Blood Transfusions in the Wild!

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@bloodman
Disclosures

• None
Case
Austere Transfusion

- Military
- Humanitarian missions
- Remote islands
- Cruise ships
- Scientific expeditions
- Remote expeditions
- Space travel
- Texas Rangers
Talk

• Whole Blood
• Why Whole Blood Transfusions?
• Blood Banking 101
• Review of data
• Practical approach
• Adjuncts to transfusions
Whole Blood

• Stuff straight out of the body
  – Red cells
  – Platelet
  – Plasma
  – White cells, etc…

https://www.trauma-news.com/2020/06/setting-up-a-whole-blood-program-5-questions-you-need-to-answer/
Whole Blood

- Blood types discovered 1901
- Blood storage devised 1914
- First used WWI Cambrai battle
- Increased use WWII
  - Red cross 13 millions units of blood
The 50 -60’s

• Korean war:
  – 400,000 units transfused- no hemolysis

• Vietnam
  – 38,000 units/month
  – 1 million during war

• Then…
Component Therapy

• Whole blood processed to:
  – Packed red cell
  – Platelet units
  – Fresh Frozen Plasma

• More efficient use of blood for most patients
Example

• One donor =
  – Packed Red Cells (42 days)
    • Surgical bleed
  – Plasma (frozen 12 months)
    • Reversal of warfarin
  – Platelets (5 days)
    • Child with leukemia

• Whole blood ~ 5 days
Whole Blood Revisited

• War experience
  – Increasing data transfusion of more red cells with insufficient plasma harmful
  – Best ratio 1:1:(1)

• Civilian experience
  – Same seen with trauma centers
Effect of FFP:RBC Ratio on Overall Mortality

- 0:22 - 1:4: 65% (n=31)
- 1:3.9 - 1:2.1: 34% (n=56)
- 1:2 - 1:0.59: 20% (n=165)

### Table 3  Mortality differences and respiratory outcome based on the ratio of blood products

<table>
<thead>
<tr>
<th>Product</th>
<th>Transfusion ratio in first 6 h</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ratio</strong></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Measure</td>
<td>&lt;1:4</td>
<td>1:4-1:1</td>
</tr>
<tr>
<td>6-h mortality %</td>
<td>37.3*</td>
<td>15.2*</td>
</tr>
<tr>
<td>FFP:PRBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital mortality %</td>
<td>54.9*</td>
<td>41.1*</td>
</tr>
<tr>
<td>Ventilator free days†</td>
<td>9</td>
<td>7.9</td>
</tr>
<tr>
<td>6 h mortality %</td>
<td>22.8</td>
<td>19.0</td>
</tr>
<tr>
<td>PLT:PRBC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital mortality %</td>
<td>43.7</td>
<td>46.8</td>
</tr>
<tr>
<td>Ventilator-free days‡</td>
<td>6*</td>
<td>9.9†</td>
</tr>
</tbody>
</table>

*Significant difference from other 2 ratios.
†$P =$ nonsignificant (.79).
‡Massive transfusion patients who survived >30 days (n = 277), Fisher exact test.

Why?

- Less coagulopathy
- Less inflammation
- Better resources
  - Bias toward place who got blood to patient faster
Civilian Trials

• PROMM tin
  – Ratios < 1:2 (less plasma) 3-4x rate of 1:1

• PROPPR
  – 1:1:1 vs 1:1:2
    – JAMA 313:471, 2015
Survival 1:1 vs 1:2

Less exsanguination at 24 hours with 1:1
NO increase in complications with 1:1

The Return of Whole Blood
Military

- Both stored and warm (fresh) whole blood
- Suggestions of better outcomes
  - Patient transfused faster
  - Balanced resuscitation
  - “Young blood”
Civilian Use

• Increasing use of whole blood
  – Via blood bank center
• More efficient massive transfusions
• Our record – 38 whole blood units
Component Therapy vs Whole Blood

1U PRBC + 6U PLT + 1U FFP + 10 pk Cryo

- Hct 29%
- PLT 87K
- Coag activity 65%
- 750 mg fibrinogen

Ok Where to you get whole blood in the middle of nowhere?
Blood Banking 101

- Not all blood compatible
- Need to match blood types
- Need to match Rh
- Need to avoid infections
- Need to avoid complications
Cross and Typing

• Goal is not to give incompatible blood!
• Elaborate system of checks and balances
  – Very risk adverse system
# ABO Blood Group

<table>
<thead>
<tr>
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<th>Group A</th>
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<td><strong>Red blood cell type</strong></td>
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- **Group A** has A antigens and antibodies against B.
- **Group B** has B antigens and antibodies against A.
- **Group AB** has both A and B antigens. No antibodies are present.
- **Group O** has neither A nor B antigens. It contains both anti-A and anti-B antibodies.

This table summarizes the blood group characteristics and their corresponding antibody presence in plasma.
Storage

- Whole blood 4° for 21 days
- PRBC for 42 days
- Expires if > 10 °
Transfusing

- Paper work checked by two people to verify unit and correct patient receiving it
- Patient with frequent vital signs
Infections

- Blood screened for a variety of viral diseases with both antigen and PCR testing
Current Screening

• Hep B
• Hep C
• HIV
• HTLV I and II
• Syphilis
• West Nile Virus
• Zika virus
• Babesia*
• Trypanosoma cruzi*
When to Consider Fresh Whole Blood

• Shock due to hemorrhage
  – Trauma
  – Gastrointestinal
  – Gynecological
  – Genitourinary

• Far away from Blood Bank
Hypotensive Resuscitation

• Concern is too much fluids “pops” clot off vessels
  – Complications with “clear fluids”

• Resuscitate until pulse barely palpable

• Sacrifice perfusion to reduce bleeding
Military Experience

- Iraq/Afghanistan war
  - > 10,000 units whole blood
- “Walking Blood Bank”
- No worse outcomes with FWB
  - Some data better outcomes
- Only option in austere environments
Fresh Whole Blood

- Cold stored FWB
- Warm FWB collected before mission
  - Stored for up 24hrs at room temp
- Walking blood bank
  - Prescreened donors
Military: Infections

• Early program with no viral screening
  – Military prescreened
  – One case of transfusion transmitted hepatitis B

• Now rapid blood screening when feasible
Cruise Ships

• Classic middle of nowhere situation

• Royal Caribbean Cruise extensive experience
  – 2008-2016
  – Presented at 2016 THOR meetings
Cruise Ship

- Not practical to store blood
- High risk patients
  - Older
  - Use of NSAID/ASA/Anticoagulants
Royal Caribbean Cruises Ltd - Blood Transfusion Protocol for Shipboard Management of Catastrophic, Non-Compressible Hemorrhage

Patient presents with active, non-compressible bleeding:
- > than 4 hours will elapse till transfer to appropriate shoreside medical facility
- Hb < 10.0 grms/dl

Hemodynamically Stable

INITIATE:
- ICU level monitoring
- IV fluid to maintain MAP > 75 mmHg (Permissive Hypotension)
- 4 hrly CBC/FBC/INR / Ionized Calcium
- Alert Captain
- Consider Tranexamic Acid (TXA) (Note 2)
- Consider Vitamin K if on warfarin
- Complete Eldon card screening of patient
- If later than 17.00 hrs local time call for blood donors (see Note 1 below)
- Routine disembark to shoreside hospital at next port/avoid helicopter use

Develops Hemodynamic Instability

INITIATE:
- ICU level monitoring
- 2 x large bore IV’s with IV fluid to maintain MAP > 75 mmHg
- Alert Captain
- Call Med Ops Hotline
- 2 hrly CBC/FBC/INR/Lactate / Ionized Calcium
- Administer Tranexamic Acid (TXA) (see Note 2 below)
- Administer Vitamin K if on warfarin
- Complete Eldon card screening of patient
- Call for donors (see Note 3 below)
- Screen donors and immediately administer first unit of Group O negative fresh whole blood (FWB)
- RE-ASSESS AFTER 1st UNIT OF FWB

Hemodynamically Unstable

If still Bleeding and/or Hemodynamically Unstable

- Continue ICU level monitoring
- Administer further two units of Group O negative FWB as rapidly as patient condition can tolerate
- Evaluate urgent MEDEVAC options with Captain/MED OPS/Notify CareTeam
- Risk of helicopter transport acceptable - prefer disembark in port
- Send 4th unit with patient to run during MEDEVAC process

Routine Medevac
Avoid Helicopter

Urgent Medevac
Risk of Helicopter Acceptable

Medical disembark to hospital with:
- Endoscopy/general surgical capability
- ICU level care
- Availability of screened, cross matched blood
- Notify MedOps/CareTeam of receiving hospital

Note 1:
- Consideration should be given to ensuring that identified Group O negative or O positive donors can be contacted should they be required to report to medical center to donate blood, without the need for ship-wide public address announcements after 21.00 hrs local time.

Note 2:
- A loading dose of Tranexamic Acid (Cyklokapron) should be mixed 1 gram in 100 ccs of 0.9% normal saline and administered over 10 minutes. (no faster than 100mg/min)
- If a maintenance infusion is required a further 1.0 gram is diluted in 100 ccs of 0.9% normal saline and administered over 4 hours.
- Use of Tranexamic Acid in stable patient requires risk/benefit analysis, i.e. risk of continuing bleeding vs inducing thrombotic event.

Note 3:
- If serum ionized Calcium is < 4.2 mg/dl then consider administering IV Calcium Chloride 10mls of 10% solution over 30 minutes

Compatible Donor Request Hierarchy
1. Sexual partners
2. Male guests with blood donor cards
3. Male guests without blood donor cards
4. Female donors with blood donor cards
5. Medical team members
6. Crew

Note: blood donated by genetically related family members increases risk of Graft vs Host Disease. Female donors increase risk of Transfusion Related Acute Lung Injury (TRALI). Only take one unit from each donor, after ensuring that the donor is not already anemic.
Donor Hierarchy

1. Sexual partners
2. Male guests with donor card
3. Male guests without donor card
4. Female donors with cards
5. Medical team members
6. Crew
NOT Family Members!!!

- Genetic related donors run risk of transfusion related graft vs host disease
- TGVHD: aplasia, volumenous diarrhea, liver failure, skin sloughing off then death
Why Men?

• Transfusion Associated Acute Lung Injury
  – Rapid development of ARD like picture within 6-12 transfusion
  – Due to HLA antibodies
    • Acquired during pregnancy
  – Incidence was 1:1000
    • Leading cause of transfusion death
  – Dramatic reduction with male only plasma
Figure 1: TRALI Cases, FY2003 - FY2017
Ship Data 2008-16

- 73 patients transfused
- Mean hgb = 6.31 g/dl
- Units/patient 1-6
- 6 deaths, 4 lost to follow up
- No infections
- 2 allergic reactions
Bottom Line

• Experience shows fresh whole blood:
  – Can be done
  – Potentially lifesaving
  – Is safe
How to Do It!
“Walking Donor”

• Advantages
  – No storage requirements
  – Fresh whole blood
  – Immediately available

• Disadvantages
  – Typing
  – Infectious diseases
When to Do It

- Clinical judgment patient is in hemorrhagic shock
  - Thready pulse
  - Tachycardia
  - SBP < 90
Importance of Blood Typing

• Incompatible blood can be fatal!
• Military
  – Dog tag inaccurate 2-11%
• Cold war
  – Tattoo program Indiana and Utah
• Point of care typing
  – Eldon cards
Step 9: Place the stick with blood drop in the center of the first reagent circle. Take a new stick and quickly repeat step 7 and 8. Transfer a drop of blood to each of the remaining circles using a new stick for each circle.
https://www.biologycorner.com/anatomy/blood/blood_typing_lab.html
Typing

- Ideally give same blood type
- If recipient blood type uncertain give “O” blood
- Ideally Rh- women of should get Rh negative blood
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Type O Blood

• Universal donor
  – Truest for packed red cells
• Group O Plasma has anti-A and B
• Ideal is “low titer” O blood
• Cannot titer in the wild
• Is this an issue?
High Titer Study

- 39 volunteers A, B, AB
- Transfused high titer O plasma
- > 1:400 hemolysis
- > 1:1000 severe hemolysis
  - No renal failure
- ~ 5% titers > 1:1000
How it's Done

• Blood type donor and recipient
• Give same type blood or type O
• Donor marks bag – double checked by blood drawer
• Double check donor and recipient blood type
• Give IV or IO

Shock 41s1, p76, 2014
Field Blood Transfusion Kit (TMM-FBTK)

Product No. #01370
NSN: 6515-01-618-3730

Designed for field forward missions in the most remote and austere environments, the Field Blood Transfusion Kit contains essential items to collect and transfuse fresh whole blood in a compact package.

READ MORE

$109.95

This product cannot be shipped outside the United States (except APO/FPO addresses).

This product is for Military, Federal Government, or Physician purchases only. If you do not meet this requirement this item will be deleted from your cart. If you are a civilian physician a medical license is required. Please call to order 800-766-1365.

Purchase of this medical device requires that the user have supervision from a licensed medical practitioner. Devices requiring such supervision may be labeled “Caution” or “RX only”. Ensuring this supervision is the purchaser’s responsibility. By adding this item to the cart I verify that I accept these terms.
Donor

- Medial cubital vein
- Keep blood bag in motion
- Keep bag 20cm below arm
- Give 500 ml water or hydration solution
Recipient

• IV or IO access
• Infuse by gravity
• Don’t mix anything else with blood
Transfusion Reactions

- 1: 50 transfusions has a reaction
- 1:1000 can be severe
- Allergic: 1:300
- TRALI 1:5,000
- Unknown how many patients get evaluated for reactions
Reactions

- Febrile reactions
  - Acetaminophen
- Allergic
  - Antihistamines
## DONOR TESTING

**1950**
- ABO/Rh
- Syphilis

**1960**
- Hepatitis B viral antigen
- HIV-1 antibody
- Non-A, non-B Hepatitis (core ab)
- ALT
- HTLV-I antibody
- HCV viral protein antibody

**1970**
- HIV-1/2 antibody
- HIV-1 antigen
- HTLV-I/II

**1980**
- HCV PCR
- HIV PCR
- WNV

**1990**

**2000**

**2010**
Infections

• Can be impractical to test in the field
• Awkward questions
• Reality: bleeding to death vs treatable viral disease
**Field Emergency Donor Panel Questionnaire and Triage Tool**

- Give blood donor briefing to potential donor group
- Confirm blood group(s) required
- Exclude air crew, HGV drivers and key machinery operators

### Primary Triage (Question as a group)

<table>
<thead>
<tr>
<th>Serial</th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Do you want to give blood?</td>
<td></td>
<td></td>
<td>Disqualify if NO</td>
</tr>
<tr>
<td>2</td>
<td>Have you given blood before</td>
<td></td>
<td></td>
<td>If yes - Consider early selection</td>
</tr>
</tbody>
</table>

### Secondary Triage (Question individually)

<table>
<thead>
<tr>
<th>Serial</th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Are you unwell now? New Fever/ Diarrhea / Vomiting Chronic medical condition and not well</td>
<td></td>
<td></td>
<td>Disqualify if YES</td>
</tr>
<tr>
<td>4</td>
<td>Are you taking medication for blood pressure; stroke or heart, lung, kidney, cancer or blood conditions?</td>
<td></td>
<td></td>
<td>Disqualify if YES</td>
</tr>
<tr>
<td>5</td>
<td>Have you had a blood transfusion or blood products in the last year</td>
<td></td>
<td></td>
<td>Disqualify if YES Accept after 1 year</td>
</tr>
<tr>
<td>6</td>
<td>Are you living with HEP B, C / HIV / AIDS - OR living with anyone with these conditions</td>
<td></td>
<td></td>
<td>Disqualify if YES</td>
</tr>
<tr>
<td>7</td>
<td>Have you ever been refused as a donor or told not to donate blood (a past history of treated anemia may be acceptable)</td>
<td></td>
<td></td>
<td>Disqualify if YES</td>
</tr>
<tr>
<td>8</td>
<td>Male donors only. Have you ever had sex with another male?</td>
<td></td>
<td></td>
<td>Disqualify if YES</td>
</tr>
<tr>
<td>9</td>
<td>Have you ever taken illegal drugs with a needle (even steroids)</td>
<td></td>
<td></td>
<td>Disqualify if YES</td>
</tr>
<tr>
<td>10</td>
<td>Are you currently pregnant or breastfeeding?</td>
<td></td>
<td></td>
<td>Disqualify if YES</td>
</tr>
<tr>
<td>12</td>
<td>Conduct a physical examination Check: Temperature / Rash / Malnutrition, Pallor / Jaundice / Cyanosis / Shortness of breath / Intoxication from alcohol or drugs / Veins</td>
<td></td>
<td></td>
<td>Disqualify any potentially unwell donor or donors with very difficult veins</td>
</tr>
</tbody>
</table>

- The remaining group form the Emergency Donor Panel (EDP)
- Use the Risk Triage Screen to risk screen
... and the donor may need psychological support if given unexpected news and in possession of firearms.”

Transfusion 56:S119, 2016
Donor Performance Issues

• 450 ml withdrawn
• One unit donation decreases VO2max by 4-10%
• But no other performance issues
• Rare situation can draw two units
Israel Defense Force

- RCT of 36 combatants
- Donor group had 450ml of blood drawn
- Control had IV’s but no blood drawn
- Performance compared one hour later
- Transfusion 60:S77, 2020
Example of Testing

• Marksmanship with M4 assault rifles
  – 100 meter sprint
  – 5 rounds fired kneeling
  – 5 round fired prone
• All in 60 seconds
Performance

- Marksmanship: no difference
- Weighted pull-ups: no difference
- Deadlifts (60lbs): no difference
- Walking Lunges: no difference
- 200m sprint: no difference
- Fatigue: no difference
- Cognition: no difference
Donor Safety

- No major performance issues
- Oral rehydration
Pretrip Preparation

• Dream world
  – Participants prescreen for viral disease
  – Blood type and anti-A, anti-B titers
    • Identify low titer “O” donor
  – Training in blood transfusion
Supplies

• Several transfusion kits
• Extra blood typing cards
• Rehydration salts
• Tranexamic acid
Adjunct Therapy

• Control hemorrhage
  – Tourniquets
  – Packing for external wounds

• Tranexamic acid
Tranexamic Acid

- Potent antifibrinolytic
- Earlier the better
- Can be given IM or IO
- 1 gram before/with transfusion
- Shown to be beneficial in traumatic bleeding
Plasma concentration curves of TXA

Any Cause of Death

TXA
(n= 10,060)
1,463 (14.5%)

Placebo
(n= 10,067)
1,613 (16.0%)

RR (95% CI)
0.91 (0.85–0.97) 2P=0.0035

ARR = 1.5%, NNT 66.7
Death Due to Bleeding

TXA (n=10,060) 489 (4.9%)
Placebo (n=10,067) 574 (5.7%)

ARR = 0.8%, NNT 125

RR (95% CI) 0.85 (0.76–0.96) 2P=0.0077
Time to TXA

- **≤1 hour**: 0.68 (0.54–0.86)
- **>1 to ≤ 3 hours**: 0.79 (0.60–1.04)
- **>3 hours**: 1.44 (1.04–1.99)

Relative Risk (RR) with 99% CI and p-value: 0.000008
The (Not so) Bright Future
“Artificial Blood”

- Limited oxygen carrying capacity
- No hemostatic function
- Stay in intravascular space ~ 24 hrs
- Not FDA approved
- Bulky
Lyophilized Plasma

- “Freeze dried plasma”
- Widely use by French Military
- No need to keep frozen
- Bulky and doesn’t carry oxygen
Figure 1 - Thrombosomes (TBX) manufacturing process and comparison to LSP. Apheresis platelets are collected from group O donors (A). The platelets are loaded with trehalose, a sugar molecule (B). The trehalose-loaded platelets are dehydrated to form a powder (C). The Thrombosomes are stored at room temperature for up to 3 years (D). The Thrombosomes can be rapidly rehydrated with sterile water (E). Within 2-3 minutes of rehydration, Thrombosomes can be rapidly administered to stop bleeding (F).
Bottom Line

• Nothing better than blood
• “Walking Blood Bank” easiest way to carry blood products in austere environments