From HEMS to SAR, from sea to mountains, from urban to combat, a thorough Congress. This is Remote.
Pre-hospital blood products “state of the art”

Dr Anne Weaver
Consultant in Emergency Medicine & Pre-Hospital Care
London’s Air Ambulance

REMOTE 2018
Milan, Italy
The problem in Europe

• Major haemorrhage is still a leading cause of death in trauma patients
• Average time for a major trauma patient to reach hospital in London = 66 minutes – same in Europe
• Patients still die pre-hospital from bleeding
• Limited availability of pre-hospital blood products
UK stats – trauma haemorrhage

• 4700 / yr major haemorrhage (1550 dead)
• 1300 / yr massive haemorrhage (585 dead)
• Deaths 50% in 24hrs (50% in first 4 hrs)
• 50% needed urgent surgery
• £150 million / yr
“State of the art”

• Product availability – development, adaptation, logistics
• Patient selection – point of care devices
• Delivery – temperature, rate of delivery, vascular access devices
• Patient safety – electronic tracking (vein to vein)
• Research – biobank, outcomes, product development
Acute Traumatic Coagulopathy

Karim Brohi, BSc, FRCS, FRCA, Jasmin Singh, MB, BS, BSc, Mischa Heron, MRCP, FFAEM, and Timothy Coats, MD, FRCS, FFAEM

**Background:** Traumatic coagulopathy is thought to be caused primarily by fluid administration and hypothermia.

**Methods:** A retrospective study was performed to determine whether coagulopathy resulting from the injury itself is a clinically important entity in severely injured patients.

**Results:** One thousand eight hundred sixty-seven consecutive trauma patients were reviewed, of whom 1,088 had full data sets. Median Injury Severity Score was 20, and 57.7% had an Injury Severity Score > 15; 24.4% of patients had a significant coagulopathy. Patients with an acute coagulopathy had significantly higher mortality (46.0% vs. 10.9%; \( \chi^2, p < 0.001 \)). The incidence of coagulopathy increased with severity of injury, but was not related to the volume of intravenous fluid administered (\( r^2 = 0.25, p < 0.001 \)).

**Conclusion:** There is a common and clinically important acute traumatic coagulopathy that is not related to fluid administration. This is a marker of injury severity and is related to mortality. A coagulation screen is an important early test in severely injured patients.

**Key Words:** Traumatic coagulopathy, Hypothermia, Fluid administration.

*J Trauma. 2003;54:1127–1130.*
25%
4x
Pre-hospital challenges

• Logistics – delivery, storage, shelf-life
• Frequency of use (wastage) – population, purpose of service
• Carriage – portability, cold chain, resilience of kit
• Limited trained team members
• Limited IV access
• Time taken to transfuse multiple products
Blood products in pre-hospital care

• Packed red blood cells
• Plasma
• Fibrinogen
• Red cells & plasma
• Whole blood

• Legislation
• Local need
International pre-hospital products

- Australia
  - PRBC
  - Not using TXA routinely
- New Zealand (Auckland)
  - whole blood
- USA
  - PRBC
  - Thawed plasma trials
  - Low titre O whole blood

- Europe
  - Austria – fibrinogen (FinTIC)
  - France, Germany, Denmark, UK – lyophilised / thawed plasma
  - Norway – plasma, low titre O WB

- Military
  - US – whole blood (Afghanistan)
  - UK MERT – PRBC & thawed plasma
  - Israel – low titre whole blood
  - Norway special forces – warm whole blood
Patient selection

• Not all hypotension is bleeding
• “bleeding mimics”
• Encourage clinicians to make a diagnosis
• Standard Operating Procedure for Pre-hospital transfusion
• Case review – retrospective, with CT / surgical findings
Point of care testing

- LAA does not use any device currently
- Mandatory to take a pre-transfusion sample
- Determine native blood group
- Plan to create a biobank for research
- Option to use i-stat or similar device – lactate, base deficit
- Future – handheld ROTEM / TEG
Pre-hospital PRBC transfusion

• London’s Air Ambulance (LAA) launched “blood on board” in March 2012
• 100 transfusions per year (5%)

• Indications:
  • Code red in extremis
  • Traumatic arrest where hypovolaemia is key factor
Golden Hour box

- Robust kit
- 4 units (each 350ml)
- Data logger 2-6C
- Steady state up to 72 hrs
Warming devices

Comparison of the performance of battery operated fluid warmers. Lehavi et al. EMJ 2018 vol 35(9)
PREHOSPITAL MORTALITY
2009 34% 2015 18%
LAA PRBC outcomes

• Reduced pre-hospital mortality (p<0.01)
• Reduced overall product use (p<0.01)
• Avoids unnecessary waste & allogeneic tissue exposure
• No difference in overall mortality
• Peak in early hospital deaths
• LAA transfusion practice is safe and feasible

Pre-hospital transfusion of red blood cells in civilian trauma patients. Rehn et al. Transfus Med. 2017
Pre-Trauma Center Red Blood Cell Transfusion Is Associated with Improved Early Outcomes in Air Medical Trauma Patients

Joshua B Brown, MD, Jason L Sperry, MD, MPH, FACS, Anisleidy Fombona, BS, Timothy R Billiar, MD, FACS, Andrew B Peitzman, MD, FACS, Francis X Guyette, MD, MPH

CONCLUSIONS: Pre-trauma center RBC was associated with an increased probability of 24-hour survival, decreased risk of shock, and lower 24-hour RBC requirement. Pre-trauma center RBC appears beneficial in severely injured air medical trauma patients and prospective study is warranted as PTC RBC transfusion becomes more readily available. (J Am Coll Surg 2015; 220:797–808. © 2015 by the American College of Surgeons)
Pre-hospital blood trials

• PRBC
• “Improved outcomes”
• 6hr survival
• 24hr survival
• Reduced blood product transfusion in 24hrs
• Improved BE / acid base balance on admission
• Feasible with low wastage
ROYAL LONDON HOSPITAL CODE RED
3 AND 24-HR MORTALITY

CODE RED INTRODUCED
TXA
PHC BLOOD
ROTEM CODE RED

Percentage patients


 Died >3h <24h
 Died <3h

???
Plasma

- Contains plasma proteins, clotting factors, fibrinogen
- Haemostatic resuscitation
- Restores glycocalyx
- Available as:
  - Fresh Frozen Plasma (FFP) – thawed for use
  - Lyophilised / freeze dried plasma - reconstituted
  - Liquid plasma – never frozen, platelets
Pre-hospital plasma

- US trials
  - COMBAT – no stat sig difference in mortality
  - PAMPPer - reduced 30 day mortality compared to standard care (Sperry et al. NEJM 2018)
- Thawed fresh frozen plasma - 5 day shelf life
- Freeze dried plasma
- Feasible but high wastage due to short shelf-life
- Liquid plasma >7 day shelf-life
**Original Investigation**

Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma

The PROPPR Randomized Clinical Trial

John B. Holcomb, MD; Barbara C. Tilley, PhD; Sarah Baraniuk, PhD; Erin E. Fox, PhD; Charles E. Wade, PhD; Jeanette M. Podbielski, RN; Deborah J. del Junco, PhD; Karen J. Brasel, MD, MPH; Eileen M. Bulger, MD; Rachael A. Callcut, MD, MSPH; Mitchell Jay Cohen, MD; Bryan A. Cotton, MD, MPH; Timothy C. Fabian, MD; Kenji Inaba, MD; Jeffrey D. Kerby, MD, PhD; Peter Muskat, MD; Terence O’Keeffe, MBChB, MSPH; Sandro Rizoli, MD, PhD; Bryce R. H. Robinson, MD; Thomas M. Scalea, MD; Martin A. Schreiber, MS; Deborah M. Stein, MD; Jordan A. Weinberg, MD; Jeannie L. Callum, MD; John R. Hess, MD, MPH; Nena Matijevic, PhD; Christopher N. Miller, MD; Jean-Francois Pittet, MD; David B. Hoyt, MD; Gail D. Pearson, MD, ScD; Brian Leroux, PhD; Gerald van Belle, PhD; for the PROPPR Study Group

PROPPR (plasma, platelet, PRBC) trial
JAMA 2015

• Multi-centre RCT
• 1:1:1 vs 1:1:2
• Low numbers
• No stat sig difference in 24 hr or 30 day mortality
• Higher rate of haemostasis
• Reduced numbers of death due to exsanguination (9.4% vs 14.6% p<0.03)
• UK guidelines changed on this basis
Impact of fibrinogen levels on outcomes after acute injury in patients requiring a massive transfusion.


Fibrinogen > 180 mg/dl, Fibrinogen 180 – 100 mg/dl, Fibrinogen < 100 mg/dl
FIB IN TIC
Fibrinogen in Trauma induced coagulopathy
Early cryoprecipitate for major haemorrhage in trauma: a randomised controlled feasibility trial

N. Curry¹,*, C. Rourke², R. Davenport², S. Beer¹, L. Pankhurst³, A. Deary³, H. Thomas³, C. Llewelyn³, L. Green⁴, H. Doughty⁵, G. Nordmann⁶,⁷, K. Brohi² and S. Stanworth¹
CRYOSTAT Mortality

Standard: 6/21 : 28%
Early CRYO: 2/20 : 10%
• Offered support to advance pre-hospital capability
• Current limitations
  • Blood donations – split for component therapy
  • Products must be leuco-reduced (vCJD)
  • Current filters remove platelets (not by design)

• Whole blood is not currently available in UK
• We are not “state of the art”......yet
Our wish list

• 1:1:1
• Plasma: PRBC: platelets
• Fibrinogen
• All in one bag
• Through one IV line
• No mixing with water
Our wish list

• 1:1:1
• Plasma: PRBC: platelets
• Fibrinogen
• All in one bag
• Through one IV line
• No mixing with water

• Platelet sparing filter.....
UK whole blood

- Routine UK military practice 1940-60
- Fresh whole blood (used within 24 hrs)
- By 1965 use faded as blood products became available with longer shelf life
- Today WB is not produced by NHSBT
- All products must be leucocyte depleted since 1999 - vCJD
Whole blood for hemostatic resuscitation of major bleeding

Philip C. Spinella,1,2 Heather F. Pidcoke,2 Geir Strandenes,3,4 Tor Hervig,4 Andrew Fisher,5 Donald Jenkins,6 Mark Yazer,7 James Stubbs,8 Alan Murdock,9 Anne Sailliol,10 Paul M. Ness,11 and Andrew P. Cap2

• Transfusion. 2016:56;S190-S202
• US Army data
• WB superior or equivalent to blood product txn
• 4C platelets have better function than warm (22C) platelets
• Leukoreduced, platelets spared.
Norway (PHC and special forces)

- Military-civilian co-operation
- 2013 - Freeze dried plasma
- 2014 – PRBC
- 2015 Special forces - warm, WB donation to “buddy”
  - Pre-screened personnel – ABO compatible
  - Fit to continue special ops work after donation
- 2018 Low titre O – all forces

- Developed protocol for Emergency Donor Panels
  - Rapid blood group – 40s
  - Blood borne virus screen – 60s
Anne Weaver @Anni...  • 25/10/2018  
Launch day for RC&plasma
@LDNairamb 🎉🩹  huge thanks to everyone who made this happen!
Amazing collaboration👏 @NHSBT @Barts_Chatry @Saracens @HSF_Foundation @RoyalLondonHosp @NHSBartsHealth transfusionteam @LGreeBartsNHS @rossdavenpont @karimbrohi @davidlbath @j0nathanjenkins
An evaluation of leucocyte depleted red cells & plasma transfusion for major traumatic haemorrhage in patients presenting in the pre-hospital setting in London – 2 year feasibility study
“RC & plasma” - why do this study?

• Interest in pre-hosp product delivery
• No safety / efficacy studies exist
• Need to establish feasibility of delivery to a Major Trauma Centre
• Shorter shelf life – 14 days vs 35 days
• Potential to increase wastage – O neg
RC&plasma progress

• 13 RC&plasma transfusions
• 12 pre-transfusion samples
• Logistical advantage – fewer actions to deliver transfusion
• 470 ml per unit
• Efficient delivery schedule
• Too early to comment on coagulation parameters
LAA - future aims

• Develop / validate a platelet-sparing filter for UK use
• Potential to provide whole blood to UK pre-hospital providers & Major Trauma Centres
• Co-ordinate a funded RCT across UK Air Ambulance teams
• Support the innovation & field testing of hand held POC devices
Catastrophic haemorrhage in PHC

• Physician – paramedic teams
• Recognition of serious haemorrhage
• Pre-alert protocols
• Massive haemorrhage protocols - logistics
• Pre-hospital transfusion
• Aggressive vascular control in the field - REBOA
KEEP CALM
ALL BLOODING STOPS EVENTUALLY