Transfusion Medicine for Surgeons

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Outline of Talk

- Blood products (How to order, when to order, etc.)
  - Red cells
  - Platelets
  - Plasma
  - Cryoprecipitate
  - Other products: Albumin, Octaplex, Niastase

- Risks of transfusion
- Costs of transfusion
Donation Process

- Blood is collected by Canadian Blood Services in all provinces/territories except Québec (where it is collected by Héma-Québec)

- Health Canada regulates all aspects:
  - Donor eligibility, blood collection, testing, processing and distribution
Donor blood is collected as a “whole blood unit”
- 480 mL blood
- 70 mL anticoagulant

Blood is filtered to remove white blood cells (leukoreduction)

Processed or separated into a variety of different components which may include:
- Red blood cells
- Platelets
- Frozen plasma
- Cryoprecipitate
Red Cells
Red Blood Cells

- A unit of red cells has a total volume of ~300mL

- Made up of:
  - 160 mL of red cells
  - 30 mL of plasma
  - 110 mL of anticoagulant (citrate) and preservative

- 1 unit of RBC raises Hb ~10 g/L
How to order RBC transfusions

- **Pretransfusion blood work**
  - Group and screen
    - When transfusion is likely going to occur
  - Hold for transfusion
    - When transfusion is possible

- **Crossmatch done at HHS is “electronic”**
  - Computer selects units based on patient’s ABO and Rh group type

- **Not necessary to order “cross for X units”**
  - Units are not held for specific patients
## Selecting compatible blood

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Antibody present in plasma</th>
<th>Donor red cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>Anti-A, Anti-B</td>
<td>O</td>
</tr>
<tr>
<td>A</td>
<td>Anti-B</td>
<td>A, O</td>
</tr>
<tr>
<td>B</td>
<td>Anti-A</td>
<td>B, O</td>
</tr>
<tr>
<td>AB</td>
<td>None</td>
<td>AB, A, B, O</td>
</tr>
</tbody>
</table>
How to order RBC transfusions

- Order one unit at a time

- Indicate timing the unit should infuse over
  - Usually ~2 hours, must be completed within 4 hours

- Give indication for transfusion (in orders or in progress notes)
How to order RBC transfusions

Order 1 unit at a time, reassess patient and Hgb between units

Jan 1st, 2008 @ 09:00h
Transfuse 1 unit of RBC over 2 hours for Hb 65 and tachycardia
I. Transfusalot, MD

Max is 4 hours per unit

Always include indication for transfusion

Slide from Dr. K. Pavenski
How to transfuse red cells

- Informed consent must be obtained (more on this on next slide…)
  - Document that informed consent was obtained in the chart

- Infuse one unit at a time
  - Assess outcome (clinical, hemoglobin) before transfusing further

- Premedications are not required
  - Consider Lasix in patients at risk for circulatory overload
    - Age > 60, decreased renal function, cardiac disease
Informed Consent

- Must be obtained for transfusion of all blood components

- What to include:
  - Description of blood or blood product
  - Benefits
  - Risks
    - Viral and bacterial infection, TRALI, acute hemolysis, common minor reactions (fever, allergic reaction)
  - Alternatives (including benefits and risks)

- Physician should disclose information which the physician knows that a reasonable person in the patient’s position would wish to be aware of prior to making a decision about undergoing treatment

- Give patient opportunity to ask questions

- For more information: [http://www.pbco.ca/ic.html](http://www.pbco.ca/ic.html) (Provincial Blood Coordinating Office, BC)
Case 1

- 55 year old man intubated in the ICU several days post-MVC with multiple trauma
  - No history of cardiac disease
  - No evidence of acute bleeding

- Vital signs: HR 85, BP 140/80
- Labs: Hb 79 g/L

- Should you transfuse??
Transfusion Trigger

● No universal transfusion “trigger”
  - Varies by patient and must be assessed individually (based on risk factors, clinical signs, symptoms, hemoglobin level)

● General indications:
  - Symptomatic anemia
  - Acute bleeding
Transfusion Requirements in Critical Care (TRICC)

- Hebert P et al. NEJM 1999

- Is a restrictive strategy of red cell transfusion that maintains Hb between 7 and 9 g/dL equivalent to a more liberal strategy of maintaining Hb between 10 and 12 g/dL in critically ill patients?

- Randomized, unblinded, controlled clinical trial

- Consecutive critically ill patients from 22 tertiary care ICUs and 3 community ICUs in Canada
Patients were assigned to one of two treatment groups; restrictive or liberal strategy of transfusion.

- **Restrictive Strategy:** Transfusion of 1 unit of PRBC when Hb < 70 g/L.
- **Liberal Strategy:** Transfusion of 1 unit of PRBC when Hb < 100 g/L.
Primary outcome:
- Death from all causes in the 30 days after randomization

Secondary outcomes:
- Mortality
  - 60 days
  - during ICU stay
  - during hospitalization
- Organ failure/dysfunction
TRICC: Results--1° and 2° Outcomes

- 1° outcome: 30-day mortality
  - Similar between groups
  - 18.7% (restrictive) versus 23.3% (liberal), p=0.11

- 2° outcome: mortality rate during hospitalization
  - Significantly lower in restrictive strategy group
  - 22.2% versus 28.1%, p=0.05

- No significant differences in other 2° outcomes
  - Mortality rate during ICU stay, 60-day mortality, multi-organ failure
Transfusion in the Critically Ill

- No general benefit (& possible harm) until hemoglobin falls to 70 g/L
  - TRICC Trial, Hebert et al., NEJM 1999

- Transfusion recommended below 70 g/L

- Consider higher levels (100 g/L) in patients with unstable angina or acute MI
Case 2

- 55 year old man intubated in the ICU several days post-MVC with multiple trauma
  - No history of cardiac disease
  - Actively bleeding from presumed GI ulcer

- Vital signs: HR 85, BP 140/80
- Labs: Hb 79 g/L

- Now should you transfuse??
RBC Transfusion in Acute Blood Loss

- Maintain hemoglobin over 70 g/L during active bleeding
  - Consider rate of bleeding, hemodynamic factors, evidence of tissue ischemia

- Anticipate need when hemoglobin drops below 80 g/L

- Consider maintaining higher level (80-100 g/L) with:
  - Impaired pulmonary function
  - Increased oxygen consumption (e.g. fever)
  - Unstable coronary disease
  - Atherosclerosis
  - Uncontrolled bleeding

- Patients with levels above 100 g/L are unlikely to benefit
Case 3

- 55 year old man intubated in the ICU several days post-MVC with multiple trauma
  - History of cardiac disease, ECG shows evidence of acute ischemia
  - No evidence of acute bleeding

- Vital signs: HR 85, BP 140/80
- Labs: Hb 79 g/L

- Should you transfuse??
RBC Transfusion in Cardiac Disease

- Conflicting evidence from various studies
  - Controversy about where to maintain the hemoglobin level

- Consider transfusing if there are clear signs of inadequate tissue oxygen delivery in a patient with a low Hb and acute coronary syndrome

- Suggest:
  - Hb < 80 g/L and no symptoms
  - Hb < 100 g/L if experiencing symptoms

Wu et al. NEJM 2001; Rao et al. JAMA 2004; Yang et al. J Am Coll Cardiol 2005
Case 4

- 80 year old man post-op surgery for hip fracture
  - History of cardiac disease (angina), no recent chest pain

- Vital signs: HR 85, BP 140/80
- Labs: Hb 85 g/L

- Should you transfuse??
  - Your colleague tells you that you should as it will improve the patient’s functional recovery….is he right?
FOCUS Study

- Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair


- To determine whether higher blood transfusion thresholds improve functional recovery and reduce mortality and morbidity in patients with underlying cardiovascular disease or cardiovascular risk factors.
Patients: ≥50 years, surgery for hip fracture, risk factors for cardiac disease, Hb < 100 g/L

Intervention:
- Transfusion when Hb < 100 g/L
- Transfusion when symptoms or when Hb < 80 g/L

Primary outcome:
- Death or inability to walk across a room without human assistance at 60 days
FOCUS Study

- 2016 patients enrolled (mean age 81.6 years)
- No difference between groups:
  - 35% dead or unable to walk in both groups
- Group transfused at 100 g/L received more blood
  - 2 units (median) versus 0 units
- Symptomatic transfusion conserved blood and had no adverse effects on ability to walk, 60-day follow-up mortality, falls, readmission rates or fatigue in this high-risk group of elderly patients with cardiovascular disease/risk factors
RBC Transfusion and the Surgical Patient

- Pre-operatively, consider alternatives in advance (at least 5 weeks) of surgery to allow planning

- Intra-operatively, meticulous attention to surgical technique

- Post-operatively, adhere to good transfusion practice, minimize blood taking for laboratory tests
<table>
<thead>
<tr>
<th>Time until Surgery</th>
<th>Blood Conservation Strategies Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 35 days</td>
<td>• Investigate and treat anemia</td>
</tr>
<tr>
<td></td>
<td>• Delay surgery until anemia corrected</td>
</tr>
<tr>
<td></td>
<td>• Iron</td>
</tr>
<tr>
<td>14–35 days</td>
<td>• Delay surgery until anemia corrected</td>
</tr>
<tr>
<td></td>
<td>• Autologous blood donation</td>
</tr>
<tr>
<td></td>
<td>• Erythropoietin weekly dosing regimen</td>
</tr>
<tr>
<td></td>
<td>• Iron</td>
</tr>
<tr>
<td>10–13 days</td>
<td>• Delay surgery until anemia corrected</td>
</tr>
<tr>
<td></td>
<td>• Erythropoietin daily dosing regimen</td>
</tr>
<tr>
<td></td>
<td>• Iron</td>
</tr>
<tr>
<td>&lt; 10 days</td>
<td>• Delay surgery until anemia corrected</td>
</tr>
<tr>
<td>before surgery</td>
<td></td>
</tr>
<tr>
<td>Intraoperative</td>
<td>• Attention to surgical hemostasis</td>
</tr>
<tr>
<td></td>
<td>• Antifibrinolytics and DDAVP</td>
</tr>
<tr>
<td></td>
<td>• Intraoperative cell salvage</td>
</tr>
<tr>
<td></td>
<td>• Regional anesthesia</td>
</tr>
<tr>
<td></td>
<td>• Other measures, mainly investigational</td>
</tr>
<tr>
<td></td>
<td>• Adherence to strict transfusion guidelines</td>
</tr>
</tbody>
</table>
Case 5

- 55 year old man in the ICU several days post-MVC with multiple trauma
  - No history of cardiac disease
  - No evidence of acute bleeding
- Vital signs: HR 85, BP 140/80
- Labs: Hb 60 g/L
- Patient is a Jehovah’s Witness and does not consent to blood transfusion....what do you do??
Jehovah’s Witnesses

- Refuse transfusion of allogenic blood based on their understanding of several Biblical passages

- Physicians should discuss the options with individual patients

- Generally considered not acceptable:
  - Whole blood, red cells, white blood cells, platelets, plasma

- Personal decision:
  - Albumin, clotting factor concentrates, IVIG, autologous blood obtained for ANH or by cell salvage, cryoprecipitate, fibrin glue
Refusal of Blood Products

- Minimize phlebotomies for laboratory testing
- Provide adequate support to minimize causes of anemia
  - Iron supplementation
  - Folic acid (5 mg OD)
  - Vitamin B12 (1 mg PO OD)
- Erythropoietin (20,000 units SC OD)
  - If Hb<100 or if Hb<120 and surgery is planned
- If ongoing bleeding, consider:
  - Antifibrinolytics (cyklokapron)
  - Desmopressin acetate
  - Niastase
RBC Transfusion and Chronic Anemia

- Consider alternatives and adjuncts to transfusion
  - Ensure adequate stores of iron, vitamin B12, folate
  - Erythropoietin
  - Treat underlying disease

- Only transfuse when there is no effective alternative

- Maintain hemoglobin at a level avoid symptoms of anemia

- Monitor long-term transfusion dependant patients for iron overload
## Summary for RBC Transfusions

<table>
<thead>
<tr>
<th>Hemoglobin</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 100 g/L</td>
<td>Likely inappropriate except in exceptional circumstances.</td>
</tr>
<tr>
<td>70-100 g/L</td>
<td>Likely to be appropriate if there are signs or symptoms of impaired oxygen delivery.</td>
</tr>
<tr>
<td>&lt; 70 g/L</td>
<td>Likely to be appropriate.</td>
</tr>
<tr>
<td>&lt; 60 g/L</td>
<td>Transfusion highly recommended.(^{10})</td>
</tr>
</tbody>
</table>
  * Young patients with low risk of ischemic cardiovascular disease can sometimes tolerate greater degrees of anemia.
Plasma
50 year old man with chronic liver failure requires percutaneous liver biopsy
   - No evidence of acute bleeding
   - Labs: INR: 1.7

What do you do? Should he receive a plasma transfusion?
Plasma

- Plasma can be used to prepare FFP or cryoprecipitate.
  - Usually male donors only (unless AB plasma)

- The plasma may also be shipped to commercial manufacturers as “Recovered Plasma” for further manufacture (fractionation)
FP

- Source clotting factors
  - Contains all clotting factors
  - Factors 8 level is slightly reduced

- Available in 2 forms:
  - recovered from regular donations
    - each unit is 250 mL
  - from apheresis donation

- Should be ABO compatible

- Blood bank requires ~30 minutes for thawing

- Infusion time 30-120 minutes (maximum 4 hours)
Dosing of FP

- Dose is 10-15 mL/kg
  - Will increase all coagulation factors by ~30% which is usually adequate for hemostasis

- Example of calculation:
  - 70 kg X 15 mL/kg = 1050 mL = 4 units

- In general:
  - 3 units for small adult
  - 4 units for large adult

- Giving less will be ineffective
## Selecting compatible plasma (and platelets)

<table>
<thead>
<tr>
<th>Recipient</th>
<th>ABO antigen(s) present on red cells</th>
<th>Donor plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>none</td>
<td>O, A, B, AB</td>
</tr>
<tr>
<td>A</td>
<td>A</td>
<td>A, AB</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>B, AB</td>
</tr>
<tr>
<td>AB</td>
<td>A and B</td>
<td>AB</td>
</tr>
</tbody>
</table>
FP

- Indications:
  - Correction of clotting factor deficiencies where clotting factor concentrates are not available or when multiple clotting deficiencies are present
  - e.g. Liver disease, warfarin reversal, DIC)

- Contraindications
  - Available specific therapy: FVIII, FIX, Vitamin K
  - Volume expansion
  - Patients with IgA antibodies or selective IgA deficiency
Plasma transfusion is NOT indicated

- To correct warfarin effect when time is available to allow for spontaneous or vitamin K-induced normalization of PT or INR

- Prior to procedures (such as percutaneous liver biopsy, thoracentesis or paracentesis) in patients with liver disease and INR or 2.0 or less

- Hypovolemia

- Plasma exchange procedures (excluding TTP)

- Treatment of immunodeficiency states

- When specific therapy is available: i.e. factor 8 or factor 9 deficiency
Platelets
Case 7

- 50 year old man admitted to ICU with severe pneumonia and sepsis
- Patient deteriorates clinically, bleeding noted from IV sites
- Labs: Hb 110, plt 19 x 10⁹/L, INR 4.0, PTT 76,
- You order:  
  - FP: 4 units
- Should you also order platelets?
Platelets

- Two main types of platelets for transfusion

- Random donor platelets (Buffy Coat)
  - From whole blood donation
  - Given in pools of 4 units (resuspended in one donor’s plasma)

- Apheresis platelets
  - Single donor collection

- Equivalent: one adult dose
- Volume 300-350 mL
Platelets

- Recommended infusion time ~60 minutes

- One adult dose of buffy coat platelets or one apheresis platelet unit, should raise the platelet count by $10-15 \times 10^9/L$

- Note: new terminology…one dose of BC platelets (pooled from 4 donors) is equivalent to 5U of platelets

- If concerns about response: check post-transfusion platelet count within 1 hour of transfusion to determine response and detect refractoriness
Clinical Use of Platelets

<table>
<thead>
<tr>
<th>Platelet count (x10⁹/L)</th>
<th>Clinical setting</th>
<th>Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>Immune thrombocytopenia</td>
<td>Transfuse platelets only with serious bleeding</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Non-immune thrombocytopenia</td>
<td>Transfuse 1 adult dose</td>
</tr>
<tr>
<td>&lt;20</td>
<td>Non-immune thrombocytopenia and fever or coagulopathy</td>
<td>Transfuse 1 adult dose</td>
</tr>
<tr>
<td>&lt;20</td>
<td>Procedures not associated with significant blood loss</td>
<td>Transfuse 1 adult dose</td>
</tr>
<tr>
<td>20-50</td>
<td>Procedures not associated with significant blood loss</td>
<td>Have 1 adult dose available, transfuse only if there is serious bleeding</td>
</tr>
</tbody>
</table>

Callum and Pinkerton, Bloody easy 2
# Clinical Use of Platelets

<table>
<thead>
<tr>
<th>Platelet count (x10⁹/L)</th>
<th>Clinical Setting</th>
<th>Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>Epidural anesthesia and lumbar puncture</td>
<td>Transfuse 1 adult dose immediately before procedure</td>
</tr>
<tr>
<td>&lt;50-100</td>
<td>Procedures associated with blood loss or major surgery (&gt;500 mL expected blood loss)</td>
<td>Transfuse 1 adult dose immediately before procedure</td>
</tr>
<tr>
<td>&lt;100</td>
<td>Pre-neurosurgery or head trauma</td>
<td>Transfuse 1 adult dose</td>
</tr>
<tr>
<td>Any</td>
<td>Platelet dysfunction and marked bleeding (e.g. post-cardiopulmonary bypass, anti-platelet agents)</td>
<td>Transfuse 1 adult dose</td>
</tr>
</tbody>
</table>

Callum and Pinkerton, Bloody easy 2
Cryoprecipitate
Case 8

- 50 year old man admitted to ICU with severe pneumonia
- Patient deteriorates clinically, bleeding noted from IV sites
- Labs: Hb 110, plt 19 x 10^9/L, INR 4.0, PTT 76,
- You have already ordered:
  - Platelets: one adult dose
  - FP: 4 units
- Additional labs: Fibrinogen 0.4 g/L
- What else should be transfused?
Cryoprecipitate

- Plasma is frozen within 8 hours of collection and then thawed slowly at 1-6°C to “slush”

- Centrifuged to separate the liquid from the precipitated proteins

- Separated plasma is called “cryosupernatant” Precipitate proteins are called “cryoprecipitate”

- Stored frozen
Cryoprecipitate

- Named because it contains factors that precipitate from FFP in the cold

- Contains:
  - Fibrinogen 500 mg
  - Factor VIII 200 IU
  - vWF 80 units
  - Fibronectin
  - Factor XIII 40-60 units

- Resuspended in 5-15 mL of plasma
- Store frozen (-18°C)
Cryoprecipitate

- 1 unit per 8-10 Kg body weight
- 8-10 units for an average sized adult
  - \( \frac{8-10}{1} \) = 2 g fibrinogen

- Volume: 5-15 mL per unit
- Infusion time 10-30 minutes
- Each dose should raise fibrinogen by 0.5-1.0 g/L
- Check post-infusion fibrinogen level to confirm outcome
Cryoprecipitate

- Indications for its use:
  - Treatment of massive or microvascular bleeding with
    - Fibrinogen < 1.0 g/L
    - Status highly suggestive of hypofibrinogenemia without time for laboratory confirmation
    - Massive rapid defibrination in the obstetrical patient
  - Hereditary Disorders of Hemostasis
    - For bleeding in vWD patients ONLY if factor concentrate is unavailable and DDAVP is ineffective
    - For the emergency management of factor VIII deficiency ONLY if manufactured factor VIII is unavailable
Cryoprecipitate

- Cryo is not indicated for:
  - Hemophilia A
  - Von Willebrand’s disease
  - Congenital fibrinogen deficiency
  - Production of fibrin glue
  - Factor XIII deficiency

- It is not a source of “concentrated” plasma, should not be used as a substitute for FFP

- Fibrinogen level should be obtained before administration
Other products:

Octaplex
Niastase
Albumin
Case 9

- 50 year old man on therapeutic warfarin for atrial fibrillation
- Presents with acute GI bleed
- Labs: INR 2.5
- What should you do?
## Elevated INR in patient on Warfarin

<table>
<thead>
<tr>
<th>INR</th>
<th>Bleeding?</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1-5.0</td>
<td>No</td>
<td>Lower dose or omit dose, monitor more frequently</td>
</tr>
<tr>
<td>5.1-9.0</td>
<td>No</td>
<td>Omit one or two doses, restart at lower dose. Consider administration of vitamin K (1-2.5 mg PO)</td>
</tr>
<tr>
<td>&gt;9.0</td>
<td>No</td>
<td>Hold warfarin therapy, give vitamin K (2.5-5 mg)</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>Serious</td>
<td>Hold warfarin therapy, give vitamin K (10 mg IV). May give Octaplex, FFP or Niastase depending on urgency</td>
</tr>
<tr>
<td>Any</td>
<td>Life-threatening</td>
<td>Hold warfarin therapy, give vitamin K (10 mg IV). Give octaplex, FFP or niastase</td>
</tr>
</tbody>
</table>

Ansell J et al., Chest 2008
Octaplex

- Prothrombin complex concentrate (PCC)
- Contains factors II, VII, IX, X, PC, PS
- Human product, but viral inactivation steps

- Indications:
  - Treatment of severe active bleeding in acquired coagulation defects caused by vit K antagonists OR
  - Rapid correction (<6 h) of the deficiency of vit-K dependent factors required for urgent surgical procedures

- Dose
  - INR 2-3: 20 IU/kg
  - INR 3-6: 30 IU/kg
  - INR > 6: 40 IU/kg

- Also give vitamin K
- THROMBO consult required
Niastase

- Recombinant activated factor VIIa

- Accepted Indications:
  - bleeding in individuals with hemophilia A or B having inhibitors
  - bleeding in patients with acquired inhibitors
  - patients with FVII deficiency
  - patients with congenital coagulopathies other than hemophilia

- Other (possible) uses
  - DIC
  - Liver dysfunction
  - Control of hemorrhage in the absence of coagulation defects (trauma, surgery, and obstetrical complications)
  - Reversal of oral anticoagulation
Niastase

- Dose varies depending on indication
  - Hemophilia: 90 mcg/kg q2h
  - FVII deficiency: 20-30 mcg/kg
  - Refractory bleeding: 40 mcg/kg

- Hematology consult required for use
- If using in patient with refractory bleeding, ensure that you have corrected all other parameters (platelet count, fibrinogen, temperature, etc)
- Associated with significant thromboembolic complications
**Albumin**

**How to order:**
- 500 mL 5% albumin (=25 g)
  - Expands plasma volume by 750 mL
- 100 mL 25% albumin (=25 g)
  - Expands plasma volume by 450 mL
- 25% albumin should not be infused faster than 2 mL/min in 70 kg adult

**Alternatives**
- Starch polymers (pentaspan, hextend, voluven)
- Crystalloid solutions (saline, Ringer’s lactate)
Albumin: Indications

- Volume replacement in nonhemorrhagic shock unresponsive to crystalloid
- Volume replacement in patient with burns (>50%) unresponsive to crystalloid
- Volume replacement after large volume paracentesis (>5 L) in patient unresponsive to crystalloid
- Replacement fluid for plasma exchange
- Volume replacement in patient with severe necrotizing pancreatitis
- Diarrhea (>2 L per day) in hypoalbuminemic patients on enteral feedings unresponsive to short chain peptide supplementation

Nahirniak S. in Clinical Guide to Transfusion, 2006
Case 8

- 55 year old man in the ICU several days post-MVC with multiple trauma
  - No history of cardiac disease
  - No evidence of acute bleeding

- Vital signs: HR 85, BP 140/80
- Labs: Hb 60 g/L

- Patient and his family are approached to give consent for a transfusion of RBC. He asks about the risks of transfusion....what do you tell him?
## Risks of not transfusing

### TABLE 3. Mortality stratified by postoperative Hb level (n = 300)

<table>
<thead>
<tr>
<th>Postoperative Hb (g/dL)</th>
<th>Total study population</th>
<th>30-day in-hospital mortality*</th>
<th>No cardiovascular disease (n = 230)</th>
<th>Cardiovascular disease (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Number</td>
<td>30-day in-hospital mortality, n (%)</td>
</tr>
<tr>
<td>1.1-2.0</td>
<td>7</td>
<td>7 (100)</td>
<td>5</td>
<td>5 (100)</td>
</tr>
<tr>
<td>2.1-3.0</td>
<td>24</td>
<td>13 (54.2)</td>
<td>19</td>
<td>10 (52.6)</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>28</td>
<td>7 (25.0)</td>
<td>20</td>
<td>2 (10.0)</td>
</tr>
<tr>
<td>4.1-5.0</td>
<td>32</td>
<td>11 (34.4)</td>
<td>20</td>
<td>4 (20.0)</td>
</tr>
<tr>
<td>5.1-6.0</td>
<td>54</td>
<td>5 (9.3)</td>
<td>40</td>
<td>3 (7.5)</td>
</tr>
<tr>
<td>6.1-7.0</td>
<td>56</td>
<td>5 (8.9)</td>
<td>44</td>
<td>5 (11.4)</td>
</tr>
<tr>
<td>7.1-8.0</td>
<td>99</td>
<td>0 (0)</td>
<td>82</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

* Results reported as number (%).

### TABLE 4. Mortality or morbidity stratified by postoperative Hb level*

<table>
<thead>
<tr>
<th>Postoperative Hb (g/dL)</th>
<th>Total study population</th>
<th>30-day in-hospital mortality and/or morbidity†</th>
<th>No cardiovascular disease (n = 199)</th>
<th>Cardiovascular disease (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Number</td>
<td>30-day in-hospital mortality and/or morbidity†</td>
</tr>
<tr>
<td>1.1-2.0</td>
<td>4</td>
<td>4 (100)</td>
<td>2</td>
<td>2 (100)</td>
</tr>
<tr>
<td>2.1-3.0</td>
<td>12</td>
<td>11 (91.7)</td>
<td>9</td>
<td>8 (88.9)</td>
</tr>
<tr>
<td>3.1-4.0</td>
<td>19</td>
<td>10 (52.6)</td>
<td>14</td>
<td>6 (42.9)</td>
</tr>
<tr>
<td>4.1-5.0</td>
<td>26</td>
<td>15 (57.7)</td>
<td>18</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>5.1-6.0</td>
<td>49</td>
<td>14 (28.6)</td>
<td>34</td>
<td>8 (23.5)</td>
</tr>
<tr>
<td>6.1-7.0</td>
<td>50</td>
<td>11 (22.0)</td>
<td>40</td>
<td>9 (22.5)</td>
</tr>
<tr>
<td>7.1-8.0</td>
<td>96</td>
<td>9 (9.4)</td>
<td>82</td>
<td>8 (9.8)</td>
</tr>
</tbody>
</table>

* Analysis limited to multicenter data (n = 256); postoperative Hb is prior to event.
† Defined as arrhythmia, congestive heart failure; myocardial infarction, bacteremia, pneumonia, deep wound infection, or death; 74 patients with at least one event. Data reported as number (%).
Alternatives to blood product usage

- Autologous donation
- Blood salvage techniques
  - Intraoperative hemodilution
  - Intraoperative cell saving techniques
- Volume expanders
  - Crystalloids (Saline, Ringer’s lactate)
  - Colloids (Pentastarch)
- Pharmacologic agents for bleeding
  - Desmopressin acetate
  - Tranexamic Acid
  - Vitamin K
- Therapeutic agents for anemia
  - Iron
  - Folic acid
  - Vitamin B12
  - Erythropoietin
Risks of transfusion
<table>
<thead>
<tr>
<th>Testing performed by CBS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Syphilis</strong></td>
</tr>
<tr>
<td><strong>Hepatitis B</strong></td>
</tr>
<tr>
<td><strong>Hepatitis C</strong></td>
</tr>
<tr>
<td><strong>HIV</strong></td>
</tr>
<tr>
<td><strong>HTLV-I and II</strong></td>
</tr>
<tr>
<td><strong>West Nile virus</strong></td>
</tr>
<tr>
<td><strong>Bacterial testing</strong></td>
</tr>
<tr>
<td><strong>CMV</strong></td>
</tr>
<tr>
<td><strong>Chagas Disease</strong></td>
</tr>
</tbody>
</table>
## Infectious complications of transfusion

<table>
<thead>
<tr>
<th>Infection</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial sepsis</td>
<td>1:10,000 (greatest risk with platelets)</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1:153,000</td>
</tr>
<tr>
<td>HTLV-I,II</td>
<td>1:4.3 million</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1:2.3 million</td>
</tr>
<tr>
<td>HIV</td>
<td>1:7.8 million</td>
</tr>
<tr>
<td>WNV</td>
<td>1:&gt;1 million*</td>
</tr>
<tr>
<td>vCJD</td>
<td>Very rare (4 cases reported)</td>
</tr>
<tr>
<td>Malaria</td>
<td>1:4 million</td>
</tr>
</tbody>
</table>

*depends on season and geographical area.

---

O’Brien et al. Transfusion 2007  
Callum and Pinkerton, Bloody easy 2
## Non-infectious Complications of Transfusion

<table>
<thead>
<tr>
<th>Complication</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hemolytic transfusion reaction</td>
<td>1:25,000</td>
</tr>
<tr>
<td>Delayed hemolytic transfusion reaction</td>
<td>1:7,000</td>
</tr>
<tr>
<td>Febrile non-hemolytic transfusion reaction</td>
<td>1:10 (plts)</td>
</tr>
<tr>
<td>Allergic reaction: Anaphylactic</td>
<td>1:40,000</td>
</tr>
<tr>
<td>Allergic reaction: Minor</td>
<td>1:100</td>
</tr>
<tr>
<td>TRALI</td>
<td>1:5,000</td>
</tr>
<tr>
<td>Transfusion-associated circulatory overload (TACO)</td>
<td>1:700</td>
</tr>
</tbody>
</table>

Callum and Pinkerton, Bloody easy 2
Risks of Transfusion

- Most common adverse events of transfusion are usually mild and not life-threatening
  - Febrile non-hemolytic transfusion reactions
    - 1:10 (pool of 5 units of platelets)
  - Minor allergic reactions
    - 1:100

- Transmissions of HIV and HCV are uncommon
  - HCV: 1 in 2,300,000
  - HIV: 1 in 7,800,000
Risks of Transfusion

- Risk of death per transfusion of 1 unit (all causes)
  - 1 in 207,894
    - TTISS, Canada (2004-2005)
  - 1 in 285,000
    - SHOT (UK) components possibly, probably or definitely related to patient death (2008)
  - 1 in 208,333

Serious Hazards of Transfusion Report 2008
Rebibo et al. Transfusion and Apheresis Science 2004
### Incidence of deaths by type of adverse transfusion event, 2004-2005, Canadian TTISS

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Number</th>
<th>Incidence (all components) N=2,078,935</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRALI</td>
<td>5</td>
<td>1:415,787</td>
</tr>
<tr>
<td>TACO</td>
<td>3</td>
<td>1:692,978</td>
</tr>
<tr>
<td>Bacterial contamination</td>
<td>1</td>
<td>1:2,078,935</td>
</tr>
<tr>
<td>Hemolytic transfusion reaction</td>
<td>1</td>
<td>1:2,978,935</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>1:207,894</td>
</tr>
</tbody>
</table>

Acute Hemolytic Transfusion Reactions (AHTR)
Etiology

- Antigen-positive red cells are transfused to a recipient who has an alloantibody
  - Results in intravascular hemolysis

- Often due to the administration of ABO incompatible blood
  - e.g., patient with blood group O transfused with group A red cells

- Usually due to clerical error or other error in patient identification which results in the administration of blood to wrong patient

- Estimations of mistransfusion rate
  - 1:14,000-18,000 units transfused (Canada, US, UK)
Clinical Presentation

- Acute onset, often within first 15 minutes of starting transfusion

- Initial Clinical Presentation:
  - Fever and/or chills, anxiety, nausea or vomiting, pain (flank, back, abdomen, chest, head, infusion site), dyspnea, hypotension, brown urine, bleeding

- Complications:
  - Renal failure, disseminated intravascular coagulation (DIC), death
AHTR—Treatment

- STOP the transfusion immediately

- Alert the blood bank, check for clerical error, send entire transfusion set-up to blood bank for testing

- Supportive care
  - Monitor vital signs closely
  - Maintain blood pressure and urine output
  - Monitor for hyperkalemia
  - Administer FFP, cryoprecipitate and platelets as required for coagulopathy
AHTR—Prevention

- Meticulous attention to:
  - Patient identification and bedside sample labeling at time of pre-transfusion sample collection
  - Identification during all phases of blood bank accession, testing, labeling at product issue
  - Identification of the recipient at start of transfusion including checking the armband
Case 10

- 65 year old woman undergoing hip replacement surgery
- Transfused with 2 units of RBC
- During transfusion of 1st unit developed fever, dyspnea and hypotension
- Transfusion stopped immediately
- Patient transferred to ICU
- Died of multi-organ failure and septic shock within 48 hours
Peripheral blood cultures of the patient and cultures of the implicated unit were positive for Yersinia enterocolitica. The patient died of a transfusion-related fatality due to bacterial contamination of the blood product.
**Bacterial Contamination**

- Most frequent infectious risk associated with transfusion
- Occurs most frequently with platelets
  - Stored at 20-24°C
  - Excellent growth medium for bacteria
- Risk of symptomatic reaction
  - ~1:10,000
- Risk of fatal septic reaction
  - ~1:40,000
- Organisms:
  - gram positive bacteria (skin flora),
  - less common: gram-negatives (*Klebsiella pneumoniae*, *Serratia marcescens*, *Pseudomonas* species, *Yersinia enterocolitica*)
Clinical Presentation

- Depends on bacterial load of product, species of implicated bacteria
- Rigours, fever, chills
- Hypotension
- Tachycardia
- Nausea and vomiting
- Dyspnea
- Disseminated intravascular coagulation
- Usually occurs during transfusion of implicated product
Bacterial Contamination—Treatment and Investigation

- Stop the transfusion immediately
- Notify the blood bank
  - Blood bank will notify CBS so that other products from the same donor can be quarantined and cultured
- Arrange for gram stain/culture of implicated unit(s)
- Blood culture of patient
- Broad-spectrum antibiotics
- Treatment of the shock and renal failure as required
Case 11

- 68 year old man undergoing endoscopy
  - INR 2.0
  - Transfused with 4 units of FFP
- Halfway through transfusion, patient developed acute dyspnea, hypoxia, and hypotension
- JVP not elevated
- Transfusion stopped immediately
- Patient given diuretics with no effect
Case 11

- Patient transferred to the ICU
- Because of poor response to diuretics, diagnosis of TRALI was considered
- Despite supportive care, patient did not recover and died within 48 hours

Transfusion-related fatality due to transfusion-related acute lung injury (TRALI)
TRALI

- Acute lung injury
  - Acute onset
  - Hypoxemia
    - $\text{PaO}_2/\text{FiO}_2 \leq 300$
    - $\text{SpO}_2 < 90\%$ on room air
  - Bilateral infiltrates on CXR
  - No evidence of circulatory overload (PCWP $\geq 18$)

- Within 6 hours of transfusion

- Indistinguishable from ARDS

Kleinman et al. Transfusion 2004;44:1774-89
TRALI—Epidemiology

- Incidence

  - Likely under-reported and under-recognized

  - 1.4 to 8 cases per 10,000 allogeneic blood product unit transfused (0.014%-0.08%)

  - 0.4 to 1.6 cases per 1,000 patients transfused (0.04%-0.16%)
TRALI — Pathophysiology

- Passive transfer of donor alloantibodies in plasma of transfused product

Donor alloantibody → Recipient WBC
TRALI—Pathophysiology

- Antigen-antibody interaction causes pulmonary leukostasis and activation of WBC

- Activation of WBC results in the production of inflammatory mediators that cause increased vascular permeability

- Leads to capillary leak and pulmonary tissue damage

- May also be caused by the infusion of “biologic response modifiers” within the blood component
  - Cytokines
  - Lipids with neutrophil-priming activity
TRALI — Treatment and Prognosis

- No diagnostic test: TRALI should be suspected if a patient has appropriate clinical findings within six hours of a transfusion.
- Exclude of other causes of cardiogenic and non-cardiogenic pulmonary edema.
- Ventilatory support as required.
- Maintenance of hemodynamic status.
- 80% of patients show clinical improvement within 48-96 hours.
  - In most patients, there are no long-term complications.
  - Fatal in 5-10% of cases.
Transfusion Associated Circulatory Overload (TACO)
TACO

- Acute pulmonary edema secondary to congestive heart failure precipitated by transfusion

- Associated with hypertension, tachycardia, positive fluid balance

- Likely the most under-recognized and potentially serious transfusion complication

- Studies have demonstrated incidence in orthopedic surgery patients (hip or knee arthroplasty) to be 1-8%

Popovskv MA, Transfusion Reactions, AABB, In press.
Popovskv MA, Transfusion and Apheresis Science, 2006
TACO: Risk Factors

- Too much blood transfused too rapidly
- Can be precipitated by even a single RBC unit
- Age <3 or >60 years
- Diminished cardiac reserve
- Chronic anemia
Treatment and Prevention

**Prevention**
- Transfuse only when indicated
- Recognize patients at risk
- If at risk, transfuse slowly
- Consider diuretics (before and/or after)
- Watch fluid balance, monitor patient closely

**Treatment**
- Stop transfusion
- Diuretics
- Oxygen
- Cardiac and respiratory support as required
## Complications of Massive Transfusion

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothermia</td>
<td>Red cells stored at 1-6°C</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>Red cells contain K with concentrations ranging from 7-77 mEq/unit. Tends to be associated with non-red cell transfusions (i.e. large volumes of FFP given to patients with liver disease)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>Stored blood is anticoagulated with citrate, which binds calcium. Tends to be associated with non-red cell transfusions (i.e. large volumes of FFP given to patients with liver disease)</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>Stored blood is anticoagulated with citrate, which binds calcium. pH of stored blood is ~6.6-7.0. Acidosis in MT patients is due to tissue hypoperfusion</td>
</tr>
<tr>
<td>Alkalosis/Acidosis</td>
<td>pH of stored blood is ~6.6-7.0. Citrate is metabolized to bicarbonate. Acidosis in MT patients is due to tissue hypoperfusion</td>
</tr>
<tr>
<td>Dilutional coagulopathy and thrombocytopenia</td>
<td>Coagulation defects are related to total volume of blood transfused, pre-existing hemostatic abnormalities</td>
</tr>
</tbody>
</table>

Sihler KC and Napolitano LM, Chest 2010
## Costs of Transfusion

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red blood cells (1 unit)</td>
<td>$400</td>
</tr>
<tr>
<td>Platelets (1 dose)</td>
<td>$500</td>
</tr>
<tr>
<td>FFP (4 units)</td>
<td>$700</td>
</tr>
<tr>
<td>Cryoprecipitate (8 units)</td>
<td>$225</td>
</tr>
<tr>
<td>Albumin 5% (500 mL)</td>
<td>$100</td>
</tr>
<tr>
<td>Pentaspan (500 mL)</td>
<td>$70</td>
</tr>
<tr>
<td>Niastase (4.8 mg)</td>
<td>$5,000</td>
</tr>
<tr>
<td>Octaplex (1500 IU)</td>
<td>$2,000</td>
</tr>
</tbody>
</table>

Cost does not include:

- Donor’s time
- Transportation of blood
- Processing unit in blood bank
- Nursing time
- Laboratory tests

Callum and Pinkerton, Bloody Easy 2, 2005
Cost of Transfusion

Amin M et al., Transfusion 2004
Take Home Messages

- Hemoglobin level not the only consideration in decision to transfuse RBC
- Obtain informed consent for transfusion of any blood product
- Be aware of risks of transfusion
- Blood transfusions should only be administered when benefits of transfusion outweigh risks
Take Home Messages

- RBC: 1 unit
  - symptomatic anemia OR
  - Hb< 70 g/L
- Platelets: 1 dose
  - Plt < 10
  - Plt < 50 and patient having surgery or bleeding
  - Platelet dysfunction suspected and patient having surgery or bleeding
- FFP: 4 units for coag factor deficiency
- Cryo: 8-10 units for fibrinogen < 1.0
Other Resources

- Bloody Easy 2
  - Available online at: http://sunnybrook.nextmovelearning.com/

- www.transfusionmedicine.ca
  - Access to “Clinical Guide to Transfusion”

- webertk@mcmaster.ca

- Hospital Blood Bank staff