Massive Transfusion

A massive transfusion is traditionally defined as the replacement of a patients blood volume or >10 units PRBCs within a 24hr period; newer definitions include ongoing blood loss >150mL/min or replacement of 50% of the blood volume in 3hrs or less. The primary goal is the treatment (or prevention) of hemorrhagic shock, but also of importance is the correction of coagulopathy to aid in the secondary goal of hemostasis.

ANESTHETIC CONSIDERATIONS:

- Emergency situation, call for help (anesthesia ± nursing/RT/anesthesia tech)
- **Airway**—ensure maintained, secure if necessary, potential for a/w edema with fluid shifts
- **Breathing**—100% O2, watch for ↑ Paw suggesting acute pulm edema (TRCO) or TRALI
- **Circulation**—ensure good IV access, level 1 infuser, warmed blood products
- ***Restore circulating volume:*** HR<100, SBP>100—treat hemorrhagic shock!
  - Send blood for CBC, PTT, INR, fibrinogen, D-dimer
  - Blood component therapy: start with PRBC, anticipate thrombocytopenia and coagulopathy
- **Drugs**—consider for TXA pre-op, or FVIIa
- **Exposure**—maintain or restore normothermia

ANESTHETIC GOALS:

- Predict risk factors for massive hemorrhage and have lines and blood products to deal with accordingly readily available
- Anticipate hematologic derangements associated with massive blood transfusion and prevent complications

EMERGENCY TRANSFUSION

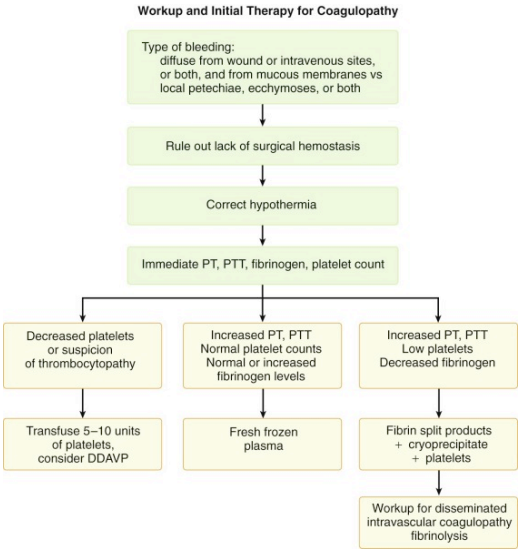
- Crossmatched blood?
  - In an emergency situation, blood can be drawn for a type and screen and depending on the urgency, either O negative Rh-typed blood may be infused or uncrossmatched blood.
  - The probable order of significance for antibodies is anti-Rh(D), Kell, C, E, and Kidd
  - If the correct ABO and Rh blood type is given, the possibility of transfusing incompatible blood is less than 1 chance in 1000. ABO-Rh typing alone results in a 99.8% chance of a compatible transfusion, with an antibody screen—99.94%, and a crossmatch increases this to 99.95%
  - For surgeries where the average number of units transfused is <0.5 determination of ABO-Rh type and screen should be sufficient. If the antibody screen is positive, a full crossmatch should be done.

HISTORY AND PHYSICAL

Factors	Class I	Class II	Class III	Class IV
Blood loss (mL)	750	750-1500	1500-2000	>2000
Blood loss (%)	15	15-30	30-40	>40
Pulse (beats/min)	<100	100	120	140 or higher
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal or ↑	Decreased	Decreased	Decreased
Capillary refill	Normal	> 3 s	>3 s	>3 s
Respirations (per min)	14-20	20-30	30-40	>35
Urine output (mL/hr)	30	20-30	5-10	Negligible
Mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic
Fluid replacement	Crystalloid	Crystalloid	Crystalloid + blood	Crystalloid + blood

INVESTIGATIONS

- **Prior to any transfusion send Crossmatch, CBC, INR, PTT and fibrinogen**
- Repeat bloodwork after blood product transfusion, further blood loss, or q4h.



OPTIMIZATION

- Hematology consult—may require to obtain FVIIa release if massive bleeding not improving, or if history/suspicion of other cause for coagulopathy
  - Anticoagulant medication
  - Hemophilia A or B
  - Von Willebrands Disease
  - Platelet dysfunction: EtOH liver disease, renal failure, uremia
- **Miller Goals for Early Resuscitation**:
  - Maintain SBP 80-10mmHg
  - Maintain Hct 25-30%
  - Maintain INR/PTT normal range
  - Maintain Plt > 50 000/hpf
  - Maintain normal Ca^{2+}
  - Maintain core temperature >35 degrees
  - Maintain function of pulse oximeter
  - Prevent increase in serum lactate
  - Prevent acidosis from worsening
  - Achieve adequate anesthesia and analgesia

ANESTHETIC OPTIONS

- **Due to concerns re coagulopathy, neuraxial anesthesia would be relatively contraindicated**
- GA

ANESTHETIC SETUP

- **Drugs:** resuscitation drugs, consider vasopressin/norepinephrine for hemodynamic support while fluid resuscitating. *Do not use in place of appropriate fluid resuscitation!*
- FVIIa: dosage suggestion in Miller is 4.8mg (one vial) for an adult—represents a 50-100mcg/kg dose
- **Equipment:**
    - Standard CAS monitors + temperature probe, foley cath
    - ± art line ±CVP, ±TEE→time permitting, resuscitation comes first
    - Crash cart—ensure nearby in case of hypovolemic arrest

MANAGEMENT OF ANESTHESIA

Goal	Procedure	Comments
Stop Hemorrhage	• Pressure/splinting • Surgical Intervention • Interventional radiology	• All attempts at early intervention should be made—importance of recognition of tamponaded patient vs surgical bleeding prior to induction of anesthesia
Request PRBC	• Severity of hemorrhage determines choice: o O negative blood o ABO group specific uncrossmatched o Fully crossmatched • Use cell saver if no contraindication	• Can use O positive blood emergently in male patients or post-menopausal females • After >2 units O blood, patient probably cannot be switched to crossmatched blood until anti A/B levels deemed low • Further cross match not required after replacement of one blood volume • Transfusion triggers below
Request FFP	• Anticipate coagulopathy after 1.5x blood volume replacement • Aim for INR<1.5, PTT <1.5x normal • 1 hr time delay for thawing	• PT and PTT> 1.5x normal is associated with greater surgical bleeding • May need to use FFP before results available, draw samples before transfusion
Request Platelets	• Anticipate PLT count <50 x10^9 after 2x blood volume replacement • Transfuse pooled PLT or 10mL/kg • Repeat PLT count 10 min and 1 hr after PLT transfusion • May have delayed delivery time	• Target PLT count >50 x10^9 unless major trauma or PLT dysfunction—then aim >100 x 10^9 • May need to transfuse PLT prior to lab results, draw prior to infusion
Request cryoprecipitate	• Aim for fibrinogen >1, 1 pack/ 10kg body weight • To replace fibrinogen and FVIII	• Fibrinogen <0.8g/L strongly associated with microvascular bleeding • Fibrinogen deficiency can develop early when plasma poor PRBC are transfused
Suspect DIC	• Correct shock, hypothermia, acidosis as they may be causative	• Low platelet count, prolonged PT and PTT, and elevated fibrin split products • The D-dimer assay most sensitive test: ↑ in 94% of patients with DIC • Fibrinogen levels may be maintained except in severe forms of DIC

- Transfusion triggers PRBC (Miller):
    1. Blood loss greater than 20% of blood volume when more than 1000mL
    2. Hgb <80
    3. Hgb <100 with major disease (emphysema, IHD)
    4. Hgb <100 with autologous blood
    5. Hgb <120 and ventilator dependent

o Indications for FFP transfusion:
1. For urgent reversal of warfarin therapy
2. For correction of known coagulation abnormalities for which specific factors are unavailable
3. For presence of microvascular bleeding with >1.5x normal INR or PTT
4. For correction of microvascular bleeding with transfusion >1 blood volume and no coags available
5. FFP should be given in doses calculated to achieve a minimum of 30% of plasma factor concentration (usually achieved with administration of 10 to 15 mL/kg of FFP), except for urgent reversal of warfarin anticoagulation, for which 5 to 8 mL/kg of FFP usually suffice. Four to five platelet concentrates, 1 unit of single-donor apheresis platelets, or 1 unit of whole blood provides a quantity of coagulation factors similar to that contained on 1 unit of FFP (except for decreased, but still hemostatic, concentrations of factors V and VIII in whole blood).
6. Contraindicated for plasma volume expansion or replacement of albumin

DISPOSITION & MONITORING

- Observation bed vs ICU: if patient warm, euvolemic, hemodynamically stable and metabolic derangements have been assessed may be able to go to Obs.

PREGNANCY

- o In an emergency, women of childbearing age must only receive Type O negative blood so as not to sensitize them against Rh which would complicate future pregnancies.
- o Pregnant women may not show signs of blood loss (like tachycardia) until they have lost up to 2L of blood, so they may present late
- o Pregnancy is inherently a hypercoagulable state; they are also at increased risk of DIC (RF: AFE, abruption)

PEDIATRICS

- Maximal Allowable Blood Loss (MABL)= Estimated Blood Volume (EBV) x Child's Hct-Minimal Accepted Hct)/ Child's Hct
- Blood product replacement:

Hazards Associated with Massive Transfusion: Barash

- Hypothermia
- Volume overload
- Dilutional coagulopathy
- Reduced O2 carrying capacity (↓2, 3-DPG)
- Metabolic acidosis
- Hyperkalemia
- Citrate intoxication
- Microaggregate delivery

- PRBCs 10-15 mL/kg will increase Hgb by 20-30 mg/dL
- Platelets 5-10 mL/kg increases Plt count by 50-100 000/mm^3
- FFP 10-15 mL/kg will increase Factor levels by 15-20%
- Cryoprecipitate 1-2 units/kg will increase fibrinogen by 60-100 mg/dL

COMPLICATIONS

- Coagulopathy
  - PRBC are low in all factors, but with massive transfusion lack of factors V and VIII are usually responsible for INR >1.5; treated with FFP which contains all coag factors (except PLT)
  - Thrombocytopenia: according to Miller ↑PTT only occurs in the presence of thrombocytopenia in clinical situations involving blood transfusions
  - FVIIa if coagulopathy persists despite appropriate blood product replacement
- Citrate toxicity
  - May occur in massive transfusion with >1 U PRBC q10min
  - Citrate intoxication → hypocalcemia: signs include hypotension, narrow pulse pressure, and increased intraventricular end-diastolic pressure and central venous pressure
  - Citrate intoxication is very rare, RF include: hypothermia, liver disease, liver transplantation, hyperventilation or being a pediatric patient
- Hyperkalemia
  - The serum K in PRBC is much higher, if giving blood at >120mL/min could see ↑K
  - If clinical signs (peaked T wave, or ↑K on ABG) give calcium chloride 10% solution
- Acidosis
  - Units of PRBCs have a pH of approx 6.9 due to the storage media and build-up of CO2 and lactic acid from cellular metabolism
  - Bicarbonate should not be administered to "correct" for this as the citrate in the storage media provides ample substrate for the endogenous generation of bicarbonate which often results in a metabolic alkalosis after transfusion
- Hemolytic transfusion reaction
  - Intravascular hemolysis occurs when there is a direct attack on transfused donor cells by recipient antibody and complement (ABO incompatibility)
  - Hemolytic transfusion reactions involving extravascular RBC destruction are generally less serious than those of the intravascular variety. In these cases, recipient antibody coats but does not immediately hemolyze the transfused RBCs. Destruction occurs primarily in the reticuloendothelial system. (Acute 1/25 000-1/50 000)
  - Delayed hemolytic transfusion reactions occur 2-21 days post transfusion due to an anamnestic response and production of RBC antibodies. May initially present with a decrease in Hgb. (1/2500)
  - The classic signs and symptoms of a hemolytic transfusion reaction—chills, fever, chest and flank pain, and nausea—are masked by anesthesia. Under general anesthesia, the only signs may be hemoglobinuria, bleeding diathesis, or hypotension. The presenting sign is usually hemoglobinuria
  - Laboratory tests that should be performed if hemolytic transfusion reaction is suspected include serum haptoglobin, plasma and urine hemoglobin, bilirubin, and direct antiglobulin determinations. The direct antiglobulin test can confirm the presence of hemolytic transfusion reaction because it shows that there is antibody attached to transfused donor RBCs.
  - Treatment of Hemolytic transfusion reaction:
    1. Stop the Transfusion
    2. Maintain urine output 75-100mL/hr by generous fluid administration, mannitol 12.5-50g ± lasix 20-40mg if no response to prior
    3. Alkalinize urine with 0.5-1mEq bicarb/kg body weight
    4. Assay urine and plasma Hgb concentrations
    5. Determine platelel count, PTT and serum fibrinogen
    6. Return unused blood to bloodbank to repeat crossmatch
    7. Send patient's blood and urine sample to blood bank for examination
    8. Prevent hypotension to ensure adequate renal blood flow
- TRALI (1/5000)
  - **Leading cause of transfusion associated mortality**
  - Non-cardiogenic pulmonary edema develops within 1-2hrs of transfusion
  - All blood components, but most commonly FFP, are implicated
  - Treatment involves stopping transfusion, supportive care and alerting Blood Bank. Patients HLA can be tested.
- Infectious risks (Miller)

Infection	Risk	Window period (days)
HIV-1	1/2 135 000	11
Human T-lymphotropic virus	1/2 993 000	51
Cytomegalovirus	Infrequent with leukocyte reduction	
Hepatitis C	1/1 935 000	40
Hepatitis B	1/205 000	
West Nile Virus	1/1 100 000	?

REFERENCES

- Miller 7th ed
- Barash 5th ed
- Chesnut 3rd ed
- Cote 4th ed
- Stainsby D, Maclennan S, Hamilton PJ: Management of massive blood loss: a template guideline. Br J Anaesth 85:487–491
- Asensio: Current Therapy of Trauma and Surgical Critical Care, 1st ed (2008)