Best practice in blood transfusion management in cardiac surgery

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OBJECTIVES

• To describe the paradigm shift in blood management
• To present the perioperative multimodalities strategies in reducing or eliminating allogeneic blood transfusion in cardiac surgery

A new disease was threatening the Canadian blood supply in the early 1980’s: AIDS. But the Canadian Red Cross was slow to introduce donor screening methods and even slower to test the blood. With the Krever Commission, those infected by the AIDS virus and hepatitis C found a compassionate ear and the answers they sought about who was to blame for this public health scandal.

Canadian Broadcasting Corporation Archives
http://archives.cbc.ca

RISKS OF BLOOD TRANSFUSION

The Krever Report: Canada’s Tainted Blood Disaster
**RISKS OF BLOOD TRANSFUSION**

**INFECTIOUS COMPLICATIONS**

<table>
<thead>
<tr>
<th>Blood Component</th>
<th>Risks</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>&lt;1:1,900,000</td>
<td>Hemolysis</td>
</tr>
<tr>
<td>HCV</td>
<td>1:1,800,000</td>
<td>Bacterial</td>
</tr>
<tr>
<td>HBV</td>
<td>1:250,000</td>
<td>TRALI (deaths)</td>
</tr>
<tr>
<td>HTLV-I&amp;II</td>
<td>1:2,000,000</td>
<td>Nonbac infection</td>
</tr>
<tr>
<td>West Nile Virus</td>
<td>1:1,200 to 1:30,000</td>
<td>GVHD</td>
</tr>
<tr>
<td>CMV</td>
<td>1:7,500</td>
<td>Mistransfusion</td>
</tr>
<tr>
<td>Malaria</td>
<td>1:5,000,000</td>
<td>TRALI (incidences)</td>
</tr>
<tr>
<td>Babesiosis</td>
<td>1:5,000,000</td>
<td>Febrile reaction</td>
</tr>
<tr>
<td>Chagas</td>
<td>1:300,000</td>
<td>Post-transfusion purpura</td>
</tr>
<tr>
<td>RBCs</td>
<td>1:1.6 x 105</td>
<td></td>
</tr>
<tr>
<td>Platelet</td>
<td>1:12,000 to 1:60,000</td>
<td></td>
</tr>
</tbody>
</table>

**AGE OF PRBC UNITS TRANSFUSED IS ASSOCIATED WITH MORTALITY**


**RISKS: ALLOGENEIC TRANSFUSION**

Transfusion risks Post-transfusion reaction

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</tr>
</tbody>
</table>

**TRANSFUSION HAZARDS**

**DIAGNOSED**

- Symptomatic
- Asymptomatic

**INCORRECTLY DIAGNOSED**

- Symptomatic
- Asymptomatic

**UNDIAGNOSED**

- Symptomatic
- Asymptomatic

**RBCS CHANGE SHAPE DURING STORAGE**

- Scanning electron micrographs of RBCs isolated from stored blood on day 1, day 21, and day 35
- During storage, the shape of RBCs changed gradually from normal discoid to echinocytes (RBCs with multiple regular spiny projections)

2. Taber’s Cyclopedic Medical Dictionary, 18th Edition

**CURRENT BLOOD SUPPLY IS THE SAFEST EVER IN TRANSFUSION HISTORY**

There will NEVER be zero risk

**PROJECTED BLOOD COLLECTIONS VERSUS PROJECTED HOSPITAL DEMAND**

Prévisions du nombre d’unités prélevées vs la demande dans le hôpitaux
Cheng CHD. Best practice in blood transfusion management in cardiac surgery

**Item** | **Price**
--- | ---
Red blood cells | $400
Autologous (whole) blood | $400
Erythropoietin 40,000 IU/week for 4 weeks | $2,280†
Erythropoietin 1,000 IU | $14.25†
5 units platelets | $500
4 units buffy coat derive platelets | $500
1 units single donor (apheresis) platelets | $500
1 unit HLA-matched single donor (apheresis) platelets | $1,250
Apheresis fresh frozen plasma | $220
4 units frozen plasma | $700
8 units cryoprecipitate | $500
Aprotinin 3 million units | $500
Tranexamic add 6 g | $150
IVIG per gram | $75
Albumin 5% 500 ml | $100
Pentaspan® per 500 ml | $70
Hexten® 500 ml | $60
CMV anigen-negative, additional cost per unit | $20
Irradiation per unit | $25
Blood group (ABO, RhD) | $10
Antibody screen | $25
Crossmatch (no antibody) | $15
Crossmatch (antibody positive patient) | $45

Callum JL, Pinkerton PH. Blood transfusions, blood alternatives & transfusion reactions. 2nd Ed. 2005
Sponsored by Ontario Ministry of Health, Health Canada, Canadian Blood Services

**PARADIGM SHIFT IN EVIDENCE-BASED BLOOD MANAGEMENT**

-Cheng, Karkouti, Belisle, Giffin, Martin. CJA 2006

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**Canadian Utilization Study: Allogeneic RBC by Procedure**

-Cheng, Karkouti, Belisle, Giffin, Martin. CJA 2006

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**Canadian Utilization Study: % Patients TX by Institutions**

-Cheng, Karkouti, Belisle, Giffin, Martin. CJA 2006
Cheng CHD. *Best practice in blood transfusion management in cardiac surgery*


Jehovah’s witnesses who require operation represent a challenge to the physician because of the patients’ refusal to accept blood transfusion. We report a 20-year experience with a consecutive series of 542 Jehovah’s witness patients ranging in age from 1 day to 89 years who underwent operation. Early mortality (within 30 days after operation) was 9.4%. In 362 patients requiring temporary cardiopulmonary bypass, early mortality was 10.7%. Mortality was 13.5% among 126 patients who had single-or double-valve replacement. The only deaths among patients who had aortic valve replacement or repair of a ventricular septal defect occurred in those who had some serious complication before operation. Preoperative or postoperative anemia was a contributing factor in 12 deaths, and loss of blood was the direct cause of three deaths. Cardiovascular operations can be performed safely without blood transfusion.

2/3 OF ALL RBC TRANSFUSIONS ARE GIVEN PERIOPERATIVELY

Stover. Anesthesiology 1998;88:327-333

BLOODLESS SURGERY


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• Acute normovolemic hemodilution
  ↓ transfusion triggers
• Shed blood salvage
• Oxygen carriers

Postoperative
• ↓ transfusion triggers
• ↑ RBC
• Shed blood salvage

Cheng D. Can J Anesth 2001;48: S41- S48

**ANEMIA: LOWER HB ASSOCIATED WITH HIGHER MORTALITY FOLLOWING AMI**

• Study of 78,974 patients over 65 yrs old admitted with acute MI
• Lower Admission Hct ≥ higher 30-day mortality and longer hospitalization

![Graph showing survival rates over time]


SAFE LEVEL OF ANEMIA IN SURGICAL PATIENTS?

![Mortality Odds Ratio graph]

Jehovah’s Witnesses, observational study
↑ risk if Preop Hb ≤ 60 g/L or ≤ 100 g/L if have CAD

Jehovah’s witnesses, observational study ³risk if Preop Hb ≥ 60 g/L or ≥ 100 g/L if have CAD


<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital acquired</td>
<td>37.3%</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>29.3%</td>
</tr>
<tr>
<td>Renal failure</td>
<td>10.7%</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>8.0%</td>
</tr>
<tr>
<td>Folate deficiency</td>
<td>4.0%</td>
</tr>
<tr>
<td>Thalassemia</td>
<td>1.3%</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>9.3%</td>
</tr>
</tbody>
</table>


**RBC: FE, FOLATE**

Advantages:
• Mainstay of treating iron-deficiency anemia

Disadvantages:
• Response to treatment is slow and must be started early - poor GI tract absorption

Spence RK. 28th ISBT, August 26-30, 2000
• In cases of ongoing iron losses, oral iron does not provide enough iron to correct the iron deficient erythropoiesis, and intravenous iron should be considered

Goodnough LT. Alter in Trans Med 2:January 2000

**RBC: ERYTHROPOIETIN**

↑ reticulocyte count, Hb levels
↓ allogeneic blood transfusion


Advantages:
• Once-weekly dose
• Measurable hemoglobin response 100–130 g/L
• Adjunct to PAD programs

Disadvantages:
• Must maintain oral iron and weekly monitoring
• Cost - $1100 - 2200 per pt
• Safety / efficacy not been established in pts with hx of seizure disorder or hematologic disease

**PREOPERATIVE AUTOLOGOUS DONATION (PAD)**

• 2-3 units of blood collected before surgery

Benefits:
— ↓ allogeneic transfusion rate
— No risk of viral transmission

Risks:
reoperation for bleeding
Solid circles = clopidogrel-pretreated pts no reoperation for bleeding

APROTININ IN CABG PATIENTS ON CLOPIDOGREL (PLAVIX)

<table>
<thead>
<tr>
<th>Transfused Patients (%)</th>
<th>75</th>
<th>50</th>
<th>25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>79</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Aprotinin</td>
<td>53</td>
<td>50</td>
<td>25</td>
</tr>
</tbody>
</table>

\[ p = 0.02 \]


**SURGERY FOR THE PATIENT RECEIVING ANTI-PLATELET DRUGS: BLOOD MANAGEMENT STRATEGIES - 1**

- Stop drug administration
- Delay operation, if safe:
  - Aspirin & Plavix: 3-5 days
  - Integrilin & Aggrastat: 2-4 hours
  - ReoPro: 12-24 hours
- However, do not delay emergency CABG when it is otherwise indicated
- Aprotinin

**SURGERY FOR THE PATIENT RECEIVING ANTI-PLATELET DRUGS: BLOOD MANAGEMENT STRATEGIES - 2**

- Use mammary artery if initial bleeding not too excessive
- Use full loading and maintenance heparin doses for CPB
- Maintain standard ACT’s for CPB
- If excessive bleeding is present, transfuse platelets after protamine to reverse effect of drug

**PERIOPERATIVE PHLEBOTOMY**
Cheng CHD. Best practice in blood transfusion management in cardiac surgery

ml/day

<table>
<thead>
<tr>
<th>Range</th>
<th>Study</th>
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<tbody>
<tr>
<td>61-70</td>
<td>Corwin et al. 1995</td>
</tr>
<tr>
<td>41</td>
<td>von Ahsen et al. 1999</td>
</tr>
<tr>
<td>41.1 (39.7)</td>
<td>Vincent et al. 2002</td>
</tr>
<tr>
<td>If arterial lines</td>
<td>73.9 vs 33.5 ml/d Smoller et al. 1986</td>
</tr>
<tr>
<td>44% more drawn</td>
<td>Low et al. 1995</td>
</tr>
</tbody>
</table>

PERIOP BLOOD MANAGEMENT MODALITIES

Preoperative
- ↑ RBC (erythropoietin, Fe, folate)
- Autologous donation (PAD)
- Anti-PLT agents

Intraoperative
- Pharmacology: Antifibrinolytics
- Anesthesia & Surgical techniques
- Acute Normovolemic Hemodilution
- ↓ transfusion triggers
- Shed blood salvage
- Oxygen carriers

Postoperative
- ↓ transfusion triggers
- ↑ RBC
- Shed blood salvage


TREATMENTS TO AVOID INTRAOP ANEMIA

<table>
<thead>
<tr>
<th>Therapeutic Control of Hemostasis</th>
<th>Therapeutic O₂ Control of Hemostasis</th>
<th>Therapeutic O₂ Delivery</th>
<th>Therapeutic Acceleration of Hematopoiesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimize excess bleeding</td>
<td>Deliver O₂ to tissues</td>
<td>To replenish RBCs</td>
<td></td>
</tr>
<tr>
<td>Trasylol®</td>
<td>Oxygen Therapeutics</td>
<td>Procrit®</td>
<td>Epogen®</td>
</tr>
<tr>
<td>Amicar®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyklokapron®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDAVP®</td>
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PROPHYLACTIC ANTI-FIBRINOLYTICS IN CARDIAC SURGERY: META-ANALYSIS

Outcomes: Chest tube blood loss, transfusion, re-exploration, perioperative mortality

Efficacy: Aprotinin = Tranexamic Acid • DDAVP

Cost: $600-$980 $50-$200


APROTININ DOSE RESPONSE


Published by edigraphic.com

COMPARISON OF OUTCOMES IN THE MATCHED GROUP

Variables | Number | Proportion | Number | Proportion | (p value)
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Received at least 1 RBC unit</td>
<td>354</td>
<td>0.79</td>
<td>342</td>
<td>0.76</td>
<td>0.3</td>
</tr>
<tr>
<td>Received at least 5 RBC units</td>
<td>157</td>
<td>0.35</td>
<td>135</td>
<td>0.30</td>
<td>0.1</td>
</tr>
<tr>
<td>Received at least 10 RBC units</td>
<td>60</td>
<td>0.13</td>
<td>46</td>
<td>0.10</td>
<td>0.2</td>
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<tr>
<td>Received at least 5 PLT units</td>
<td>252</td>
<td>0.56</td>
<td>223</td>
<td>0.50</td>
<td>0.06</td>
</tr>
<tr>
<td>Received at least 1 FFP unit</td>
<td>296</td>
<td>0.66</td>
<td>275</td>
<td>0.61</td>
<td>0.1</td>
</tr>
<tr>
<td>Surgical reexploration</td>
<td>59</td>
<td>0.13</td>
<td>51</td>
<td>0.11</td>
<td>0.4</td>
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<tr>
<td>Myocardial infarction</td>
<td>12</td>
<td>0.03</td>
<td>10</td>
<td>0.02</td>
<td>0.7</td>
</tr>
<tr>
<td>Stroke</td>
<td>15</td>
<td>0.03</td>
<td>13</td>
<td>0.03</td>
<td>0.7</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>107</td>
<td>0.24</td>
<td>75</td>
<td>0.17</td>
<td>0.01</td>
</tr>
<tr>
<td>Renal failure</td>
<td>25</td>
<td>0.056</td>
<td>14</td>
<td>0.031</td>
<td>0.08</td>
</tr>
<tr>
<td>Serious infection</td>
<td>21</td>
<td>0.05</td>
<td>21</td>
<td>0.05</td>
<td>1.0</td>
</tr>
<tr>
<td>Death</td>
<td>30</td>
<td>0.07</td>
<td>33</td>
<td>0.07</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Karkouti K et al. Transfusion 2006


Cheng CHD. *Best practice in blood transfusion management in cardiac surgery*

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**FVIIa MECHANISM OF ACTION: BOOSTS THROMBIN GENERATION ON ACTIVATED PLATELETS**

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**GUIDE LINE FOR CONSIDERATION OF RFVIIA USE AS RESCUE THERAPY IN CV SURGERY**

- Excessive blood loss
  - > 2,000 ml blood loss OR transfusion of ≥ 5 units of RBC
- Ongoing blood loss
  - > 200 cc/h OR inability to close sternum
- Eliminate surgical bleeding
  - further exploration or re-exploration
- Normalize/optimise coagulation
  - Full dose of antifibrinolytics
  - Transfused at least: 5 U platelets and 4 U FFP
  - Hemoglobin concentration at least 80 g/L
  - INR/PTT/Fibrinogen corrected to at least 50% normal

Karkouti et al, TGH-UHN 2005

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**rFVIIa POTENTIAL COMPLICATIONS**

- Myocardial infarction
- DVT
- Pulmonary embolism
- Anastomotic/vascular occlusion

Brown JL. Anaesthesia 2003;58:1245.
ANESTHESIA TECHNIQUES: CONTROLLED HYPOTENSION; NORMOTHERMIA

COAGULATION MONITORING

- Thromboelastograph (TEG) whole blood test of viscoelastic blood clot formation
- Ultegra platelet response to a thrombin receptor agonist peptide (TRAP)
- Clot Signature Analyzer (CSA) measure platelet reactivity
- Plateletworks platelet count ratio to assess platelet reactivity

ACUTE NORMOVOLEMIC HEMODILUTION (ANH)

PERIOPERATIVE BLOOD LOSS: COLLOID VS COLLOID

ACUTE NORMOVOLEMIC HEMODILUTION

Blood loss scale

HES 0.4

Gel

HES >0.4

CRIC
Canadian Research Initiative on Colloids
Cheng CHD. Best practice in blood transfusion management in cardiac surgery

PATIENTS TRANSFUSED: HES 0.4 VS (HES 0.5 OR HES 0.7)

SURGICAL TECHNIQUES: OPCAB SURGERY, MINIMALLY INVASIVE SURGERY

SURGICAL TECHNIQUE: MINIMALLY INVASIVE SURGERY
SURGICAL TECHNIQUE:
ENDOSCOPIC VEIN HARVESTING WOUND DRAINAGE, NECROSIS, INFECTION, AND LEG EDEMA

SURGICAL EQUIPMENT:
HARMONIC SCALPEL

PERFUSION TECHNIQUES

- Prime reduction
  - Smaller circuits
  - Mini circuits
  - Retrograde autologous prime
  - Micoplegia systems

- Hemoconcentration
  - Cell Salvage
  - Ultra filtration

Cross-Linked Hb

Red blood cells, 7 μ

0.2μ Oxygen emulsion particles (Perfluorocarbon)
OXYGEN THERAPEUTICS

<table>
<thead>
<tr>
<th>Product</th>
<th>Source</th>
<th>Hb Conc &amp; Cross-link</th>
<th>T 1/2 (hr)</th>
<th>Trial Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb raffimer / Hemolink™</td>
<td>Human RBCs</td>
<td>100 g/L raffinose cross-linked polymerized</td>
<td>14-20</td>
<td>II Orthopedic</td>
</tr>
<tr>
<td>HBOC-201/ Hemopure®</td>
<td>Bovine RBCs</td>
<td>130 g/L glutaraldehyde polymerized</td>
<td>9-24</td>
<td>II Cardiac/Vascular II Orthopedic</td>
</tr>
<tr>
<td>Poly SFH - IV/ PolyHeme™</td>
<td>Human RBCs</td>
<td>100 g/L glutaraldehyde polymerized</td>
<td>24</td>
<td>II Trauma III Vascular/AAA</td>
</tr>
<tr>
<td>DCLHb / HemAssist™</td>
<td>Human RBCs</td>
<td>100 g/L diaspirin cross-linked</td>
<td>2-11</td>
<td>III Cardiac III Trauma</td>
</tr>
<tr>
<td>AF0144®/ Oxygent™</td>
<td>Human RBCs</td>
<td>100 g/L glutaraldehyde polymerized</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


STATUS OF OXYGEN THERAPEUTICS

<table>
<thead>
<tr>
<th>Product name</th>
<th>Type of product</th>
<th>Areas of investigation</th>
<th>Stage of development</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gelenpol</td>
<td>Polymerized human Hb</td>
<td>Approved in Russia for blood loss resuscitation</td>
<td>N/A</td>
<td>Institute of Macromolecular Compounds, St Petersburg Russia</td>
</tr>
<tr>
<td>Hemospan™</td>
<td>PEG-Hb (human)</td>
<td>Temporary substitute for bloodTx during Sx, injuries with loss of blood</td>
<td>Phase I completed July 2002</td>
<td>Sangart, San Diego CA, USA</td>
</tr>
<tr>
<td>Hemozyme®</td>
<td>Polynitrolaxated human</td>
<td>Surgery, hemorrhagic shock</td>
<td>Preclinical</td>
<td>Synzyme Technologies, Irvine CA, USA</td>
</tr>
</tbody>
</table>

POTENTIAL CLINICAL APPLICATIONS

- **Elective Surgery**
  - Plasma expansion, IAD, cardioplegia
- **Trauma and Emergency Resuscitation**
  - Transfusion immediately available
  - Bank blood spared until bleeding controlled
  - Hypotension associated with septic shock
- **Replacement in patients with multiple antibodies, sickle cell anemia, JW**
- **Extracorporeal organ perfusion**
- **Radiosensitive tumors**

PERIOP BLOOD MANAGEMENT MODALITIES

- **Preoperative**
  - ↑RBC (erythropoietin, Fe, folate)
  - Autologous donation (PAD)
  - Anti-PLT agents

- **Intraoperative**
  - Pharmacology: Antifibrinolytics
  - Anesthesia & Surgical techniques
  - Acute Normovolemic Hemodilution
  - ↓Transfusion triggers
  - Shed blood salvage
  - Oxygen carriers

- **Postoperative**
  - ↓transfusion triggers
  - ↑RBC
  - Shed blood salvage


TOLERANCE OF ANEMIA: VO₂ VS DO₂

<table>
<thead>
<tr>
<th>Haemoglobin (g/l)</th>
<th>Risk</th>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 100</td>
<td>Very low</td>
<td>Avoid</td>
</tr>
<tr>
<td>80-100</td>
<td>Low</td>
<td>Avoid; May occasionally require transfusion based on clinical evaluation†</td>
</tr>
<tr>
<td>60-80</td>
<td>Moderate</td>
<td>Try to avoid; Decrease oxygen consumption; Base transfusion decision on clinical evaluation†</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>High</td>
<td>Usually requires transfusion</td>
</tr>
</tbody>
</table>

†Clinical evaluation: volume, respiratory, cardiac, and cerebrovascular status, duration of anaemia, symptoms, ongoing blood loss, risk of rebleed, extent of surgery

Perioperative Transfusion Medicine, Chapter 3
A SUCCESSFUL BLOODLESS MEDICINE AND SURGERY PROGRAM

- Commitment $: Hospital
- Leadership, Knowledge Translation: A coordinated multidisciplinary approach to avoid allogeneic transfusion in patients for both elective and emergent situations
- More than just NOT administering blood to patients
- Risks of not transfusing must be weighed against the Morbidity, Mortality and Cost

“Blood transfusion is like a marriage: It should not be entered into lightly, unadvisedly, or wantonly, or more often than is absolutely necessary.”