A place for fresh blood against blood bank policies?

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I provide services to the pharmaceutical and biotechnology industry, including the manufacturers of therapies described in this presentation, who are also major sponsors of this Symposium.
Historical Background

• Over last 40 years, transfusion therapy evolved from use of predominately whole blood to now largely component therapy.

• Whole blood: still used in many developing countries and in military situations, however

• Component therapy predominates primarily due to resource utilization and safety.

• Change occurred without strong evidence of clinical outcomes between whole blood and component therapy in multiple trauma patients.
National blood services funded by government

Provide transfusion needs – through components

Embedded in the manufacturing/inventory paradigm

- “Blood factories”
- GMP, QC etc
- Detached from clinical environment
Developing and developed countries

Age and gender distribution of transfused patients

<table>
<thead>
<tr>
<th></th>
<th>Benin</th>
<th>Denmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>9099922</td>
<td>5580413</td>
</tr>
<tr>
<td>GDP/cap (PPP) $</td>
<td>1481</td>
<td>37151</td>
</tr>
<tr>
<td>Transfusions/10^3 population</td>
<td>6.1</td>
<td>9.6</td>
</tr>
</tbody>
</table>
The red cell storage lesion

ATP depletion

Lipid peroxydation

Protein oxidation

Erythrocyte

2,3-DPG depletion

Increased osmotic fragility and haemolysis

Membrane vesiculation and decreased deformability

Increased O2 Hb affinity

Increased K+, iron, RBC micro-particles, oxidized proteins and lipids, lactate, cytokines

Decreased pH

Red blood cells

Storage Medium
RBC squeezing through a capillary bed
Microhemodynamic aberrations created by transfusion of stored blood
Red cell deformability and elasticity
Mortality Decrease with Higher FFP:PRBC Ratios

- **≤1:8 Low**: 90% (56/62)
- **>1:8 and ≤1:3 Medium**: 49% (47/95)
- **>1:3 and ≤1:2 High**: 25% (28/111)
- **>1:2 Highest**: 26% (30/115)

*p<0.01 compared to >1:2*
Survival of patients receiving high ratios versus patients receiving low ratios of fresh frozen plasma (FFP) and platelets to PRBCs
Transfusion in Trauma
Patient mortality by transfusion type

<table>
<thead>
<tr>
<th>Variable (Reference Group)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>.32</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>.09</td>
</tr>
<tr>
<td>Injury Severity Score</td>
<td>.004</td>
</tr>
<tr>
<td>EMS time</td>
<td>.035</td>
</tr>
<tr>
<td>Transfer (no)</td>
<td>.58</td>
</tr>
<tr>
<td>Blood product (whole)</td>
<td>.01</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval;
aLogistic regression analysis was used.

Independent Predictors of Mortality in Adult Patients With Trauma
• Thawed FFP exerts protective effect on endothelium
• Independent of coagulation factor content
• Decreases over storage
• Argues against storage of thawed FFP
EXTENDED LIFE PLASMA:
A FRAMEWORK
FOR PREPARATION,
STORAGE AND USE
Predicted risk of death against maximum age of red blood cells

Lowess smoother

Estimated Probability of Death

Maximum age of red blood

bandwidth = 0.8
Transfusion in Man’s Best Friend
Old vs less old blood

A
Survival

Proportion Surviving

Time (h) before and after S. Aureus challenge

7 day old transfused blood
n=12

42 day old transfused blood
n=12

P=0.0005

B
Lung Injury

A-A Gradient (mmHg)

Time (h) before and after S. Aureus challenge

42 day old transfused blood

7 day old transfused blood

p = 0.01

p = 0.005

C
Shock Score

Better

Worse

Time (h) before and after S. Aureus challenge

7 day old transfused blood

42 day old transfused blood

P=0.01

D
Pulmonary Pressure during Transfusion

Mean Pulmonary Artery Pressure (mmHg)

Time (h) after S. Aureus challenge

4h

7h

10h

13h

p = 0.005

Age of Stored Transfused Blood days (d)

Post

42d

7d

Pre
The age of red blood cells is associated with bacterial infections in critically ill trauma patients.
Fresh blood in battlefield trauma

Log-Rank Test, (p=0.002)
Reiteration – The extinction of fresh whole blood transfusion

- Bigger inventory – One donor - Many patients

- Blood screening
  - Donor recruitment – millions of $€£
  - Donor selection – a million questions
  - Testing – a million tests

- Need for recovered plasma
Whole Blood in the Management of Hypovolemia Due to Obstetric Hemorrhage

Women receiving transfusions for obstetric hemorrhage N=1,540

Only whole blood given n=659
- 1,443 units transfused
  - Mean of 2.2 units per woman transfused

Only packed red blood cells given n=593
- 1,375 units transfused
  - Mean of 2.3 units per woman transfused

Combination of blood products given n=288
- 1,591 units transfused
  - Mean of 5.5 units per woman transfused

The University of Western Australia

Transfusion of fresh whole blood (FWB) versus platelet concentrates (PC) after cardiac operations

- To evaluate FWB vs PC after cardiac operations
- Platelet aggregation on extracellular matrix model
- 24 patients one unit FWB (12 patients) or 10 platelet units (12 patients) after cardiopulmonary bypass.
- One unit FWB restored platelet aggregation on extracellular matrix to preoperative status (3.0 +/- 1.0), eight PC needed for the same result (3.2 +/- 0.8).
- One unit FWB increased platelet count to level achieved by six PC.
- The effect of one unit of FWB on platelet aggregation after cardiopulmonary bypass is equal or superior, to the effect of 8 to 10 PC.
Much of transfusion practice lacks an evidence base

In particular, the assumption that transfusion and resuscitation following massive blood loss requires individual stored components needs to be challenged

Component therapy in the developed economies was an inevitable outcome of recovered plasma manufacture
More reflections

- Fresh whole blood has been rendered extinct but is therapeutically superior.

- We suggest that the emerging Patient Blood Management movement represents the future of transfusion.

- This can be achieved by closely integrating the transfusion service within the clinical environment.
A pragmatic approach to embedding patient blood management in a tertiary hospital

**1st Pillar**
Optimize erythropoiesis
- Detect anemia
- Identify underlying disorder(s) causing anemia
- Manage disorder(s)
- Refer for further evaluation if necessary
- Treat suboptimal iron stores/iron deficiency/anemia of chronic disease/iron-restricted erythropoiesis
- Treat other hematologic deficiencies
- Note: Anemia is a contraindication for elective surgery

**2nd Pillar**
Minimize blood loss & bleeding
- Identify and manage bleeding risk
- Minimizing iatrogenic blood loss
- Procedure planning and rehearsal
- Preoperative autologous blood donation (in selected cases or when patient choice)
- Other

**3rd Pillar**
Harness & optimize physiological reserve of anemia
- Assess/optimize patient's physiological reserve and risk factors
- Compare estimated blood loss with patient-specific tolerable blood loss
- Formulate patient-specific management plan using appropriate blood conservation modalities to minimize blood loss, optimize red cell mass, and manage anemia
- Restrictive transfusion thresholds

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