Anaesthetic/perioperative management of mothers who decline blood products
"I’d like you to meet Dr. Bloodgood from U of T. He’s an expert on hemoglobin."
Outline

- **Physiology**
  - Haemoglobin and the carriage of oxygen
  - Haemostasis
- **Blood conservation techniques**
  - Antenatal preparation
  - Acute normovolemic haemodilution
  - Intraoperative cell salvage
  - Pharmacological – Antifibrinolytics
- **Recombinant blood products**
- **Oxygen carrying blood substitutes**
## What is Acceptable to Jehovah’s Witnesses

<table>
<thead>
<tr>
<th>Unacceptable</th>
<th>Acceptable</th>
<th>May be acceptable ('matters of conscience')</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole blood</td>
<td>Cardiopulmonary bypass</td>
<td>Platelets</td>
</tr>
<tr>
<td>Packed red cells</td>
<td>Renal dialysis</td>
<td>Clotting factors</td>
</tr>
<tr>
<td>Plasma</td>
<td>Acute hypervolaemic haemodilution</td>
<td>Albumin</td>
</tr>
<tr>
<td>Autologous pre-donation</td>
<td>Recombinant erythropoietin</td>
<td>Immunoglobulins</td>
</tr>
<tr>
<td></td>
<td>Recombinant factor VIIa</td>
<td>Epidural blood patch</td>
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<tr>
<td></td>
<td></td>
<td>Acute normovolemic haemodilution</td>
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<td></td>
<td></td>
<td>IOCSalvage</td>
</tr>
</tbody>
</table>
Haemoglobin

- Haem – complex of porphyrin ring and iron in Fe$^{2+}$ state
- Globin – polypeptide which comprises 4 subunits (Adults 2α and 2β subunits)
- Oxygen binds reversibly with ferrous iron to form oxyhaemoglobin
Oxygen Carriage

- Relationship between O$_2$ and HB – sigmoid shaped
- Normal PO$_2$ HB is 95-98% saturated (plateau)
- Steep part of curve – fall in PaO$_2$ much greater affect on O$_2$ content and saturation
- Position of curve - right (favours unloading) or left (increases affinity)
Oxygen delivery

- Global O2 delivery (DO2) amount delivered to whole body from lungs
- Product of arterial O2 content and blood flow (CO)
  \[ \text{DO2} = \text{CO} \times \text{CaO2} \ (800 - 1,200 \text{mls/minute}) \]
- In health 98% of O2 bound to HB and 2% dissolved
- Reduction in HB reduces the DO2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal</th>
<th>Anaemic</th>
<th>Anaemic + oxygen therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspired oxygen (%)</td>
<td>21</td>
<td>21</td>
<td>100</td>
</tr>
<tr>
<td>( P_{a.o_2} ) (kPa)</td>
<td>12</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>( S_{a.o_2} ) (%)</td>
<td>98</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>Hb concentration (g litre(^{-1}))</td>
<td>150</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Dissolved oxygen (ml litre(^{-1}))</td>
<td>3</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Hb-bound oxygen (ml litre(^{-1}))</td>
<td>197</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>Total ( \text{CaO}_2 ) (ml litre(^{-1}))</td>
<td>200</td>
<td>101</td>
<td>117</td>
</tr>
<tr>
<td>( D_{O_2} ) (ml min(^{-1})), assuming a cardiac output of 5 litre min(^{-1}))</td>
<td>1000</td>
<td>505</td>
<td>585</td>
</tr>
</tbody>
</table>
Oxygen Consumption – VO2

- VO2 - aerobic metabolism, cell integrity and homeostasis (200-300 mls/min)
- Normal conditions only use 25% of DO2
- Anaemia - Critical DO2 critical HB concentration VO2 decreases (hypoxia)
  - Health 50g/L
  - Critical illness 70-90g/L
Haemostasis

- Interaction between sub endothelium coagulation proteins and platelets
- Thrombin generated
  - Initiation
  - Amplification
  - Propagation
- Loss and consumption of coagulation proteins
- Exacerbated by hypothermia and acidosis
Antenatal Preparation

- Adequate advance multidisciplinary discussion and planning
- Consider need for radiological and intensive care expertise and facilities
- Optimise haematological status
  - Iron, B12 and folate supplementation
- Recombinant erythropoietin (rEPO)
  - Erythropoiesis in 3 days
  - Equivalent of 1 unit of RCC in 5 days
General Measures

### Anaesthetic

- Anaesthesia type

### Surgical

- Thorough planning
- Diathermy type
  - Argon beam
  - Spray coagulation
- Biological haemostats

- Attention to thermoregulation
- Avoidance of venous congestion/high intrathoracic pressures
- Maintain normocapnia
- Invasive monitoring
Acute Normovolemic Haemodilution

- Practice of immediate preoperative collection of whole blood from patient with simultaneous volume replacement with crystalloid/colloid
- Reduces the number of red cells lost when bleeding occurs
- Autologous fresh whole blood available once haemostasis secured
- Volume of blood to be removed calculated according to blood volume and haematocrit (2-3 units)
Acute Normovolemic Haemodilution

- Each unit of autologous whole blood
  - 1 unit RCC
  - 1 unit plasma
  - 55-225 $\times 10^9$ platelets
- Well tolerated in healthy, term parturients where major haemorrhage predicted*
- Elective setting

*Grange CS et al; Am J Obstet Gynecol 1998; 178: 156-60
Intraoperative Cell Salvage

- Technique of recycling operative blood loss
- Principals of:
  - Collection
  - Anticoagulation
  - Washing/separation
  - Reinfusion
- RCC with haematocrit of 0.5-0.8
- Infused up to 6 hours later
Evidence in Obstetrics

<table>
<thead>
<tr>
<th>Publication</th>
<th>Publication type</th>
<th>Number of subjects</th>
<th>Clinical setting</th>
<th>Clinical outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grimes, 1988</td>
<td>Case report</td>
<td>2</td>
<td>Abdominal pregnancy, PPH</td>
<td>Uneventful</td>
</tr>
<tr>
<td>Jackson, 1993</td>
<td>Retrospective series</td>
<td>64</td>
<td>CS</td>
<td>Uneventful</td>
</tr>
<tr>
<td>Rainaldi, 1998</td>
<td>Prospective, controlled</td>
<td>68 (34 in salvage group)</td>
<td>CS</td>
<td>Salvage group: reduced length of stay + allogeneic blood transfusion, higher postoperative Hb</td>
</tr>
<tr>
<td>Rebarber, 1998</td>
<td>Historical cohort</td>
<td>139</td>
<td>CS</td>
<td>Heparin toxicity (n = 1)</td>
</tr>
<tr>
<td>Potter, 1999</td>
<td>Case report</td>
<td>1</td>
<td>Placenta praevia/CS</td>
<td>Pyrexia/endometritis</td>
</tr>
<tr>
<td>Catling, 2002</td>
<td>Case reports</td>
<td>4</td>
<td>Extraverte placentia/CS</td>
<td>ARDS/Pneumonia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PPH</td>
<td>Pyrexia/respiratory tract infection</td>
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<td>Jehovah’s witness/CS</td>
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<td>Uneventful</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Anaemia</td>
</tr>
<tr>
<td>Waters, 2003</td>
<td>Case report</td>
<td>1</td>
<td>Beta thalassaemia/CS</td>
<td>Uneventful</td>
</tr>
<tr>
<td>De Souza, 2002</td>
<td>Case report</td>
<td>1</td>
<td>Placenta praevia/CS</td>
<td>Uneventful</td>
</tr>
<tr>
<td>Qei, 2000</td>
<td>Case report</td>
<td>1</td>
<td>PET + HELLP/CS</td>
<td>Cardiac arrest/death</td>
</tr>
</tbody>
</table>

CS = caesarean section; PPH = postpartum haemorrhage; HELLP = haemolysis, elevated liver enzymes and low platelets; ARDS = acute respiratory distress syndrome; Hb = haemoglobin.

- Theoretical risk of precipitating AFE syndrome
- Experience in obstetrical setting approx 400 cases
- No proven case of any serious adverse maternal outcome
- Use does not appear to increase the rate of AFE, infection or DIC
Intraoperative Cell Salvage

- Salvaged blood at least equal to banked blood in terms of red cell survival, morphology, pH and levels of 2-3DPG*
- Plasma, platelets, activated clotting factors and complement are removed
- Use limited by need for adequately trained personnel
- Use now endorsed by several bodies worldwide with following precautions
  - Separate suction device for after delivery of placenta and fetus
  - Use of a leucocyte depletion filter mandatory

*Allam J et al; IJOA 2008; 17: 37-45
Antifibrinolytic therapy

- Synthetic lysine analogue
  Tranexamic acid
- Inhibits plasminogen activation on surface of thrombin and direct plasmin inhibitor
- No evidence of increase in thrombo-embolic complications*
- Wide variation in dosage regimes; 1-2gms before surgery

DOI: 10.1002/14651858.CD001886.pub2.
Recombinant blood products

- Many available including factors VIII, IX and VIIa
- rFVIIa – use described in obstetrics 50 case reports
- Dose 90µg/Kg IV over 2-5mins, repeated at 2 hourly intervals
- Requires non-acidotic conditions, normothermia and appropriate levels of platelets/clotting factors/ fibrinogen
- Not a licensed indication
- Concerns: thrombo-embolic events and costly
Oxygen Carrying blood substitutes

- 2 categories
  - Perfluorocarbons
  - HB based O2 carriers

- PFC’s
  - Synthetic, inert compounds
  - Linear O2-dissociation curve
  - Most O2 released before arrival at microvasculature
  - Use suspended, no clinical trials ongoing

Box 1
Characteristics of an ideal blood substitute

- No risk of disease transmission
- No immunosuppressive effects
- No interaction with the immune system
- Maintenance of arterial blood pressure and pH
- Availability of abundant supply
- Universal compatibility (no need to type and crossmatch)
- Rapid metabolism and elimination in vivo
- Prolonged shelf life and stability at a range of temperatures
- In vivo half-life similar to the red blood cell
- Similar viscosity to blood
- Availability at a reasonable cost
- Ease of administering
- Ability to access all areas of the human body (including ischemic tissue)
- No interference with capillary circulation
- Effectiveness at room air or ambient conditions
Haemoglobin based Oxygen Carriers

- Oxygen carriers that use purified human, animal or recombinant HB in a cell free preparation
- Under development for decades – side effect profile
- Currently 8 second generation products, 4 in clinical trials
- Hemopure and PolyHeme clinical arena
- Hemopure* approved for use in adult surgical patients in SA

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Hemopure (HBOC-201)</th>
<th>RBCs</th>
</tr>
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<tbody>
<tr>
<td>Storage</td>
<td>Room temperature (20–30°C)</td>
<td>Refrigerated</td>
</tr>
<tr>
<td>Shelf life</td>
<td>36 months</td>
<td>42 days</td>
</tr>
<tr>
<td>Preparations</td>
<td>Ready to use</td>
<td>Testing, typing, and cross-matching</td>
</tr>
<tr>
<td>Compatibility</td>
<td>Universal</td>
<td>Type specific</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>Immediate oxygen delivery</td>
<td>Dependant on length of storage</td>
</tr>
<tr>
<td>Purity</td>
<td>Processed to remove infectious agents</td>
<td>Tested and screened for infectious agents</td>
</tr>
<tr>
<td>Raw material</td>
<td>Bovine Hb abundant, controlled source</td>
<td>Limited availability, not controlled</td>
</tr>
</tbody>
</table>
Summary

- Blood conservation techniques becoming more applicable
- Most require advance planning – limitations in this particular setting
- Increasing use of IOCS – several bodies endorsing its use in obstetrical setting
- Future possible role for HBOC’s
- Effective multidisciplinary communication