
Whole Blood Through The Generations
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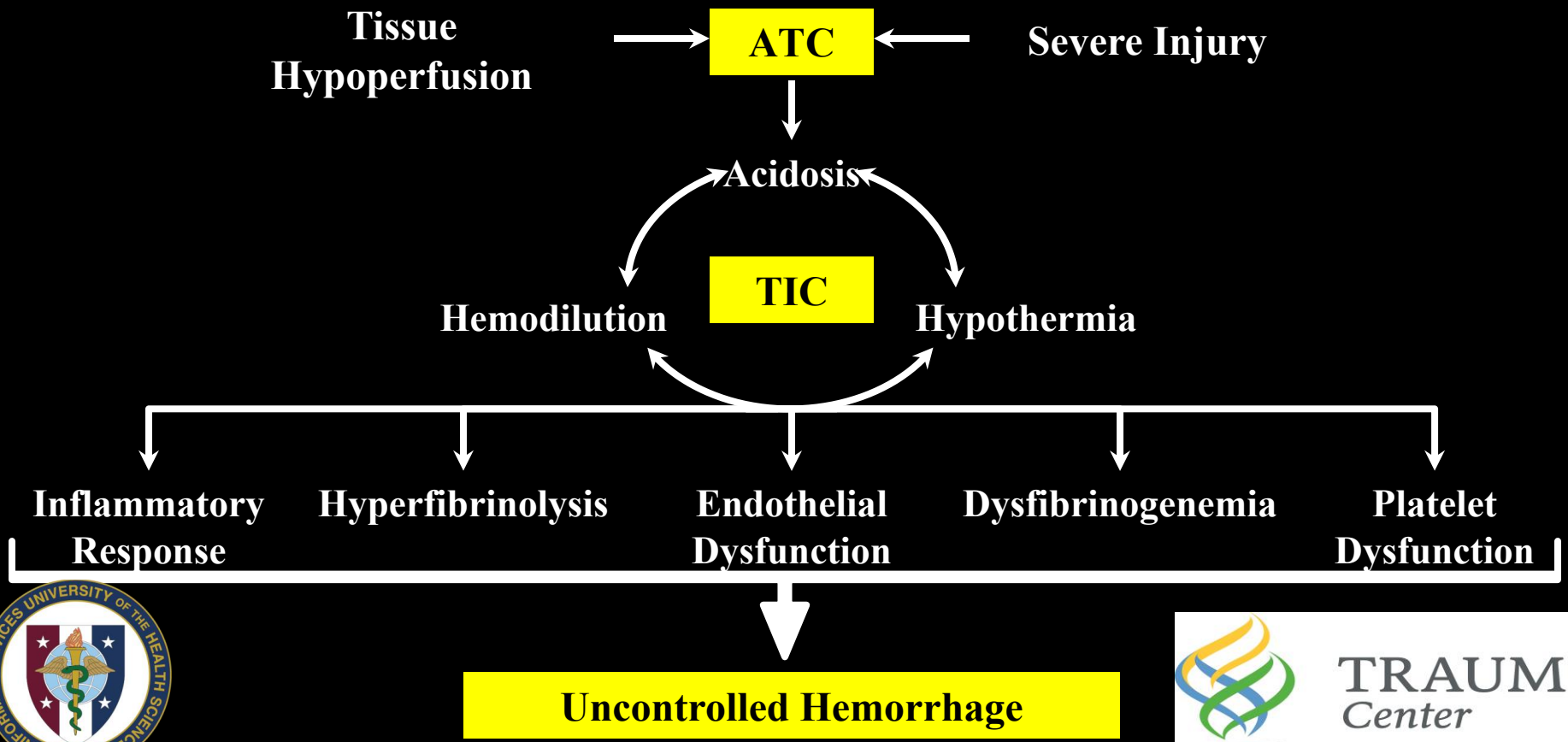
Introduction

- Hemorrhage leading cause of preventable death after trauma
- Hemorrhage control 1st step
- Replace what is lost
- Novel products in development

Acute Traumatic Coagulopathy (ATC)



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History of Whole Blood

- Richard Lower (1665) – Keeps exsanguinated dogs alive
- Philip Syng Physick (1795) – 1st human transfusion
- Civil War – 2 successful transfusions
- Alexis Carrel (1908) – Vein to vein
- 1970s – Whole blood to components


4
3
2
1

Sydney Ringer

- 1835 – 1910
- British physiologist, MD
- Outstanding bedside teacher
- True early clinical investigator
- Fanatically punctual
- Climbed building when lab door locked
- “. . . first and foremest to be open eyed and open – minded; then to be honest”

Ringer's Fluid

- Isolated frog heart studies
- Saline produced ventricular dilatation
- Blood and albumin reverse
- Calcium - normal heart beat
- Potassium – increased period of organ functionality

Normal Saline

- Hamburger 1886 to treat cholera patients
- Studied freezing point of salt solutions
- 0.92% saline freezes at same temp as human serum (-0.52C)

Hartog Jakob Hamburger
Dutch Physiological Chemist

"What is wanted is a fluid that will have the advantages of salt solutions together with the antagonism to the state of acidosis"

Captain Walter B. Cannon

Observations WWI

Cannon WB. JAMA. 1918;70;618-621.

THE TRANSFUSION OF WHOLE BLOOD:
A SUGGESTION FOR ITS MORE FREQUENT EMPLOYMENT IN WAR SURGERY.

BY

L. BRUCE ROBERTSON, B.A., M.B.TORONTO,

CAPTAIN C.A.M.C.,

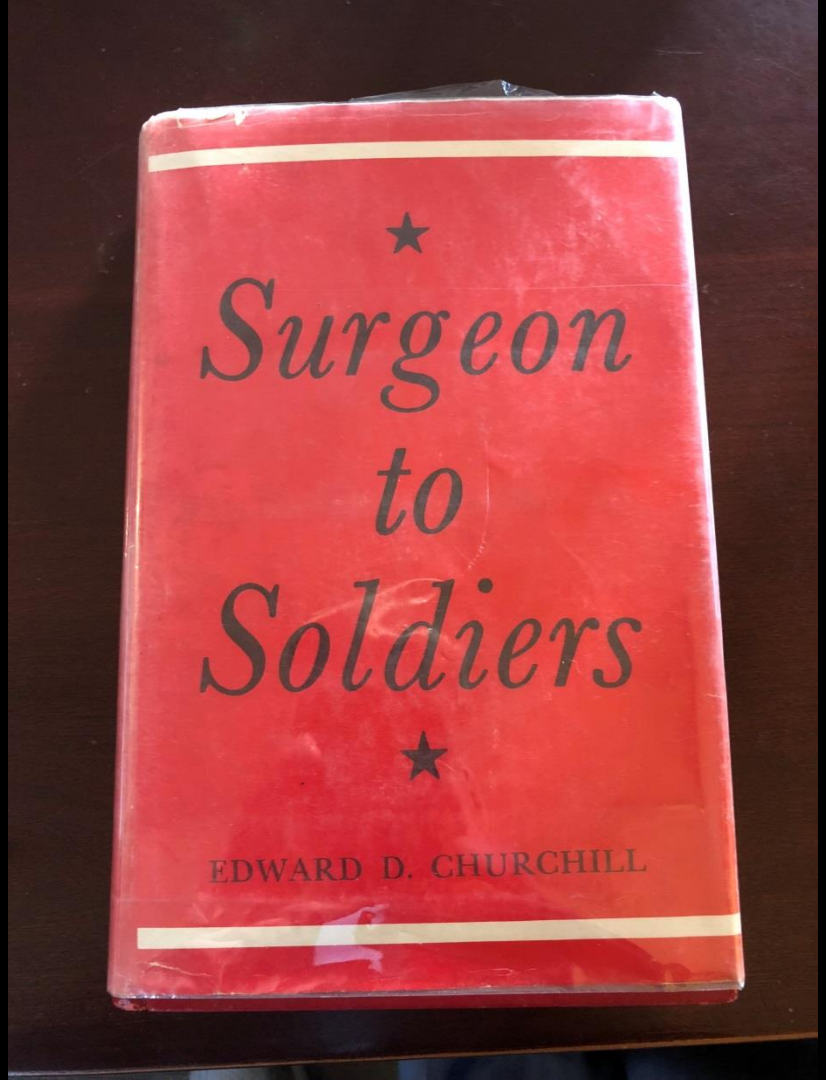
JUNIOR ASSISTANT SURGEON, HOSPITAL FOR SICK CHILDREN, TORONTO, CANADA.

THE investigations of Crile and Carrel and the more recent clinical and experimental work of Satterlee and Hooker,[1] and of Lindeman,[2] have shown the enormous value of the introduction of whole blood into the circulation, and have emphasized its limitations.

The *British Medical Journal*, July 8, 1916.

Lyophilized Plasma

WWII


Surgeon
to
Soldiers
EDWARD D. CHURCHILL

War in Vietnam

- Crystalloid increases in dominance
  - ARDS, Shock lung, Da Nang lung
- Whole blood transfusion continues
- Blood frequently shipped from US
- Known clotting deficiencies
- FFP routinely transfused with every 5 – 10 units

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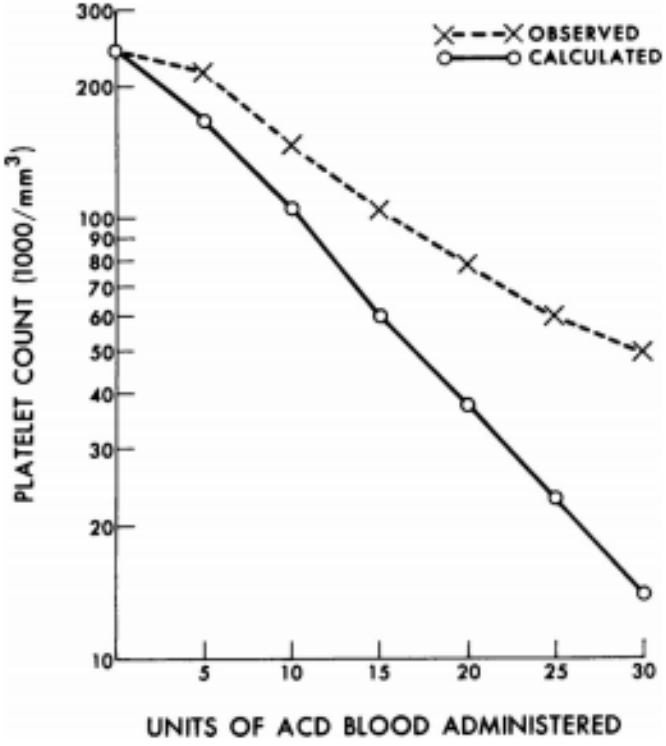
David S. Warner, M.D., Editor

Anesthesiology 2009; 110:1412–6 Copyright © 2009, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Massive Blood Transfusions

The Impact of Vietnam Military Data on Modern Civilian Transfusion Medicine

Ronald D. Miller, M.D.



CRITICAL CARE MEDICINE
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Vol. 4, No. 2
Printed in U.S.A.

Fluid resuscitation following injury: rationale for the use of balanced salt solutions

CHARLES J. CARRICO, MD; PETER C. CANIZARO, MD; G. TOM SHIRES, MD

- Controlled hemorrhage studies in dogs
- No trauma
- LR at rapid rate to replace interstitial fluid until whole blood available
- Base further <u>whole blood</u> resuscitation on patient response

CCM, 1976

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PAPER

Supranormal Trauma Resuscitation Causes More Cases of Abdominal Compartment Syndrome

Zsolt Balogh, MD; Bruce A. McKinley, PhD; Christine S. Cocanour, MD; Rosemary A. Kozar, MD, PhD; Alicia Valdivia, RN; R. Matthew Sailors, PhD; Frederick A. Moore, MD

- **Massive resuscitation to increase O2 delivery**
- **Resulted in increased fluid given**
- **Increased ACS**
- **Increased MOF**
- **Increased death**
- **Michelin people**

Arch Surg 2003

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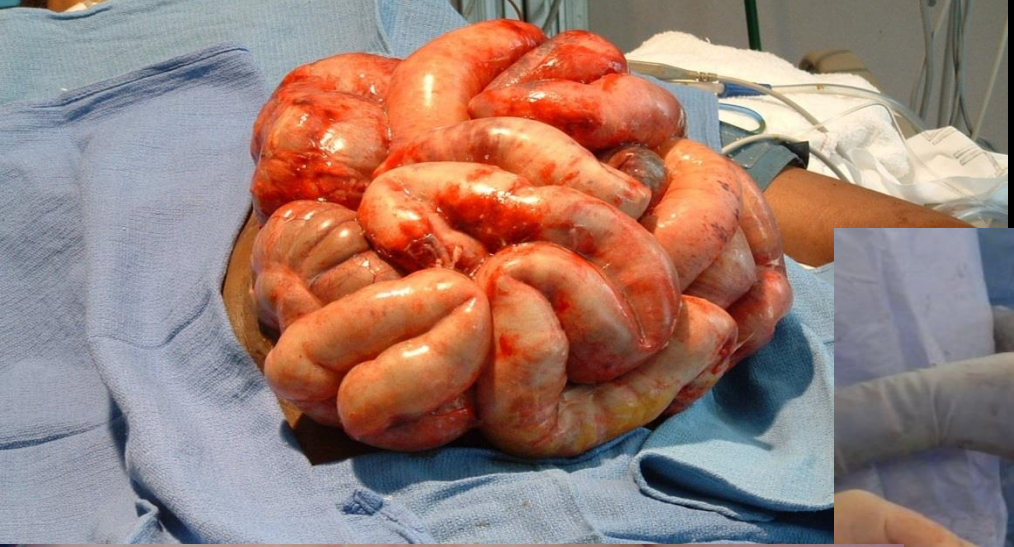
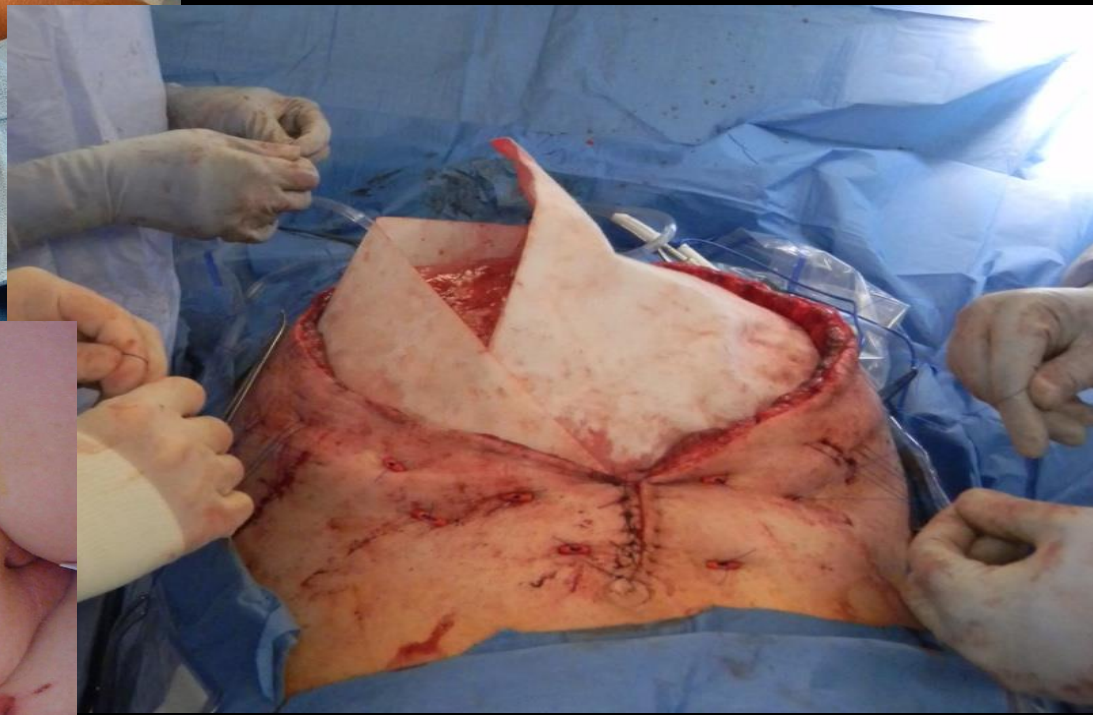
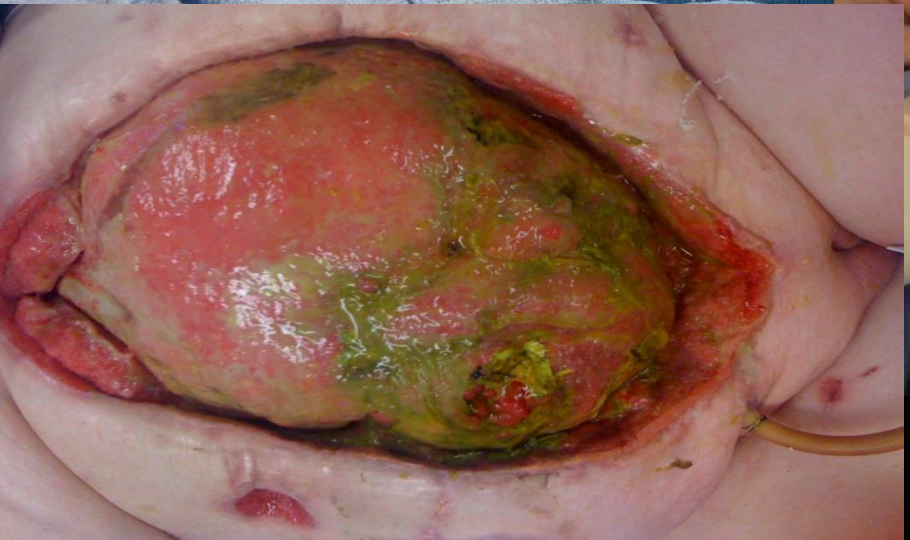
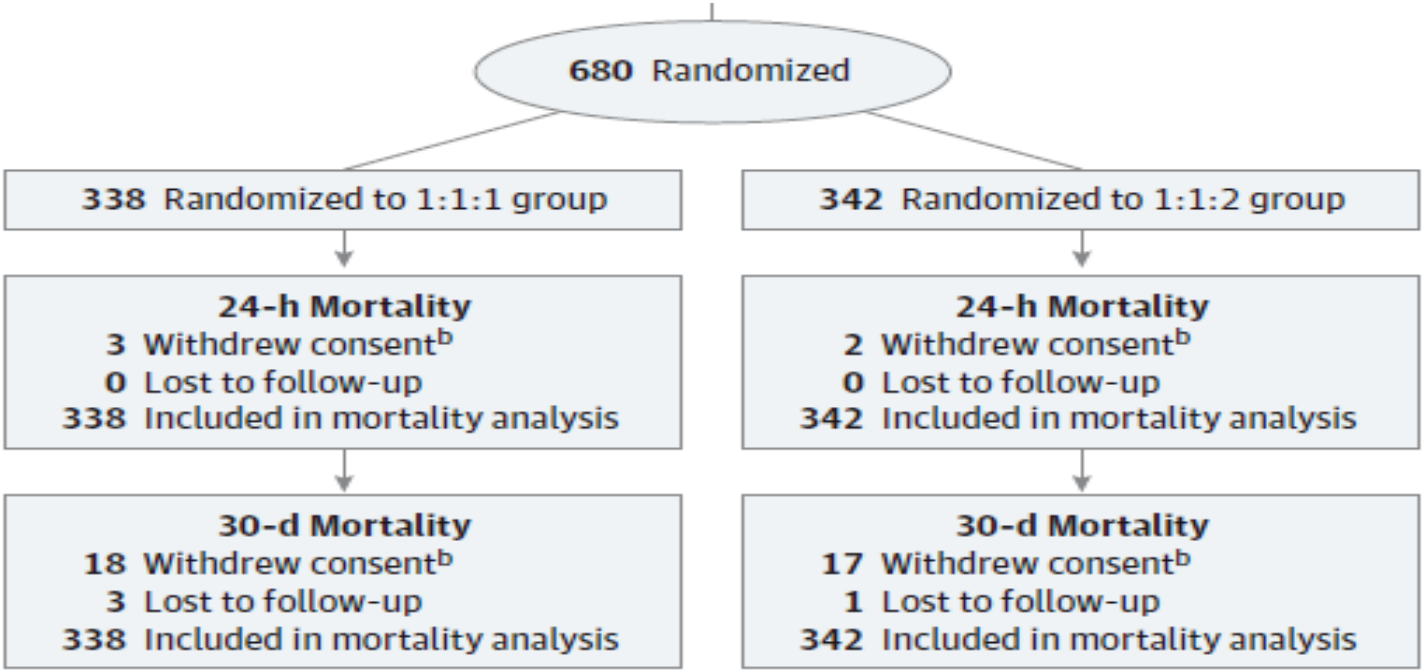






PROPPR Patient Flow



Holcomb et al *JAMA* 2015;313:471 – 482.

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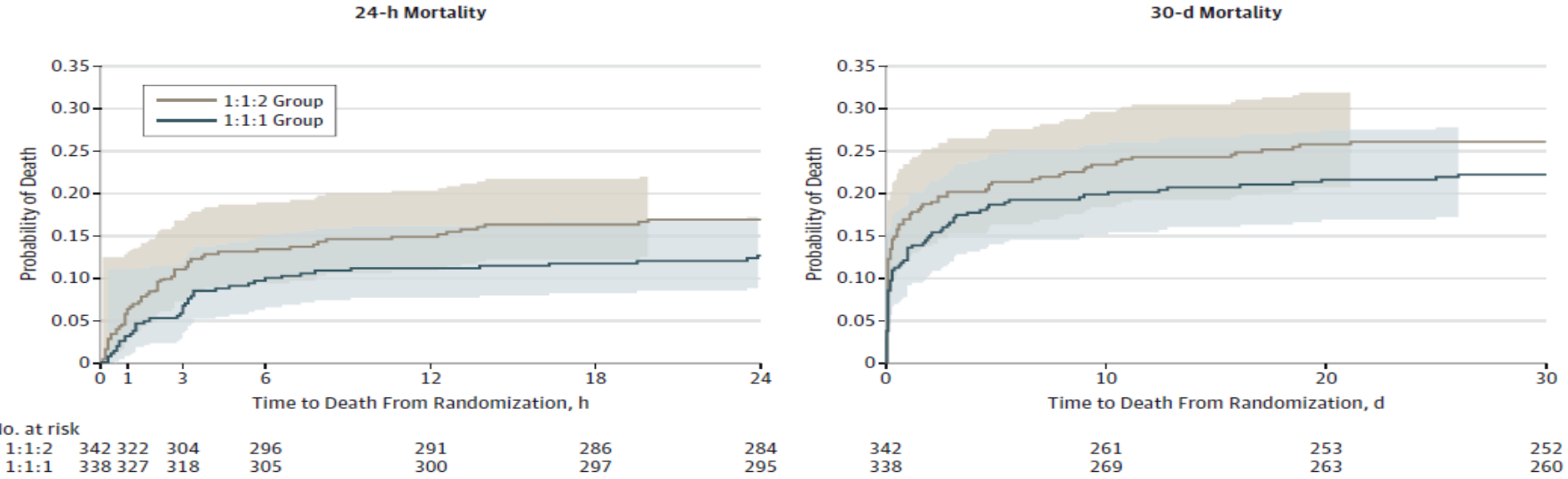
Kaplan – Meier Curves



Holcomb et al *JAMA* 2015;313:471 – 482.

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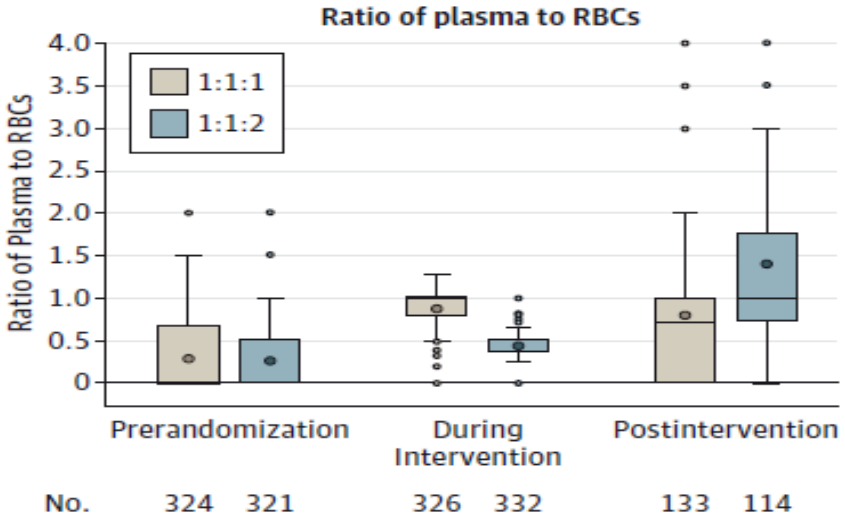
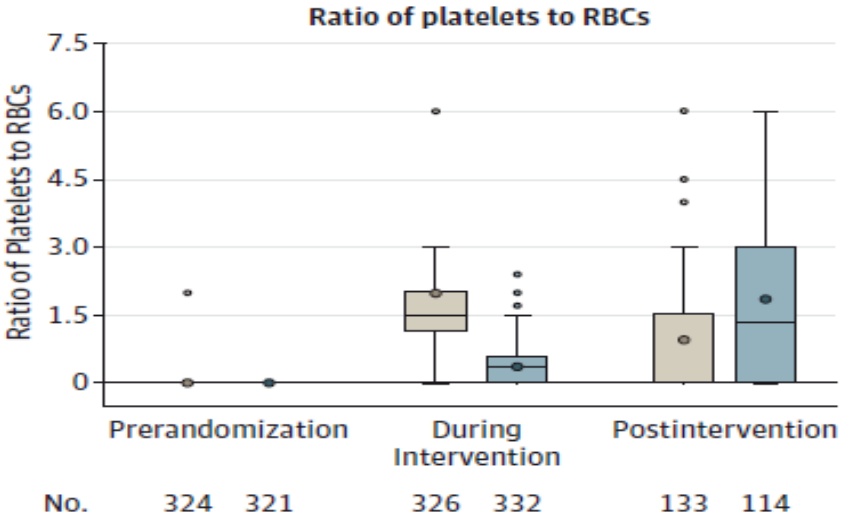
Product Ratios





Holcomb et al *JAMA* 2015;313:471 – 482.

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Cause of Death

	First 24 Hours			30 Days		
	No. (%)			No. (%)		
	1:1:1 Group (n = 338)	1:1:2 Group (n = 342)	Difference (95% CI),%[a]	1:1:1 Group (n = 335)	1:1:2 Group (n = 341)	Difference (95% CI), %[a]
Total No. of deaths	43	58		75	89	
Cause of death[b]						
Exsanguination	31 (9.2)	50 (14.6)	−5.4 (−10.4 to −0.5)	36 (10.7)	50 (14.7)	−3.9 (−9.1 to 1.2)
Traumatic brain injury	11 (3.3)	12 (3.5)	−0.3 (−3.2 to 2.7)	27 (8.1)	35 (10.3)	−2.2 (−6.7 to 2.2)
Respiratory, pulmonary contusion, or tension pneumothorax	3 (0.9)	1 (0.3)	0.6 (−0.9 to 2.4)	5 (1.5)	2 (0.6)	0.9 (−0.8 to 3.0)
Sepsis	0	0	0 (−1.1 to 1.1)	1 (0.3)	2 (0.6)	−0.3 (−1.9 to 1.2)
Multiple organ failure	0	0	0 (−1.1 to 1.1)	10 (3.0)	8 (2.3)	0.6 (−2.0 to 3.4)
Type of cardiovascular event						
Stroke	0	1 (0.3)	−0.3 (−1.7 to 0.9)	2 (0.6)	1 (0.3)	0.3 (−1.1 to 1.9)
Myocardial infarction	1 (0.3)	1 (0.3)	0 (−1.4 to 1.4)	1 (0.3)	2 (0.6)	−0.3 (−1.9 to 1.2)
Pulmonary embolism	0	1 (0.3)	−0.3 (−1.7 to 0.9)	0	1 (0.3)	−0.3 (−1.7 to 0.9)
Transfusion-related fatality	0	0	0 (−1.1 to 1.1)	1 (0.3)	0	0.3 (−0.8 to 1.7)

Holcomb et al *JAMA* 2015;313:471 – 482.

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Massive
Transfusion
Runner

Whole Blood Definitions

- Warm fresh whole blood – Transfused immediately or stored up to 8 hours at 22C. Can be stored an additional 24 hours at 4C.
- Cold whole blood – Stored at 1- 6C
  - Fresh if transfused within 48 hours
  - CPD, CP2D – Stored up to 21 days
  - CPDA – 1 Stored up to 35 days

Additive Solution Volume

The quantity of preservatives and anticoagulants in various blood products. Derived from reference [18].

Blood product	Volume of CPD (mL)	Volume of AS (mL)	Total volume
Plasma	48	0	48
Red blood cell	8	110	118
Apheresis platelet	35	0	35
Whole blood derived platelet	14	0	14
Whole blood	70	0	70

Seheult et al. *Transfusion Clin et Biol* 2019;26:174 – 179.

Whole Blood vs Components

TABLE 2. Blood products use by fresh whole blood (FWB)

	No FWB (n – 394)	FWB (n – 94)	p Value
FWB (U)	0	4.4 ± 4; 3 (2,6)	<0.001
Total RBCs (U)	4.7 ± 3.7; 4 (2, 6)	12.7 ± 9.4; 10 (6, 16)	<0.001
Total plasma (U)	2.6 ± 2.7; 2 (0, 4)	10 ± 7.1; 8 (5, 12)	<0.001
Total blood products (U)	7.3 ± 5.8; 6 (3, 10)	18.3 ± 13.1; 14 (10, 24)	<0.001
Factor VII given	23 (5.8)	24 (25.5)	<0.001
Massive transfusion	46 (11.6)	49 (52.1)	<0.001

Continuous variables reported as mean ± SD; median (LowerQ, UpperQ).
Categorical variables reported as n (%).
RBCs = red blood cells; SD – standard deviation.

Nessen et al. *Transfusion* 2013;53:107S-113S.

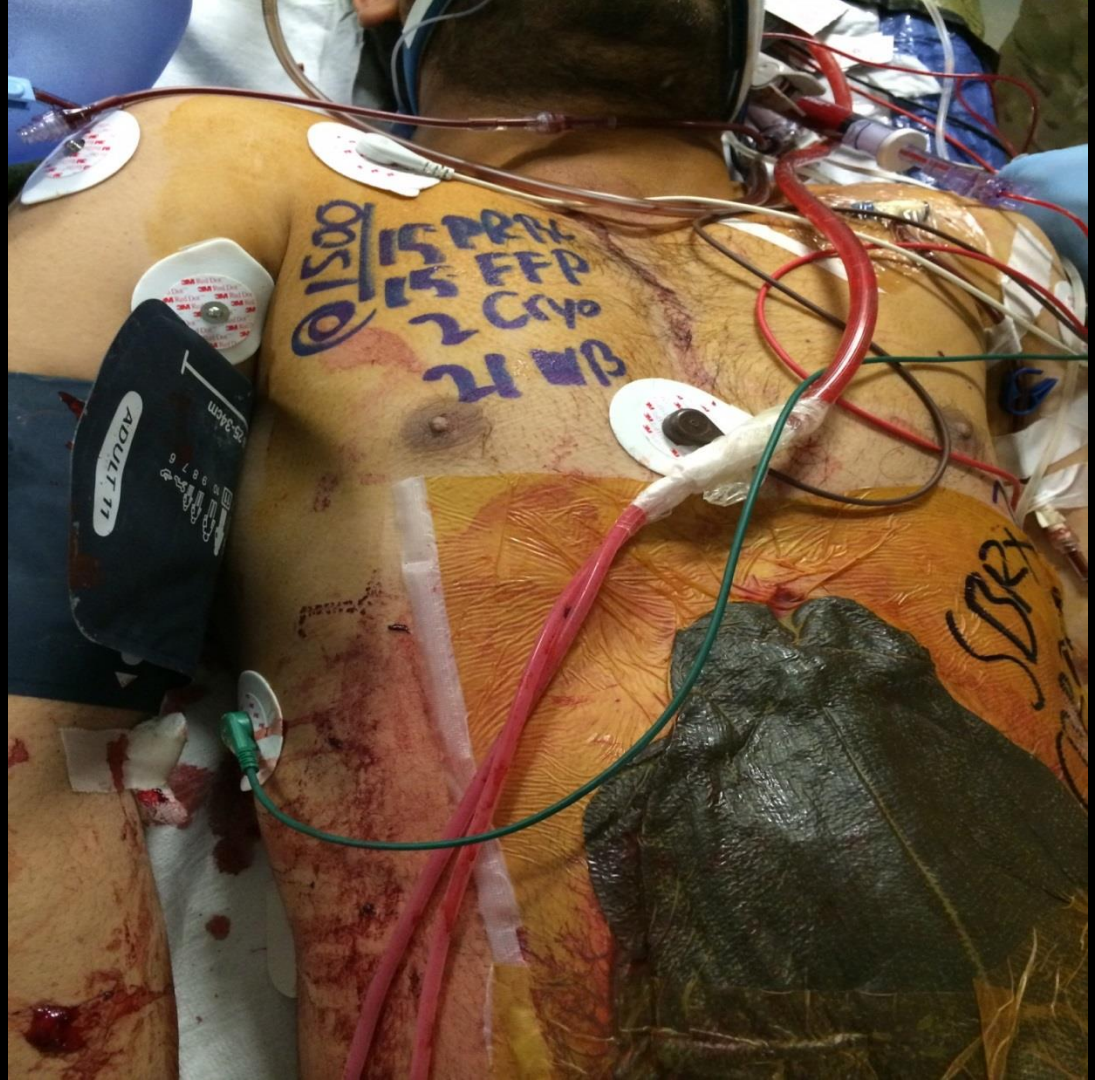
Propensity Analysis

TABLE 7. Stratified propensity score analysis predicting the effect of the use of FWB on death

	Odds ratio	95% CI	p Value
FWB use	0.11	0.02, 0.78	0.03
Injury Severity Score	1.06	1.01, 1.11	0.01
Glasgow Coma Score	0.71	0.63, 0.79	<0.001

CI = confidence interval; FWB – fresh whole blood.

Nessen et al. *Transfusion* 2013;53:107S-113S.



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Whole Blood Portland

- Program started July 9th, 2018
- 20 units provided per week
- Whole blood provided ARC
  - Low titer Ab to A and B (< 200)
  - Mixture of Rh + and Rh –
  - Leukoreduced with platelet sparing filter

Storage

- Stored up to 14 days in CPD solution
- If not utilized converted to RBCs
- Stored at 4C
- No special storage requirement

Elegance in Simplicity

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Resource Nurse

- TEGs, calciums every 30 minutes
- Guide adjunctive therapies
- Coordinate with blood bank
- Organize and transfuse with Belmont
- TXA for MTPs


O
Rh POSITIVE
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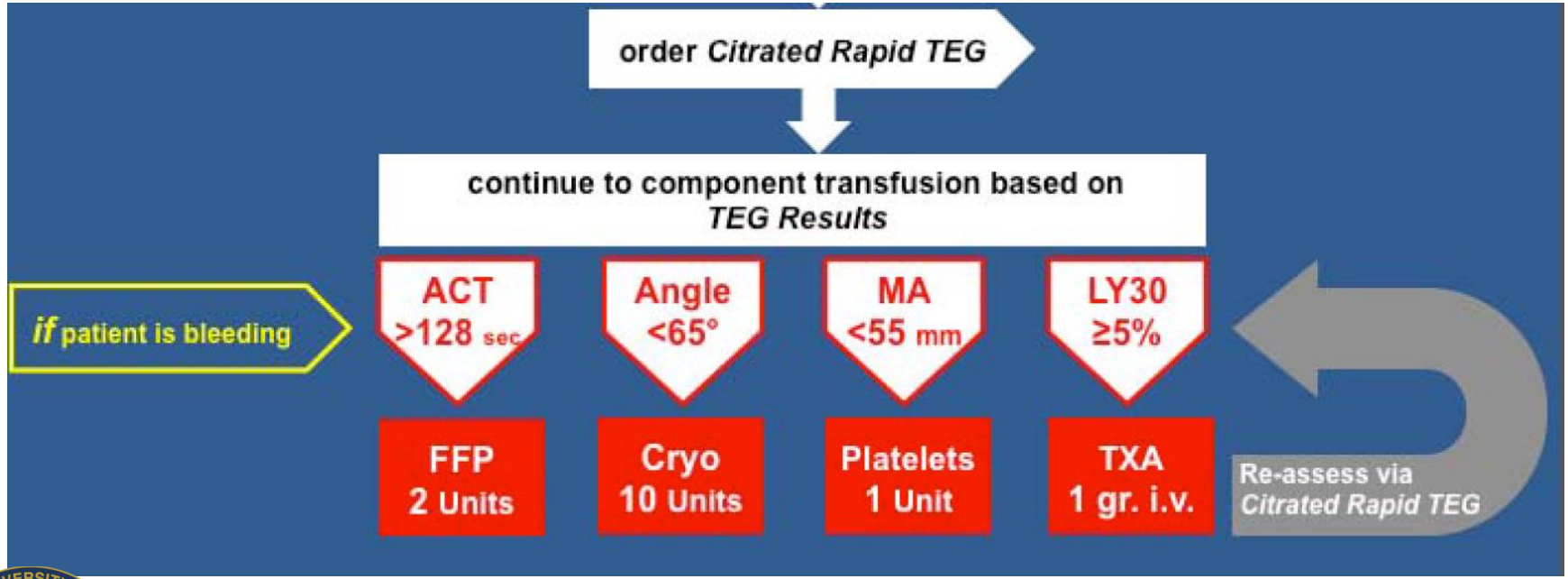
Adjunctive Therapy



Einersen et al. *JTACS* 2017;82:114 – 119.

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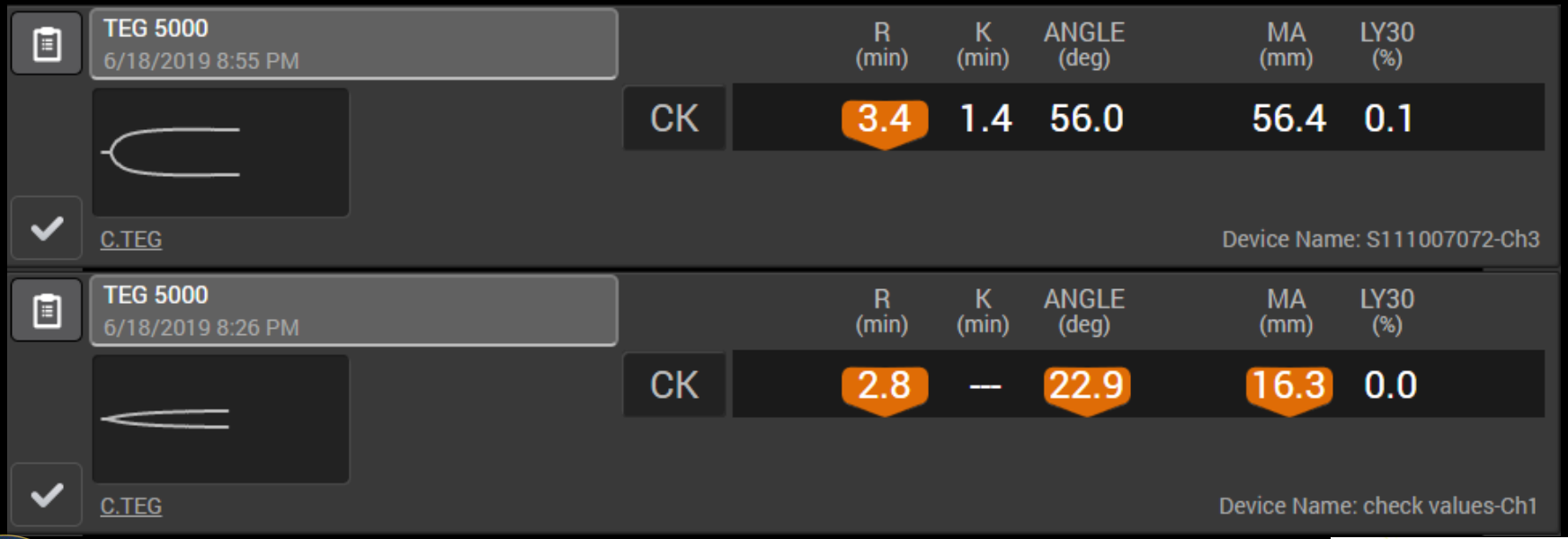
Cirrhotic Motorcyclist 3 Weeks s/p MI on Plavix



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CASE REPORT

Massive transfusion of low-titer cold-stored O-positive whole blood in a civilian trauma setting

Mary Condron,[1,†] Mick Scanlan,[2] and Martin Schreiber[3]

Condron et al. *Transfusion* 2018;9999;1 – 4.

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TABLE 2. Quantity of Blood Products Administered Within 24 Hours of Presentation by Cohort

Units of Blood Products Median (IQR)	Component Therapy Only n = 83	Received WB n = 42	*p* Value
WB Units	—	6.5 (3–11)	—
RBCs	6 (3–12)	4 (1–8)	0.003
FFP	5 (2–10)	4 (0–6)	0.01
Platelets	0 (0–2)	1 (0–2)	0.2
Cryoprecipitate	0 (0–0)	0 (0–0)	0.9
Total bags of product	12	18.5	0.19

Gallaher et al. *JTACS* 2020;89:238 – 245.

Whole Blood Barnes

- Prospective observational trial
- Leukoreduced WB, anti-A and B titers < 200
- Max dose 8 units
- 42 CT, 44 whole blood
- No difference organ failure

Shea et al. *Transfusion* 2020;60:S2 – S9.

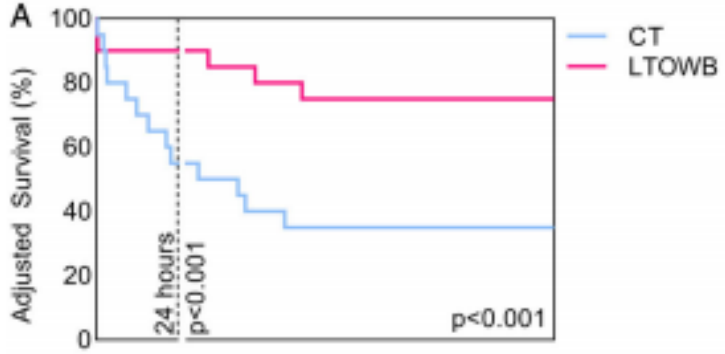
Whole Blood Barnes

TABLE 2. Blood products and other treatments

Parameter	CT Cohort	LTOWB Cohort	
Blood Product Volumes, weight-adjusted	*median (IQR)*	*median (IQR)*	*p*
RBCs, mL/kg	43.3 (25.0-70.0)	12.3 (0-29.9)	***<0.001***
Platelets, mL/kg	2.8 (1.7-5.5)	0 (0-6.0)	0.100
Plasma, mL/kg	25.7 (12.7-38.1)	7.6 (0-18.6)	***<0.001***
Cryoprecipitate, mL/kg	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.526

WB, ml/kg

23.6 (11.9 – 45.2)



Shea et al. *Transfusion* 2020;60:S2 – S9.

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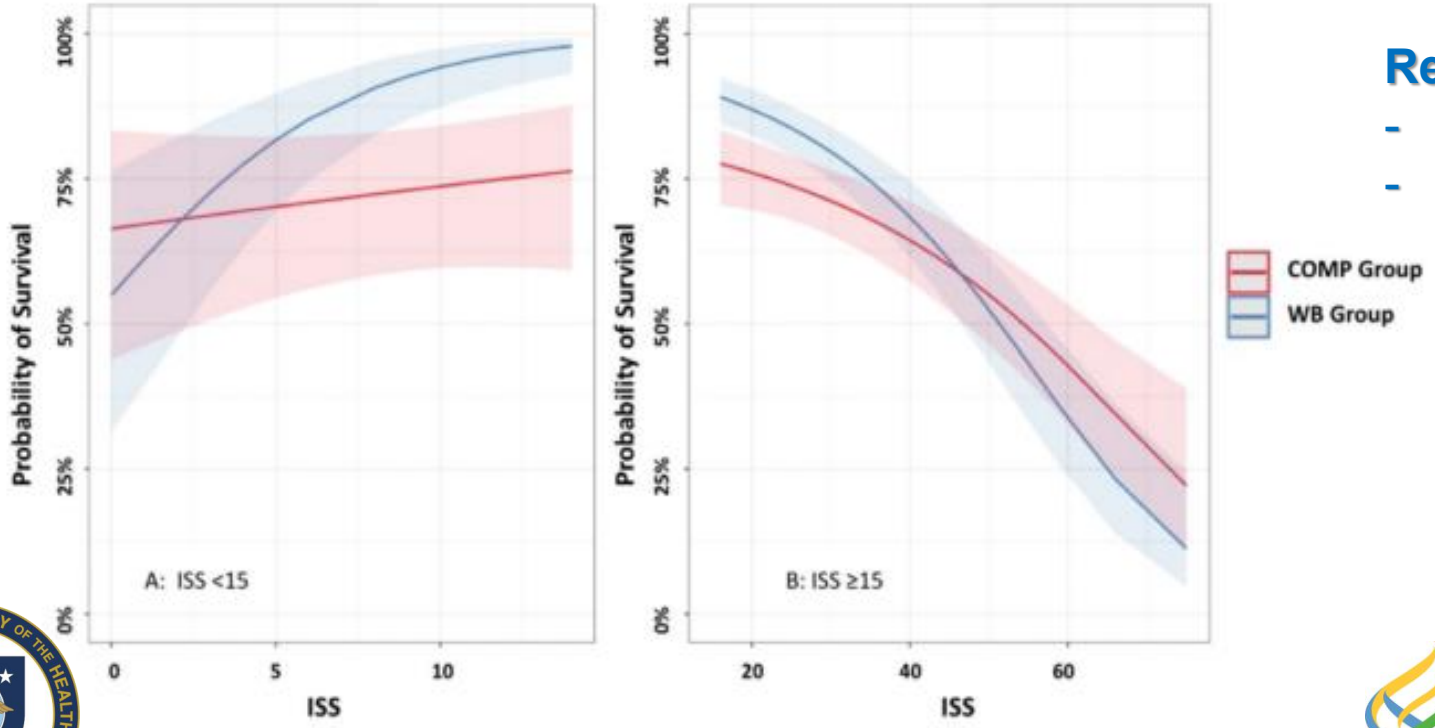
UT Houston – 1377 Patients



Reduced
- **Blood Use**
- **Mortality**

Brill et al. *JACS* 2022;234:408 – 418.

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Whole Blood LITES

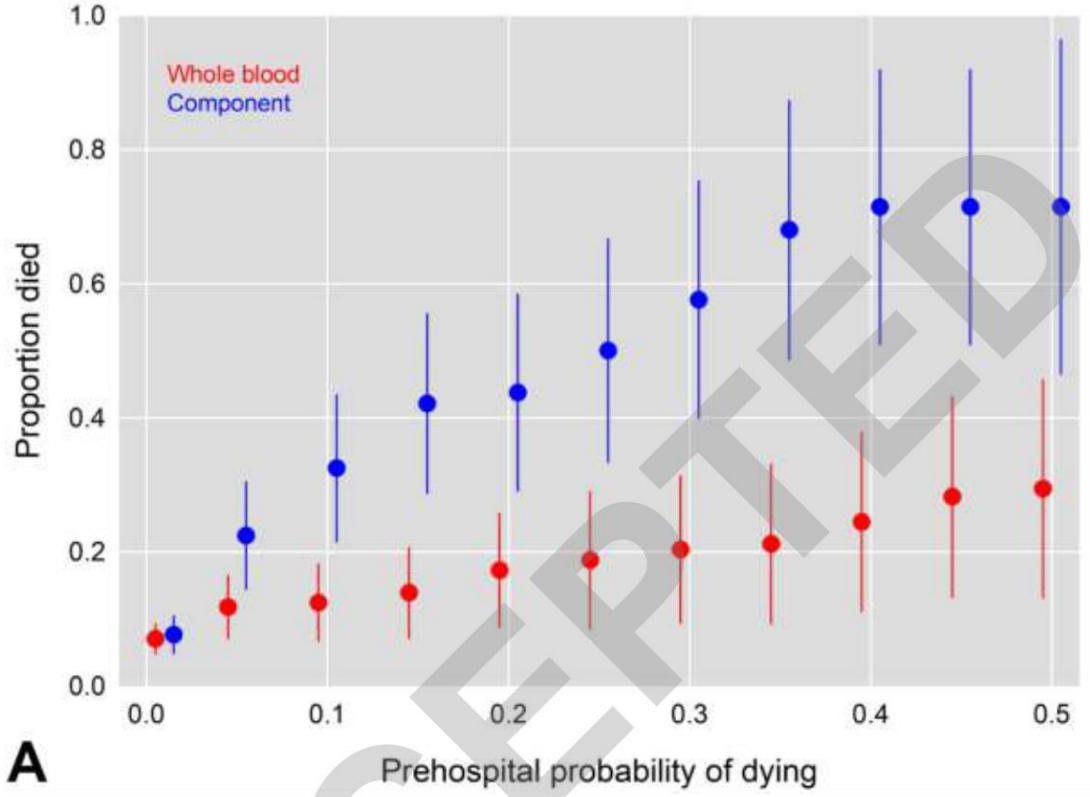
Outcomes	LTOWB (n = 624)	COMPONENT (n = 427)	Unadjusted			Adjusted*		
			RR	95% CI	p Value	RR	95% CI	p Value
Primary								
4-h mortality†	50 (8.2)	32 (7.5)	1.09	(0.71 to 1.66)	0.70	0.90	(0.59 to 1.39)	0.64
TBI subgroup	6 (6.4)	2 (4.5)	1.40	(0.29 to 6.68)	0.67	0.61	(0.14 to 2.70)	0.51
Secondary								
24-h mortality	82 (13.4)	49 (11.5)	1.16	(0.83 to 1.62)	0.37	1.08	(0.77 to 1.52)	0.67
TBI subgroup	19 (20.2)	6 (13.6)	1.48	(0.64 to 3.45)	0.36	0.89	(0.41 to 1.96)	0.78
28-d mortality	110 (17.9)	66 (15.5)	1.16	(0.88 to 1.53)	0.30	1.10	(0.83 to 1.47)	0.51
TBI subgroup	25 (26.6)	11 (25.0)	1.06	(0.58 to 1.96)	0.84	0.84	(0.45 to 1.56)	0.57

*Adjusted for age, sex, injury type, head Abbreviated Injury Scale score, prehospital

PTED

Sperry et al. *JACS* 2023; DOI: 10.1097/XCS.0000000000000708.

Whole Blood LITES



CEPTED

Sperry et al. *JACS* 2023; DOI: 10.1097/XCS.0000000000000708.

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THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

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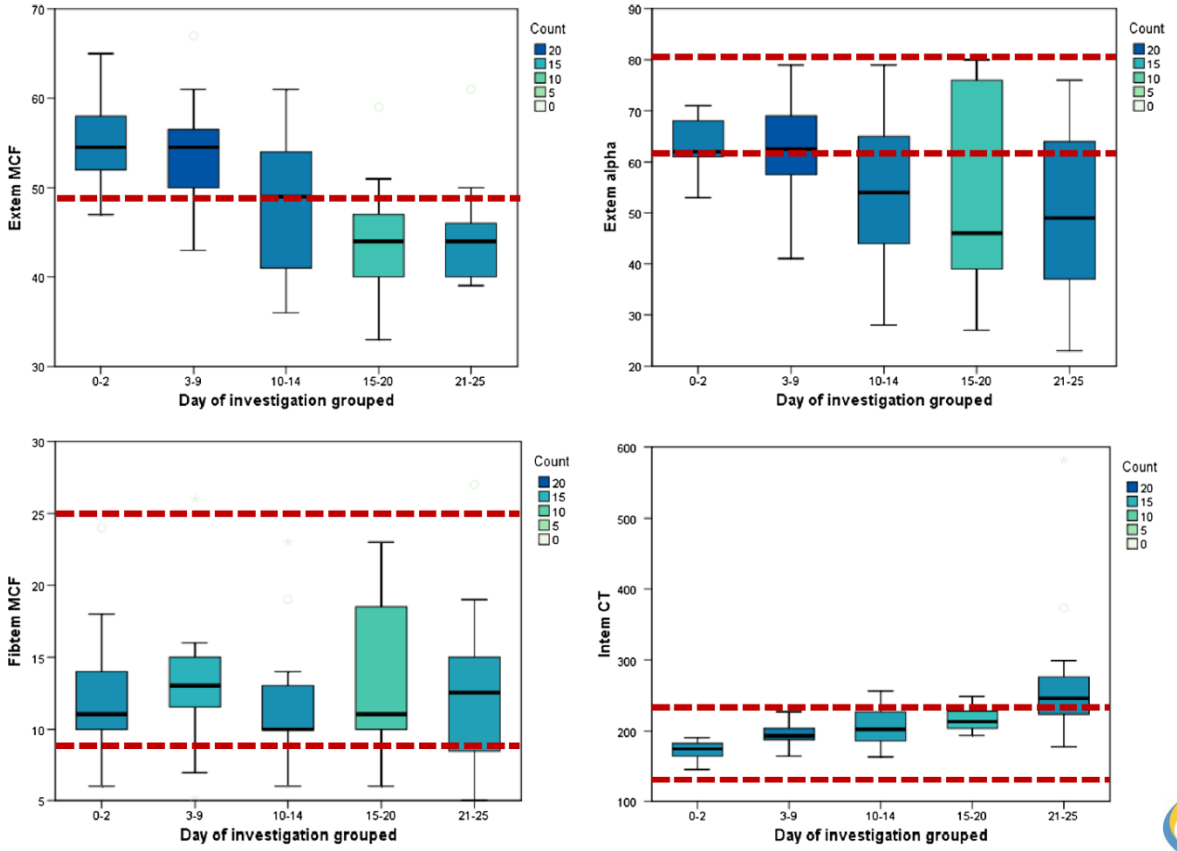
TOWAR

WB Coagulation Function Over Time



Strandness et al. *JTACS* 2015;78:S31 – S38.

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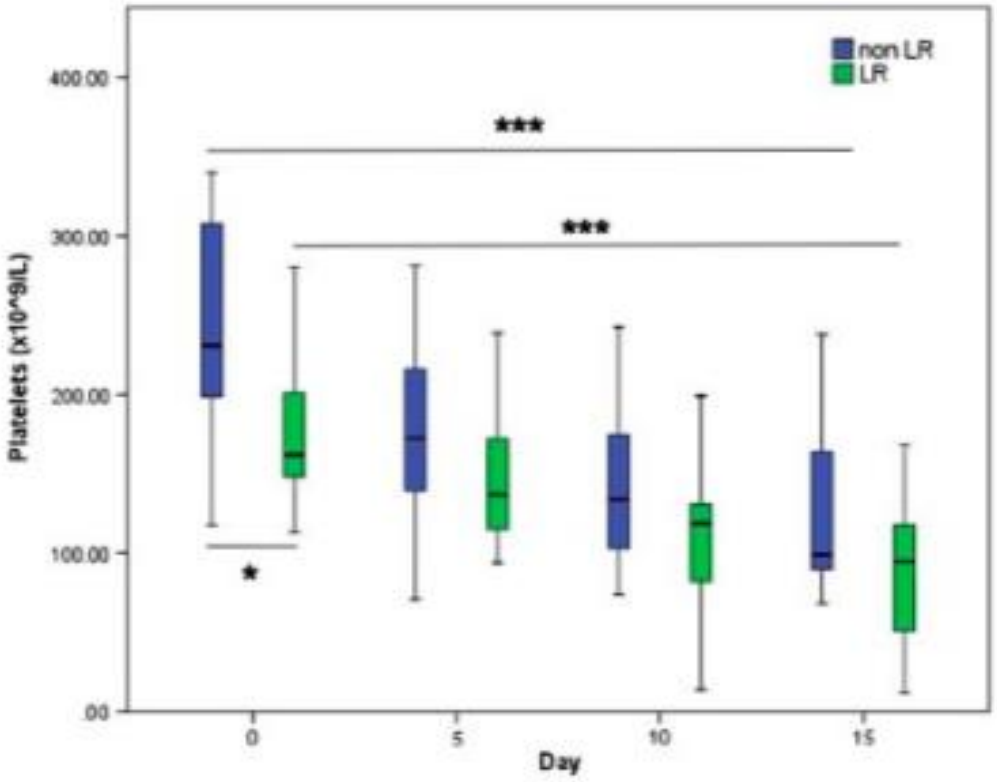
Effects of Leukoreduction



Remy et al. *JTACS* 2018;84:S104 – S114.

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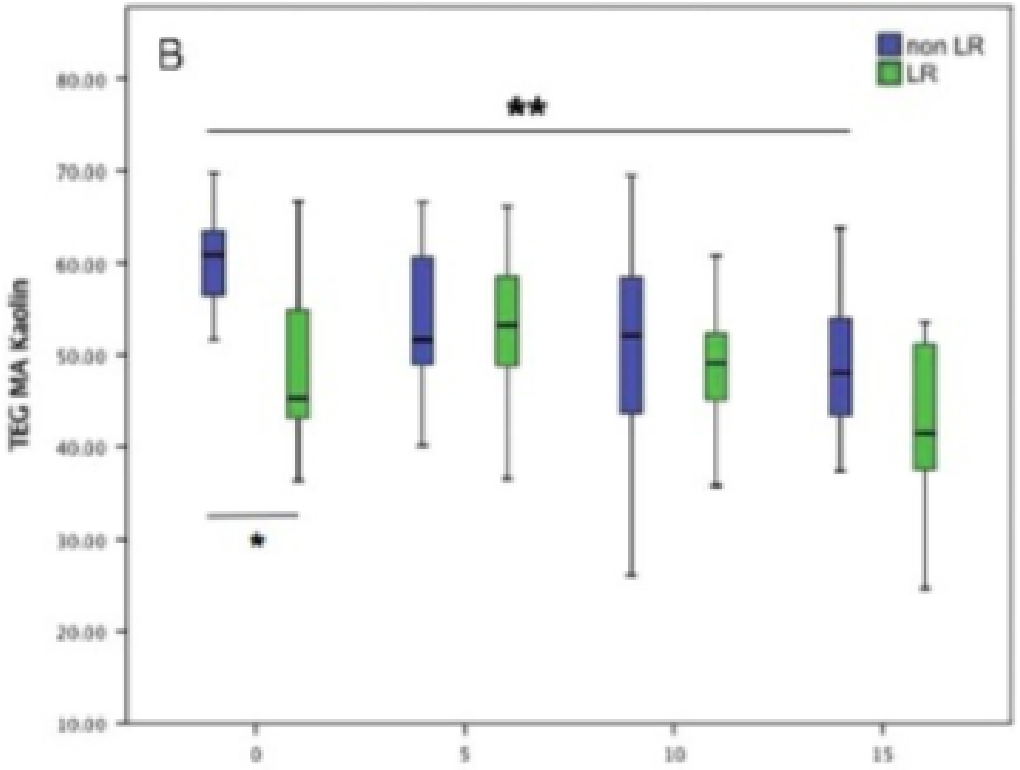
Effects of Leukoreduction



Remy et al. *JTACS* 2018;84:S104 – S114.

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Leukodepletion and Belmont

Blood Cell Count Components Pre and Post Cold Stored Leukoreduced Whole Blood infusion via Belmont RI (Rapid Infuser)

Component	Average Pre-Belmont (SD)	Average Post-Belmont (SD)	Mean Difference (SD)	95% Confidence Interval	*p* Value
Red Cell Count (thousand cells/μL)	3.90 (0.77)	4.12 (0.91)	−0.23 (1.09)	−1.01 ⟨−⟩ 0.55	0.552
Hemoglobin (mg/dL)	11.97 (2.80)	12.44 (2.72)	−0.47 (3.30)	1.89 ⟨−⟩ 2.83	0.663
Hematocrit (Liter of cell/ liter blood)	37.30 (7.82)	39.33 (9.03)	−2.03 (10.56)	−9.58 ⟨−⟩ 5.52	0.558
Mean Cell Volume (fL)	95.78 (5.21)	95.50 (5.96)	0.28 (1.38)	−0.71 ⟨−⟩ 1.27	0.538
Platelet Count (100,000 cells/μL)	75.50 (27.32)	59.60 (24.96)	15.9 (13.37)	6.35 ⟨−⟩ 25.44	0.004

Cell count components compared between the Pre and Post Belmont whole blood samples. *P* values represent one-sided Student-t-test.

Thromboelastography Component Comparison Pre and Post Cold Stored Leukoreduced Whole Blood infusion via Belmont RI (Rapid Infuser).

Component	Average Pre-Belmont (SD)	Average Post-Belmont (SD)	Mean Difference (SD)	95% Confidence Interval	p Value
R time (minutes)	10.03 (4.97)	8.12 (2.62)	1.91 (3.19)	−0.37 ⟨−⟩ 4.19	0.091
K time (minutes)	4.76 (3.37)	4.66 (0.91)	0.10 (3.47)	−2.39 ⟨−⟩ 2.59	0.929
α Angle (degrees)	57.49 (11.39)	57.22 (1.92)	0.27 (9.40)	−6.46 ⟨−⟩ 7.00	0.930
Maximum Amplitude (mm)	49.64 (6.06)	45.12 (1.44)	4.52 (5.75)	0.40 ⟨−⟩ 8.64	0.035
Clot Strength (Kdynes/cm^2)	5059.29 (1212.01)	4166.34 (769.70)	892.95 (1045.80)	144.82 ⟨−⟩ 1641.08	0.028

Thromboelastography components compared between the Pre and Post Belmont whole blood samples. P values represent one-sided Student-t-test.

14 Day old leukodepleted LTOWB before and after Belmont infusion

Hoyos Gomez T et al. *Injury* 2022 PMID 36180259.

OHSU vs BAMC

Variable	CIV (N=137) N		MIL (N=310) N		*p*-value
Age [a]	137	49.2 (20.0)	310	44.0 (19.0)	<0.01
Sex					<0.01
Male	97	70.8%	260	83.9%	
Female	40	29.2%	50	16.1%	
Mechanism					<0.01
Blunt	104	75.9%	196	63.2%	
Penetrating	33	24.1%	114	36.8%	
ISS [a]	117	21.6 (13.5)	108	21.1 (13.9)	0.73
Prehospital Blood					<0.01
Yes	1	0.7%	116	37.4%	
No	117	85.4%	194	62.6%	
Unknown	19	13.9%	0	0.0%	
AIS [b]	137		310		
Head/Neck		0 (0, 3)		0 (0, 2)	0.38
Face		0 (0, 0)		0 (0, 1)	0.03
Chest		2 (0, 3)		2 (0, 3)	0.99
Abdomen		2 (0, 3)		1 (0, 3)	0.72
Extremity		0 (0, 3)		1 (0, 2)	0.68
External		1 (1, 1)		0 (0, 0)	<0.01

[a] Data presented as mean (SD)
[b] Data presented as median (Q1, Q3)

Leukodepleted
Max age 14d

NLR
Max age 35d

Beiling et al Presented at 2022 AAST

OHSU vs BAMC

Variable	CIV (N=137)	MIL (N=310)	*p*-value
HFD [a]	15.8 (0, 22.36)	11 (0, 23)	0.15
ICU FD [a]	24.6 (3, 27.69)	22 (0, 27)	0.10
ARDS [b]	3 (2.2)	5 (1.6)	0.71
AKI [b]	16 (11.7)	10 (3.2)	<0.01
TR [b]	4 (2.9)	0 (0.0)	0.01
24-hour Transfusions [a]			
Whole blood	3 (1, 5)	2 (1, 4)	0.01
Platelets	0 (0, 2)	0 (0, 0)	<0.01
Red blood cells	2 (1, 6)	0.5 (0, 2)	<0.01
Plasma	3.5 (1, 7)	0 (0, 2)	<0.01
Cryoprecipitate	0 (0, 0)	0 (0, 0)	<0.01

[a] Data presented as median (Q1, Q3)
[b] Data presented as total events-N (%)

Leukodepleted
Max age 14d

NLR
Max age 35d

Beiling et al Presented at 2022 AAST

Domaine Leroy
Musigny Grand
Cru – France
Cost - $75,000

Low Titer O
Fresh whole blood
Still warm!

Cost - Priceless

Charles Shaw
Cabernet
California
Cost - $2.99

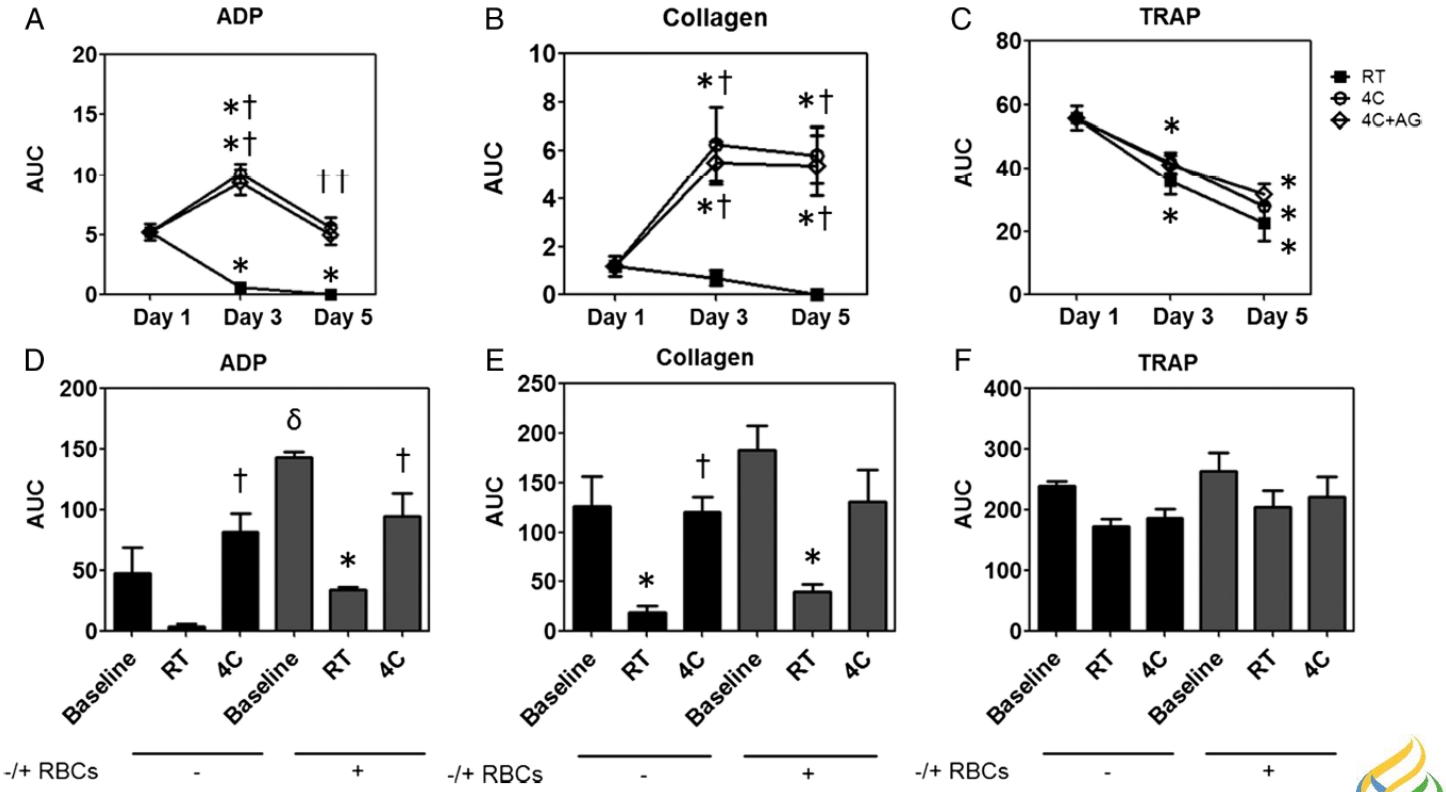
LTOWB – CPDA
Leukoreduced
35 Days old

Cost - $600

Cold Platelets

- Platelets currently stored at 22C in incubators for up to 5 days
- Risk of infection limits storage
- Warm platelets survive longer in vivo
  - 1.3 vs 3.9 days
- Trauma patients don't need 3.9 days

Platelet Function



Reddoch et al *Shock* 2014;41 Suppl 1:54 – 61.

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Cardiac Surgery - Norway

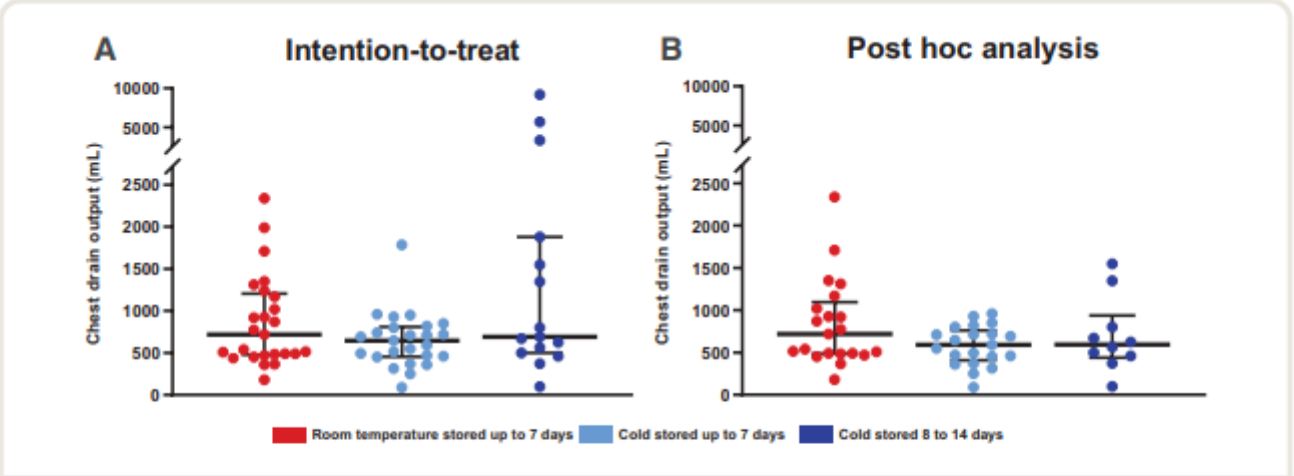

Fig. 2. Postoperative blood loss as measured by chest drain output for intention-to-treat patients (*A*) and *post hoc* analysis patients receiving room temperature–stored platelets, 7 days cold-stored platelets, and 8 to 14 days cold-stored platelets (*B*). The *dots* represent the individual study patients. The *lines* show median with interquartile range. The difference between the room temperature– and cold-stored for 7 days arms was not statistically significant ($P_{\text{intention-to-treat}} = 0.265$, $P_{\text{post hoc}} = 0.115$, two-tailed Mann–Whitney U test; SPSS Statistics for Windows, version 24.0, IBM, USA). The nonconcurrent stage II cold-stored for 8 to 14 days arm was not compared with the two stage I arms.

Strandeness et al. *Anesthesiology* 2020;133:1173 – 1183.

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Blood Product Use

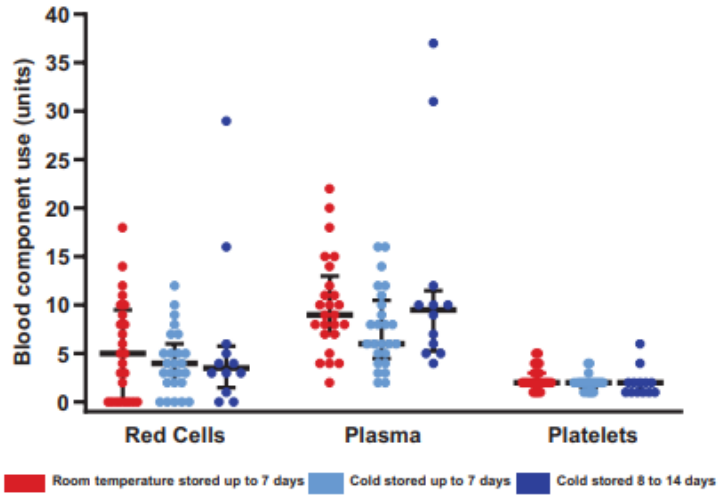

Fig. 3. Overall blood component use in patients receiving room temperature–stored platelets, 7 days cold-stored platelets, and 8 to 14 days cold-stored platelets. The *dots* represent the individual study patients. The *lines* show median with interquartile range. The difference between the room temperature– and cold-stored for 7 days arms was not statistically significant for number of transfused red cells ($P = 0.543$), plasma units ($P = 0.079$), or platelets ($P = 0.124$; two-tailed Mann–Whitney U test; SPSS Statistics for Windows). The nonconcurrent stage II arm was not compared with the two stage I arms.

Strandeness et al. Anesthesiology 2020;133:1173 – 1183.

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Safety Endpoints

Table 3. Safety Endpoints

	Room Temperature–stored up to 7 Days (n = 25)	Cold-stored up to 7 Days (n = 25)	Cold-stored for 8 to 14 Days (n = 15)
Arterial thromboembolism*	6 (24%)	6 (24%)	2 (13%)
Venous thromboembolism†	2 (8%)	0 (0%)	2 (13%)
Transfusion reaction caused by platelet transfusion	0 (0%)	0 (0%)	0 (0%)
Time to extubation, h	1.6 (5.08–21.37, 3.37–212.72)	6.6 (5.12–19.45, 3.67–349.02)	19.3 (4.28–27.27, 3.28–135.58)
Length of stay in intensive care unit, days‡	2 (1–5, 1–28+)	2 (1–6, 1–28+)	4 (2–14, 1–28+)
28-Day mortality	3 (12%)	2 (8%)	2 (13%)

The results are given as median (interquartile range, minimum, maximum) or count (percentage).

* Days from surgery: room temperature–stored up to 7 days: 3, 9, 10, 13, 16, and 22. Cold-stored up to 7 days: 2, 4, 4, 7, 8, and 14. Cold-stored from 8 to 14 days: 2 and 6.

†Days from surgery: room temperature–stored up to 7 days: 1 and 6; cold-stored for 8 to 14 days: 1 and 9.

‡‡ patient in the group with room temperature–stored up to 7 days, one patient in the cold-stored up to 7 days group, and two patients in the cold-stored for 8 to 14 days remained in intensive care at the conclusion of the 28-day study period. These were defined as 28 days for statistical analysis.

Strandeness et al. Anesthesiology 2020;133:1173 – 1183.

FDA and CSPs

- 2015 – FDA approves CSPs stored up to 3 days for resuscitation
- 2019 – FDA grants South Texas Blood & Tissue Center approval to manufacture and distribute CSP up to 14 days when conventional platelets not available or not practical
- Approved for battlefield use

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Fresh Frozen Plasma

- Obtained from whole blood and frozen at -20C within 8 hours
- Stored up to 1 year
- Freeze/thaw diminishes function
- Approximately 30 minutes to thaw
- Greatest source of waste at OHSU

Thawed FFP

- Once thawed, FFP can be maintained at 1 – 6C for up to 5 days
- Minimal degradation of factor function
- Mitigates logistical difficulties of maintaining a balanced resuscitation

Decrease (%) in FFP Coagulation Factor Levels Day 0 to Day 5

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FP24

- Similar to FFP and used interchangeably
- Frozen between 8 and 24 hours
- Additional testing (anti - HLA antibodies, TRALI)
- Further fractionation of plasma
- Not approved to create thawed plasma

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Liquid Plasma

- Never frozen
- Approved for 26 days
- Minimal factor degradation
- Immediately available

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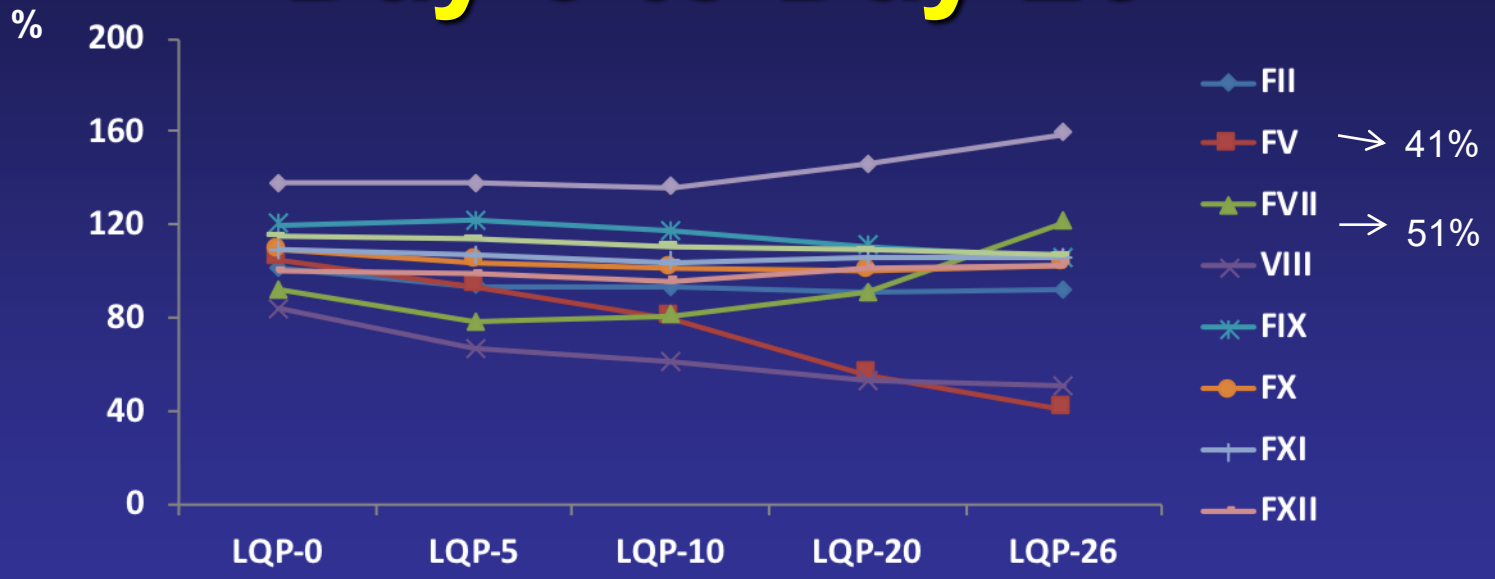
Clotting Factors in LQP
Day 0 to Day 26



>88% of the initial activities retained

Increase in FVII, XII and vWF in some plasma units: cold promoted activation

Dried Plasma

- Logistically superior
- US products are in early FDA trials
- German LyoPlas
  - Single donor (Blood type compatibility)
  - Stored up to 15 months
  - 200,000 TFNs – 0.023% major complications similar to FFP

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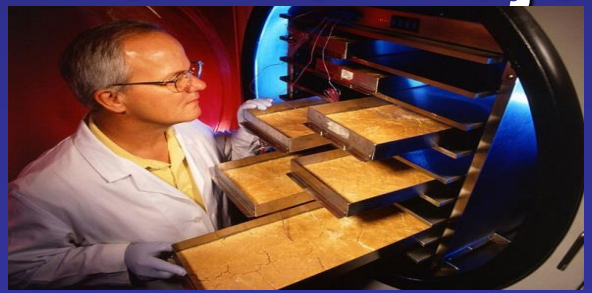
French Flyp

- Up to 11 donors/unit (Universal)
- Pathogen reduced
- Stored up to 24 months
- Available to US SF on IRB protocol
- 1000 TFNs with no major adverse events



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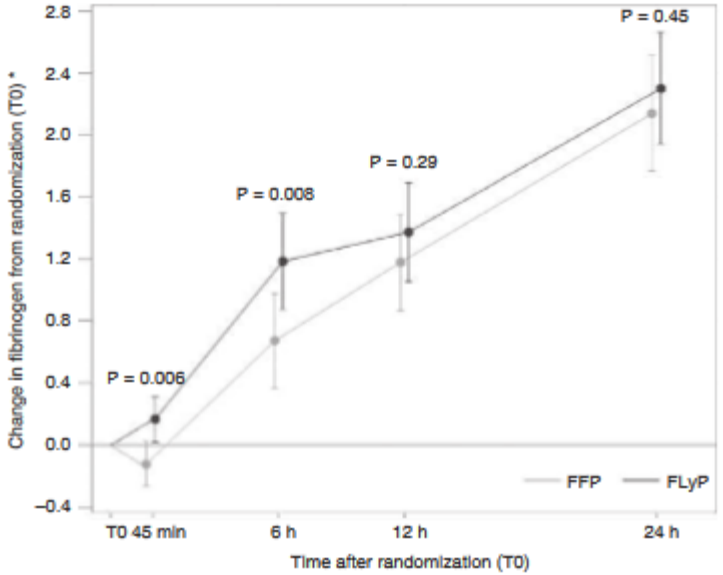
Randomized Trial FLyP

- Open label randomized trial
- 48 trauma patients requiring emergent transfusion
- Exclusion criteria
  - Received blood prior to randomization
  - Moribund

Garrigue et al *Journal of Thrombosis and Haemostasis* 2017;16:1 – 9.

Outcomes FLyP Trial



	FLyP		FFP		
	No.	Median [IQR]	No.	Median [IQR]	*P*-value
Fibrinogen concentrates, 1.5-g doses	23	2 [0–3]	24	3 [2–4]	0.052
Crystalloids, 500-mL doses	21	3 [2–4]	22	4 [3–5]	0.28
Colloids, 500-mL doses	22	1.5 [1–2]	23	2 [1–4]	0.12
Platelet concentrate, units	23	0 [0–1]	24	1 [0–2]	0.14
Red blood cell, units	23	6 [4–10]	24	7 [6–11.5]	0.12
Plasma, units	23	4 [4–8]	24	5.5 [4–9]	0.27

Garrigue et al *Journal of Thrombosis and Haemostasis* 2017;16:1 – 9.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 26, 2018 VOL. 379 NO. 4

Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock

J.L. Sperry, F.X. Guyette, J.B. Brown, M.H. Yazer, D.J. Triulzi, B.J. Early-Young, P.W. Adams, B.J. Daley, R.S. Miller, B.G. Harbrecht, J.A. Claridge, H.A. Phelan, W.R. Witham, A.T. Putnam, T.M. Duane, L.H. Alarcon, C.W. Callaway, B.S. Zuckerbraun, M.D. Neal, M.R. Rosengart, R.M. Forsythe, T.R. Billiar, D.M. Yealy, A.B. Peitzman, and M.S. Zenati, for the PAMPer Study Group*

TRAUMA
Center

PAMPer Trial

- Pragmatic, multicenter, cluster randomized
- Air transport, scene or transfer
- Thawed plasma vs standard care
- 501 patients
  - 271 standard care
  - 230 thawed plasma

Sperry et al. *NEJM* 2018;379:315 – 326

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Group Comparisons

	Standard	Plasma
Transported from referral hospital — no. (%)	59 (21.8)	52 (22.6)
Median prehospital volume of crystalloid solution (IQR) — ml§	900 (0–1500)	500 (0–1250)
Prehospital red-cell transfusion — no. (%)¶	114 (42.1)	60 (26.1)
Initial Glasgow Coma Scale score <8 — no. (%)‖	129 (47.6)	103 (44.8)
Median prehospital systolic blood pressure (IQR) — mm Hg**	69 (61–81)	71 (64–81)
Median prehospital heart rate (IQR) — beats/min	115 (96–126)	117 (104–128)
Prehospital intubation — no. (%)	141 (52.0)	115 (50.0)
Prehospital cardiopulmonary resuscitation — no. (%)	18 (6.6)	13 (5.7)
Median prehospital transport time (IQR) — min	40 (33–51)	42 (34–53)
Median Injury Severity Score (IQR)††	21 (12–29)	22 (14–33)

Sperry et al. *NEJM* 2018;379:315 – 326

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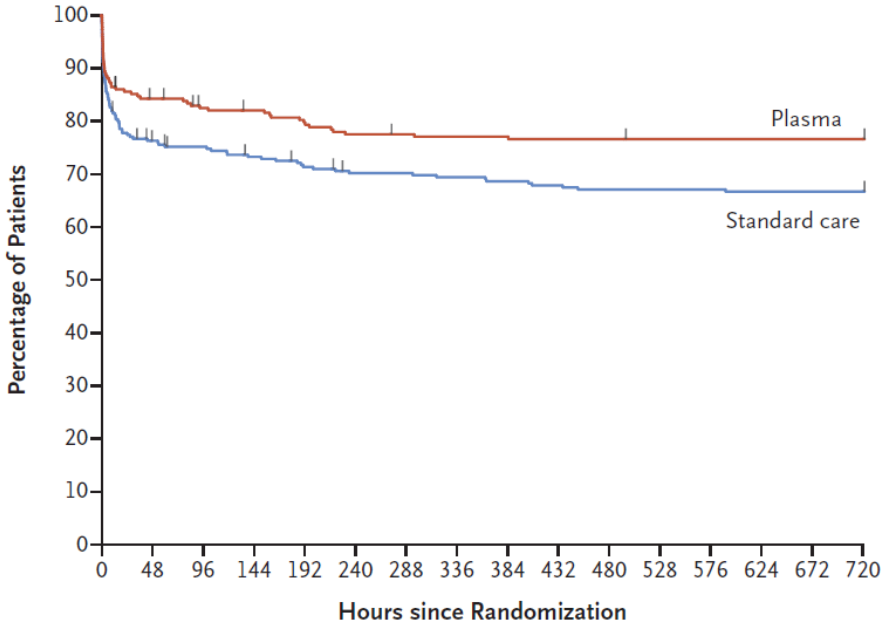
Kaplan – Meier Survival

A Survival



No. at Risk							
Plasma	230	183	172	170	169	168	168
Standard care	271	194	181	179	173	172	172

Sperry et al. *NEJM* 2018;379:315 – 326.

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Potential Benefits

- Over 1000 proteins in plasma
- Many are biologically active
- Many have unknown functions
- Suppression of dysfunctional inflammation
- Decreased endothelial permeability
- Rebuilding the glycocalyx

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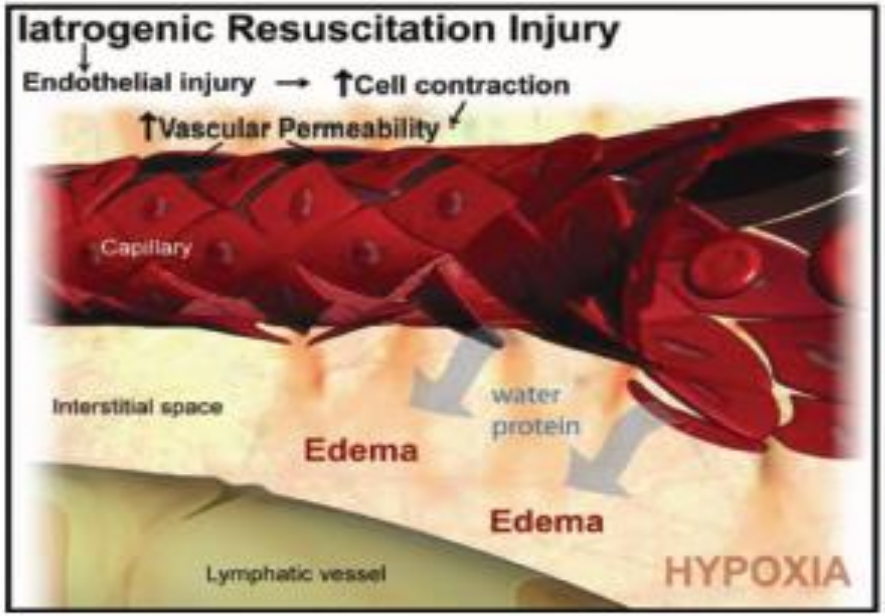
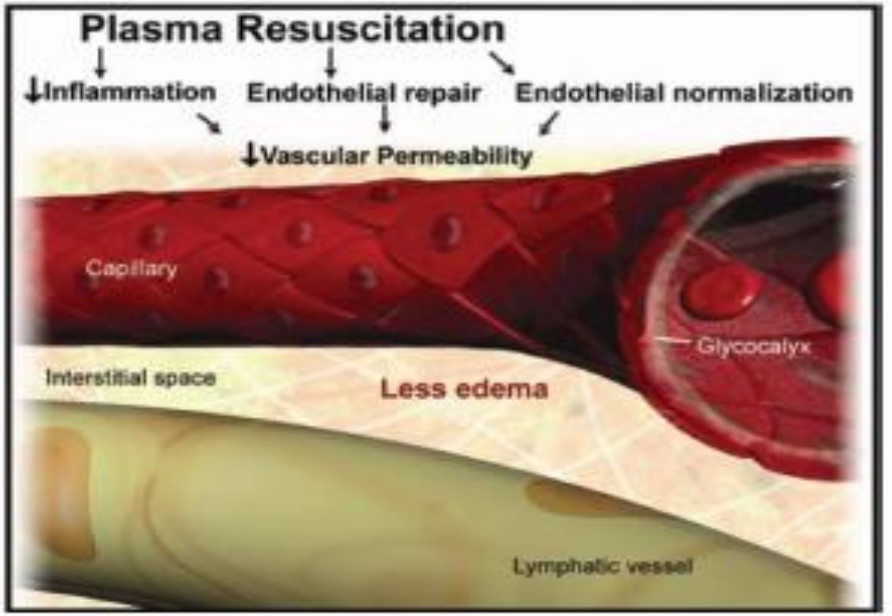
Working Biological Model
Endotheliopathy of Trauma

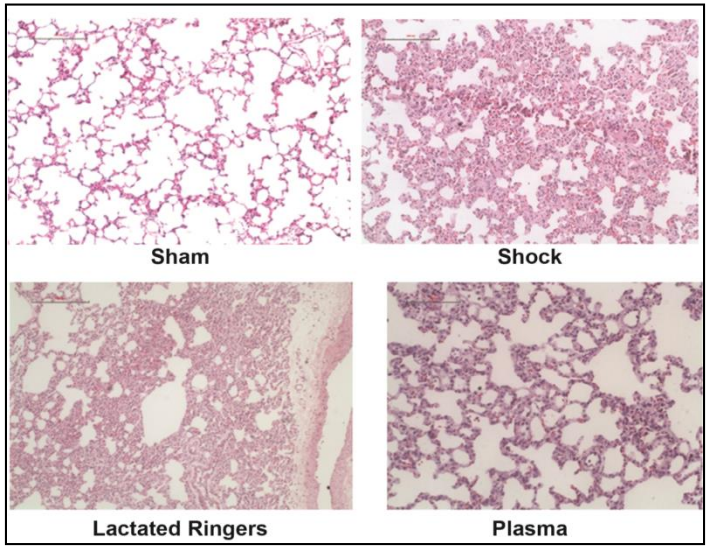


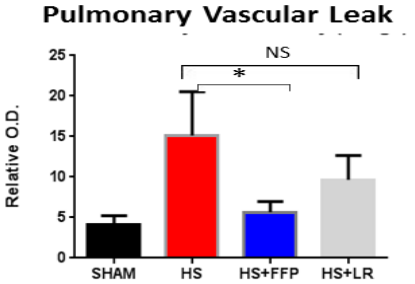


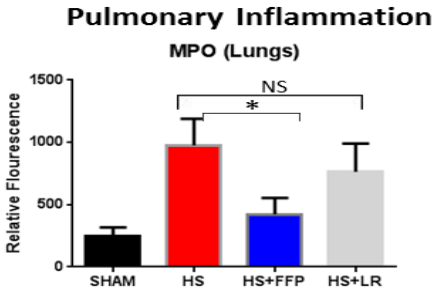
Pati et al. *J Trauma* 2010;69 Suppl 1:S55 – S63.

Lung Injury in HS is inhibited by FFP

Lung Tissue







N=5 mice/group

Peng et al *Shock* 2013;40:195 – 202.

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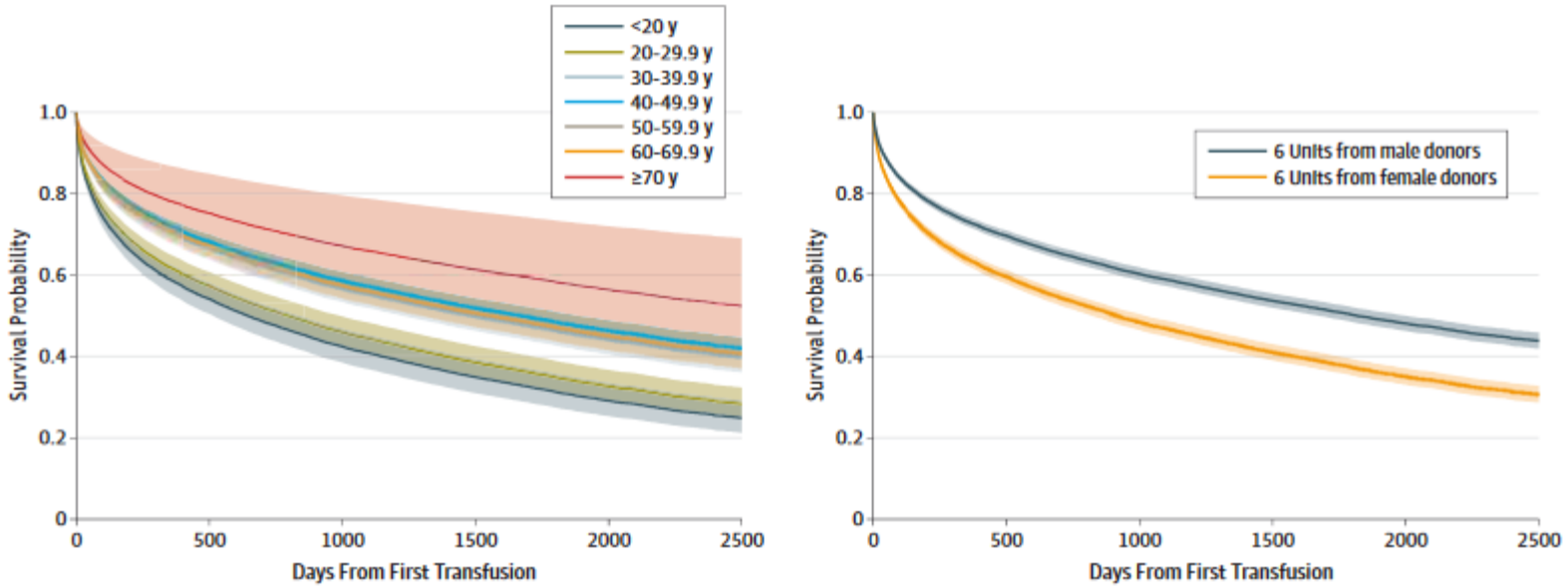
Donor Characteristics

Figure 2. Patient Survival According to Donor Age and Sex Using a Base Case of 6 Total Transfusions (Study Mean) Over the Study Period Between 2006 and 2013



This figure represents the survival of a recipient of 6 units of only one donor characteristic vs the other at baseline at the study mean recipient age and median Charlson Score.

Chasse et al *JAMA Internal Medicine* 2016;176:1307 – 1314.

Was Bram Stoker Right?

nature medicine

Nature Med May 2014

Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice

Saul A Villeda[1–6], Kristopher E Plambeck[1,2,10], Jinte Middeldorp[6,10], Joseph M Castellano[6,10], Kira I Mosher[6,7,10], Jian Luo[6], Lucas K Smith[1,2], Gregor Bieri[1,2,6,7], Karin Lin[1–3], Daniela Berdnik[6], Rafael Wabl[6], Joe Udeochu[1,2,4], Elizabeth G Wheatley[1,2,5], Bende Zou[8], Danielle A Simmons[6], Xinmin S Xie[8], Frank M Longo[6] & Tony Wyss-Coray[6,7,9]

Exposure of aged mice to young blood late in life is capable of rejuvenating cognitive function

Science May 2014

Restoring Systemic GDF11 Levels Reverses Age-Related Dysfunction in Mouse Skeletal Muscle

Manisha Sinha,[1,2,3,4*] Young C. Jang,[1,2,4*] Juhyun Oh,[1,2,4] Danika Khong,[1,2,4] Elizabeth Y. Wu,[1,2,4] Rohan Manohar,[1,2,4] Christine Miller,[1,2,4] Samuel G. Regalado,[1,5] Francesco S. Loffredo,[1,6] James R. Pancoast,[1,6] Michael F. Hirshman,[2] Jessica Lebowitz,[1,2,4] Jennifer L. Shadrach,[1,2,3] Massimiliano Cerletti,[1,2†] Mi-Jeong Kim,[2] Thomas Serwold,[2] Laurie J. Goodyear,[2,7] Bernard Rosner,[8] Richard T. Lee,[1,6] Amy J. Wagers[1,2,3,4‡]

Exposure of aged mice to young blood is capable of rejuvenating skeletal muscle

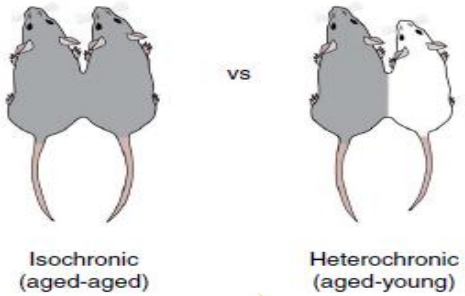
a

Parabiosis Model

Questions to consider:

1) Does the age and gender of the donor blood affect outcomes in recipients?

2) What are the soluble factors that modulate outcomes?



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Wartime Special Forces Medic

- Liquid cold stored whole blood
  - Type O
  - Low titer
  - Not leukodepleted
- Cold stored platelets
- Lyophilized plasma

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The Future

- Whole blood on the shelf
- Thrombosomes – Freeze dried platelets
- Platelet extracellular vesicles
- Oxygen carriers – Not Hgb substitutes
- Products as curative drugs beyond resuscitation


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