

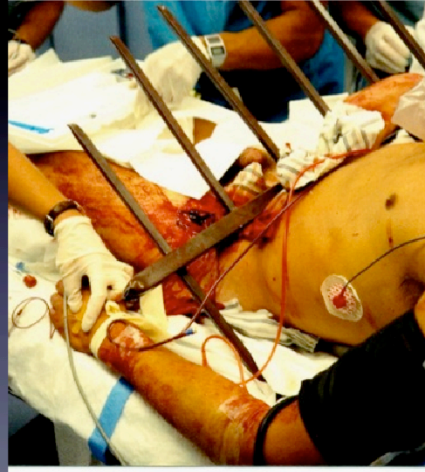
A Sanguine Approach: The Use of Blood Products and Substitutes in the Field

Christopher B. Colwell, M.D.

Denver Paramedic Division and Denver Fire
Department

Current State

- Blood loss associated with trauma carries potential complications
- Current therapy
 - Salt solutions
 - Volume



I would submit to you that bleeding is a problem, and even if you subscribe to the rather Darwinian opinion that all bleeding eventually stops, it still probably makes sense for us to do everything we can to minimize the damage that occurs before it stops.

Eagles Survey – Blood Products

- 35 agencies
 - No ground ambulances
 - Some air medical or physician opportunities



They have also tried a variety of things in various military settings as well.

The Problem with Blood

- Availability issues
- Compatibility issues
- Storage issues



Recognized Transfusion Risks

Febrile Reaction 1 : 200

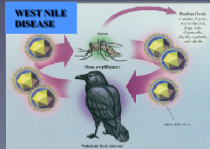
TR Acute Lung Injury 1 : 5000

Hemolytic Transfusion Reaction 1 : 6000

Hepatitis C 1 : 100,000

Hepatitis B 1 : 200,000

Human Immunodeficiency Virus 1 : 1,000,000

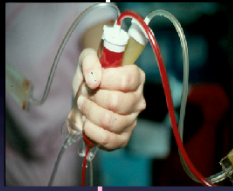


? Future Risk

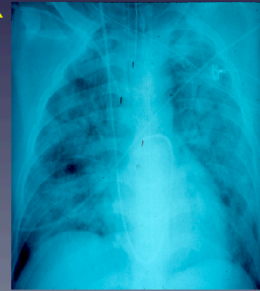
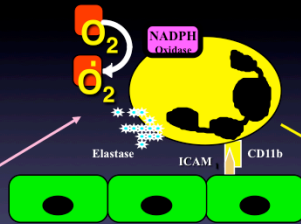


RBC Transfusion → PMN Priming → Postinjury MOF

TNF, IL₁, IL₆, IL₈, IL₁₈



LTB₄, Lyso PCs



Massive Transfusion?

- Platelets?
- Fresh Frozen Plasma?



Significant risk of DIC when these are not added

Unavailability Situations

- Military
- Remote locations
- Unplanned “elective” hemorrhage
- Multiple simultaneous injuries
- Inventory imbalance
- Religious objection



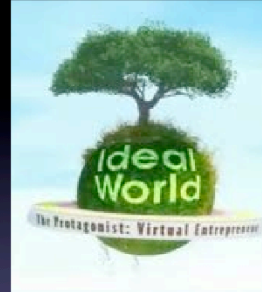
Today the blood supply is superb in this country and that is not news to any of you. However, there are situations where blood is not available and can occur in either military or civilian settings.

It can occur in remote locales or in urban areas. It can occur where the amount of blood loss in so-called elective settings is greater than that which is planned.

Certainly, we have experienced occasions where multiple simultaneous injured patients deplete the immediately available blood supply. Some patients present with rare antibodies and pose incompatibility issues with the available blood supply. The vagaries of inventory imbalances occur seasonally, like during holidays, when collections of blood fall. And of course, there are those patients who object to blood transfusion on religious ground and for whom no alternative oxygen carrier exist.

Ideal Resuscitation Fluid

- Low cost
- Abundant
- Safe
- Universally compatible
- Easy to store and transport
- Carries oxygen
- Effective at low volumes



So I don't believe it is ever going to be practical to bring blood products out into the field in most EMS systems, and yet there still needs to be a better way.

Blood Substitutes – The Future is Now



We are really close to this ideal resuscitative fluid with the blood substitutes, but we aren't there yet.

HBOC Development 1930's → 1940's → 1950's → 1970's → 1980's → 1990's

II. Hemolysates

II. Purified Hemolysates

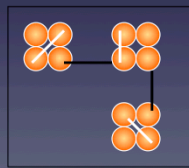
III. Tetrameric Hemoglobin (Stroma Free Hemoglobin)

IV. Modified Tetrameric Hemoglobin

V. Polymerized Hemoglobin



Human



Bovine

The hemoglobin-based oxygen carriers have undergone a number of stages of development to where we are today with polymerized hemoglobin, which has reduced the side effects dramatically. We started with hemolysates which had neurologic complications in animals and evolved into purified hemolysates, on to tetrameric and modified tetrameric hemoglobins and then to polymerized hemoglobin

PolyHeme Recipients

Critical Safety Data

- Universally compatible
 - Immediately available
- No febrile reactions
- No renal dysfunction
- No pancreatic/GI dysfunction
- No cardiac dysfunction
- No disease transmission
- No significant adverse events
- Allows rapid, massive transfusion

PolyHeme



Prehospital Randomization



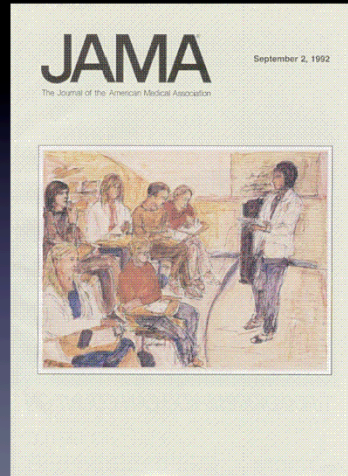
Primary Endpoint
Increased Survival at 30 days

Secondary Endpoints
Reduce use of stored blood
Reduce multiple organ failure
Reduce adverse events

This study was done at multiple sites across the country. We ended up enrolling over 100 patients. The medics loved it!

Blood Substitutes

- Meta – analysis
- Natanson et al
 - JAMA, 2008
- Vasoconstriction remains a risk
 - Higher risk of MI
 - Over 80?
- FDA response



When the numbers from across the country were all in, there was still a concern about an unacceptable degree of vasoconstriction that led to a higher risk of myocardial infarction. It was clearly to a much lesser degree than it ever had been before, but it was still too high. FDA response was to place a moratorium on human studies involving blood substitutes in late 2010.

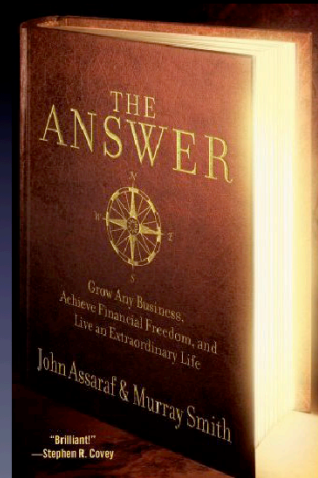
FDA



This is what the FDA is telling us, but ultimately I believe the answer will be in the next generation of blood substitutes

The Answer!

- A better blood substitute



Blood products in the field is not the answer. If we want to take the next step in trauma care in the field, the next step is going to be blood substitutes, and we need to support and encourage the final steps in getting us there. We are very close. I really believe this is where a potential answer lies and the impact could be enormous. The moratorium still exists, but the amount of work going into this is going to justify lifting it at some point, so don't give up on this yet.