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Consider…</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 y/o male GSW to chest</td>
</tr>
<tr>
<td>Responsive, HR 125, BP 88/40</td>
</tr>
</tbody>
</table>
**Patient Blood Management (PBM)**

- Multi-disciplinary approach
- Blood Bank
- Lab
- Nursing
- Hematology
- Surgery
- Anesthesia
- Medicine
- Critical Care

**Mass Transfusion Protocols**

- No generally accepted format
- Streamline efficient delivery of life-saving products when needed
- Facilitate identification of decision points in mass bleeding situation
- Standardize optimization of patient care

**Mass Transfusion Protocols**

- Should be developed by multi-disciplinary committee
- Should address triggers for initiation
- Products available for immediate transfusion
- Continued management during patient transfers (ex. ER → OR)
- Use of adjunct agents
- Termination

**Massive transfusion protocol (MTP) template**

- Senior clinician determines if patient meets criteria for MTP activation
- Notify transfusion laboratory:
  - Blood type
  - Rh factor
  - Crossmatch
  - Notify hematology/transfusion specialist

- Notify critical care staff
- Notify operating room staff
- Notify anesthesia
- Notify blood bank

**Laboratory staff**

- Crossmatch
- Type and screen
- Compatibility testing
- Platelet and frozen plasma
- Fibrinogen
- Hemoglobin
- PT/INR
- PT/INR

**Senior clinicians**

- Blood transfusion
- Medications
- Vascular access
- Fluids

**NURSING**

- Monitor vital signs
- Blood pressure
- Oxygen saturation
- Pulse rate
- Core temperature

**ARM**

- Hemoglobin > 10 g/L
- Platelets > 50,000/μL
- INR ≤ 1.5
- PT ≤ 1.5 x control
- APTT ≤ 1.5 x control
- Fibrinogen > 1 g/L
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 hemorrhage 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. rFVIIa is not licensed for use in this situation; all use must be part of practice review.

Considerations for use of rFVIIa:

- Warfarin: add vitamin K, prothrombinex/FFP
- Obstetric hemorrhage: early DIC often present; consider cryoprecipitate
- Head injury: aim for platelet count > 100 × 10⁹/L
- Permissive hypotension contraindicated
- Avoid hypothermia, institute active warming
- Avoid excessive crystalloid
- Tolerate permissive hypotension (BP 80–100 mmHg systolic) until active bleeding controlled
- Do not use hemostatic scores as a transfusion trigger

Initial management of bleeding

- Vital signs
- Intubation
- Compression
- Fluids
- Wide awake, family present

Specific surgical considerations

- Significant pre-existing medical condition
- Damage control measures on angiography

Dosage

<table>
<thead>
<tr>
<th>Condition</th>
<th>rFVIIa dose</th>
<th>FFP dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>100 U/Kg</td>
<td>15 mL/kg</td>
</tr>
<tr>
<td>Massive</td>
<td>1000 U/Kg</td>
<td>120 mL/kg</td>
</tr>
</tbody>
</table>

Initial measures:

- Compression
- Tourniquet
- Packing

Surgical assessment:

- Early surgery or angiography to stop bleeding

If significant physiological derangement, consider damage control surgery or angiography

Consider use of cell salvage where appropriate

- Actual or anticipated 4 units RBC in < 4 hrs, + hemodynamically unstable, +/- anticipated ongoing bleeding
- Serious blunt, penetrating, or multiple long bone fractures
- Major electrical, gastroenteral or surgical bleeding
- Massive transfusion protocol outside the trauma room...

Consider patients with massive hemorrhage

How to treat patients with massive hemorrhage

A. Johnson,1 2 Jakob Bennike,3 4 Robert Cullen,1 Charles E. Wade,5 Sune R. Ostrowski,1 and John B. Holcomb2

1 Section for Trauma Medicine, Capital Region Blood Bank, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark. 2Department of Surgery, Division of Acute Care Surgery, Centre for Translational Injury Research, University of Texas Health Science Center, Houston, TX, and 3The Trauma Centre, Department of Anesthesiology, Centre of Head and Orthopaedics, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark.

Blood 2014 Nov; 124(20)

MTP outside the trauma room...

54 y/o male undergoing routine laparoscopic surgery at your community hospital

Unexpected mass hemorrhage intraop
Community/Specialty Hospital MTP

- MTP may improve rapid response in settings where hemorrhage is anticipated but rarely seen
- Consider the resources at your hospital based on multi-disciplinary group feedback
- Organize and develop a plan for action
- ...then in-service / drill / debrief / repeat

Obtaining Blood Products Checklist

Massive Transfusion Protocol (MTP)

For any issues or concerns, please contact the Attending Apheresis Pathologist from the Pathology/Clinical Lab on call schedule search on WebXchange

- Call the Blood Bank to notify the initiation of MTP
  - Caller must state the words “MASSIVE TRANSFUSION PROTOCOL” and the name of the ATTENDING PHYSICIAN initiating the MTP.
  - Caller must provide the Blood Bank with the patient name and location, sex, and MRN
- An Order to Initiate the MTP is Not Needed
  - Blood Bank will contact the Attending Physician after the MTP is concluded to obtain an order for all products used during the MTP.
- Type and Cross
  - Obtain Type and Cross specimen
  - Send to Lab as soon as possible
  - Blood Bank Must Not Transport or Call When Blood Products are Ready
  - OR/ED Staff will be sent to obtain blood products immediately following the initiation of the MTP
  - A Blood Product Release white paper slip must be taken to the Blood Bank

Blood Products Included in MTP

- (2) PRBCs; (2) FFP; (1) Pool of Platelets
- Platelets will NOT be immediately available. Blood Bank will notify Staff when available.
- NOTE: While only 2 units will be sent each time, a continuous supply of blood product will be prepared and the receiving unit will need to contact Blood Bank to arrange subsequent times to pick up additional product.

Communication

- Transfer of Patient Receiving MTP
  - Inform Receiving Unit that MTP is activate
  - RN to Call Blood Bank to inform of new patient location.
- Conclusion of MTP
  - Once Attending Physician Cancels the MTP, the patient’s primary nurse should call Blood Bank to cancel the MTP.
  - Blood Bank will contact the Attending Physician after the MTP is concluded to obtain an order for all products used during the MTP.

ALL RBC AND PLASMA UNITS MUST REMAIN IN THE BLOOD BANK COOLERS UNTIL READY TO TRANSFUSE.

Summary

- Patient blood management involves a multi-disciplinary approach to care of patients who may require transfusion
- Improves patient safety, reduces waste, lowers cost and optimizes efficient delivery
- Mass transfusion protocols have been well supported in military and civilian trauma literature
- May improve response to mass hemorrhage in settings where it is anticipated but rarely seen
- Develop then in-service / drill / debrief / repeat

Fluid and Blood Management in Active Bleeding

Daniel S. Eiferman, MD, FACS
Assistant Professor of Surgery
Department of Surgery
Division of Critical Care, Trauma, and Burn
The Ohio State University Wexner Medical Center
**Objective**

Provide a practical approach to the management of active bleeding

**Remember the Goal**

Ensure that patients who need blood and blood products get every drop they need, and not a drop more

**Other Interventions Besides Transfusion To Assist With Hemostasis**

- temperature > 35°C
- pH > 7.2
- lactate < 4 mmol/L
- Ca²⁺ > 1.1 mmol/L

**Surgical Bleeding (i.e. Holes in Blood Vessels!)**

- Require operative management
- Transfusion strategy: Give blood and blood products in 1:1 ratio until bleeding controlled
Medical Bleeding (i.e. Coagulopathy) Who Remembers This?

The three pathways that make up the classical blood coagulation pathway:

- Intrinsic: surface contact
- Extrinsic: tissue damage
- Common: prothrombin to thrombin

How To Determine What To Transfuse When Coagulopathy present?

“Classic” Coagulation Assays:
- PT/INR
- PTT
- Platelets

Problem: PT/aPTT do not reflect fibrin polymerization, FXIIIa, platelet quality, or fibrinolysis
Problem: Turnaround time for results ~45-60 mins

Thromboelastography (TEG)
Assesses for impaired thrombin generation, poor clot firmness and premature lysis in the bleeding patient to guide transfusions

What additional information does TEG yield?
- Hyperfibrinolysis and/or poor fibrin contribution to clot firmness
- Heparin Effect, Anti-coagulant Effects
- Clot Firmness
- Thrombin Generation
- Can differentiate between intrinsic and extrinsic factor deficiency
How To Use TEG Output to Guide Therapy and Transfusions

<table>
<thead>
<tr>
<th>Hyperfibrinolysis</th>
<th>Tranexamic acid 25 mg/kg as a single bolus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clot Firmness</td>
<td>Fibrinogen concentrate OR Platelet concentrate, 1-2 pooled</td>
</tr>
<tr>
<td>Thrombin Generation</td>
<td>PCC 20-25 IU / kg bw OR FFP 10-15 ml / kg bw</td>
</tr>
</tbody>
</table>

Remember: Transfusion Risks

- Risks
  - TRALI (#1 mortality)
  - TACO (#2 mortality)
  - Infection
  - Immunomodulation
  - Transfusion rxns

“There’s no such thing as a free lunch.”

Summary

Surgical Bleeding—Transfuse in 1:1 ratio until hemorrhage controlled
Coagulopathy—Classical parameters inadequate and long turnaround time for results
TEG identifies the defect in the coagulation pathway causing inadequate clot formation
Summary

• Transfusions are not benign and have significant side effects
• Transfuse what is needed and nothing more!
• Use TEG to give targeted therapy to address the issue and avoid unnecessary transfusions