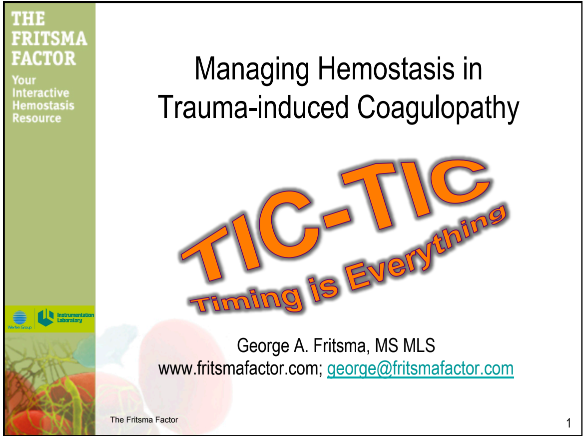
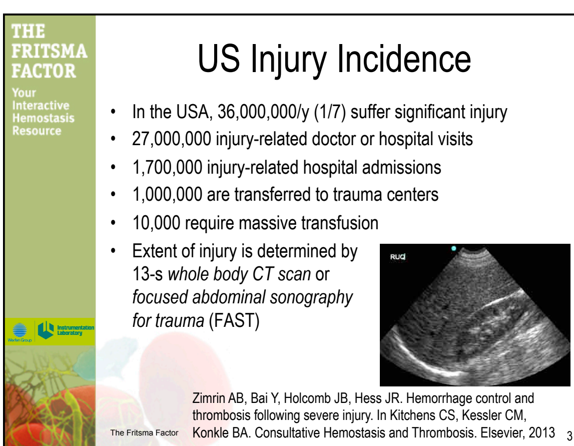
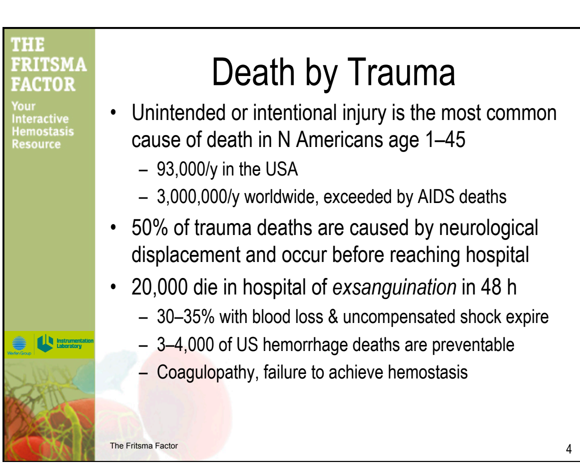
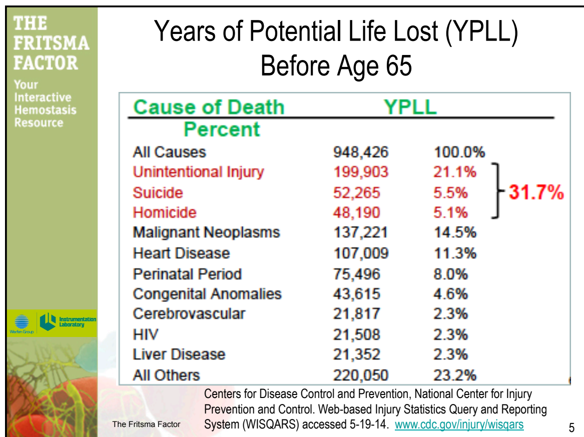
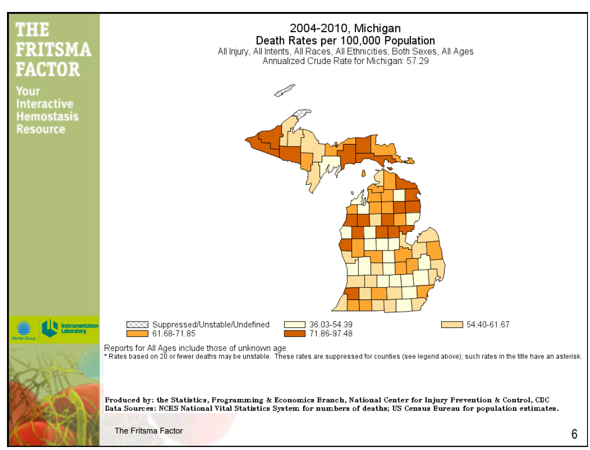

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Managing Hemostasis in
Trauma-induced Coagulopathy
TIC-TIC
Timing is Everything
George A. Fritsma, MS MLS
www.fritsmafactor.com; george@fritsmafactor.com
The Fritsma Factor
1

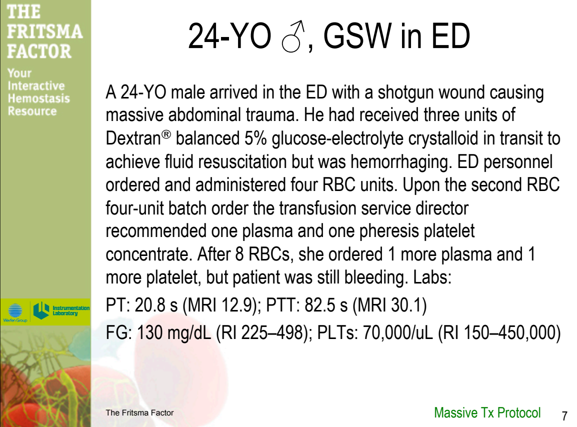
THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Sponsored By…
Werfen Group
Instrumentation Laboratory
The Fritsma Factor
2

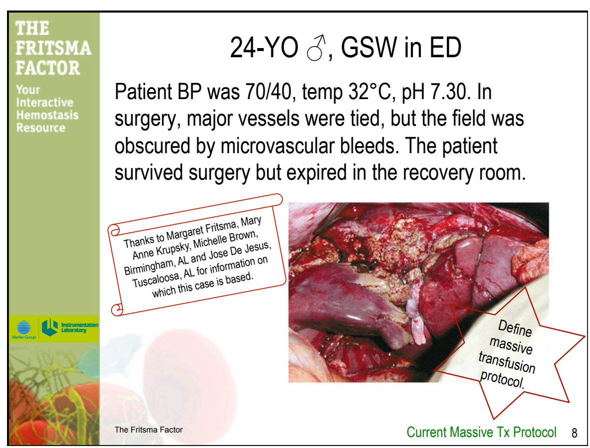

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
US Injury Incidence
• In the USA, 36,000,000/y (1/7) suffer significant injury
• 27,000,000 injury-related doctor or hospital visits
• 1,700,000 injury-related hospital admissions
• 1,000,000 are transferred to trauma centers
• 10,000 require massive transfusion
• Extent of injury is determined by 13-s whole body CT scan or focused abdominal sonography for trauma (FAST)
Zimrin AB, Bai Y, Holcomb JB, Hess JR. Hemorrhage control and thrombosis following severe injury. In Kitchens CS, Kessler CM, Konkle BA. Consultative Hemostasis and Thrombosis. Elsevier, 2013
The Fritsma Factor
3

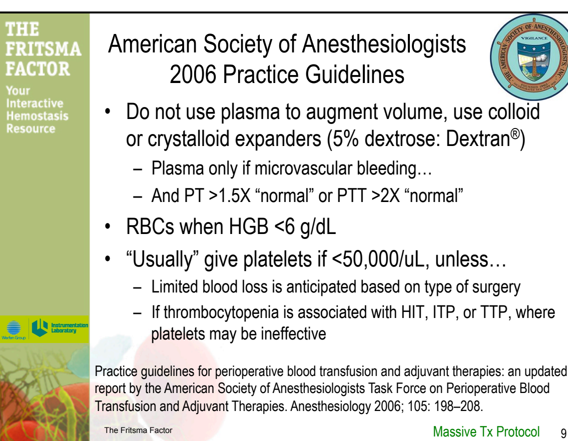

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Death by Trauma
• Unintended or intentional injury is the most common cause of death in N Americans age 1–45
– 93,000/y in the USA
– 3,000,000/y worldwide, exceeded by AIDS deaths
• 50% of trauma deaths are caused by neurological displacement and occur before reaching hospital
• 20,000 die in hospital of exsanguination in 48 h
– 30–35% with blood loss & uncompensated shock expire
– 3–4,000 of US hemorrhage deaths are preventable
– Coagulopathy, failure to achieve hemostasis
The Fritsma Factor
4

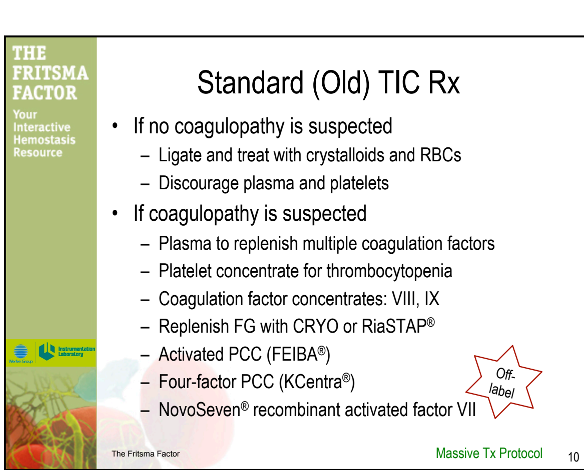

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Years of Potential Life Lost (YPLL)
Before Age 65
Cause of Death YPLL Percent
All Causes 948,426 100.0%
Unintentional Injury 199,903 21.1%
Suicide 52,265 5.5%
Homicide 48,190 5.1%
31.7%
Malignant Neoplasms 137,221 14.5%
Heart Disease 107,009 11.3%
Perinatal Period 75,496 8.0%
Congenital Anomalies 43,615 4.6%
Cerebrovascular 21,817 2.3%
HIV 21,508 2.3%
Liver Disease 21,352 2.3%
All Others 220,050 23.2%
Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Web-based Injury Statistics Query and Reporting System (WISQARS) accessed 5-19-14. www.cdc.gov/injury/wisqars
The Fritsma Factor
5

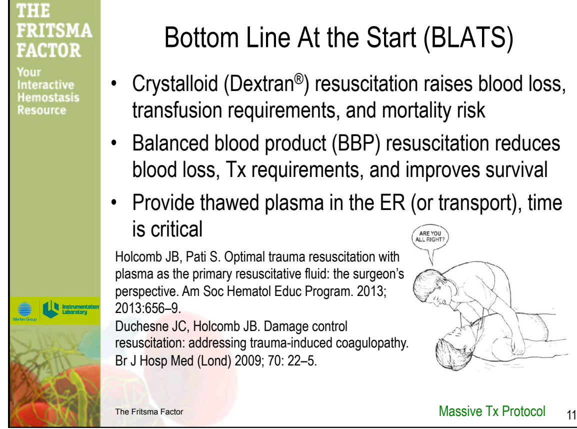

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
2004-2010, Michigan
Death Rates per 100,000 Population
All Injury, All Intents, All Races, All Ethnicities, Both Sexes, All Ages
Annualized Crude Rate for Michigan: 57.29
Suppressed/Unstable/Undefined
36.03-54.39
54.40-61.67
61.68-71.85
71.86-97.48
Reports for All Ages include those of unknown age.
Produced by: the Statistics, Programming & Economics Branch, National Center for Injury Prevention & Control, CDC
Data Sources: NCES National Vital Statistics System for numbers of deaths; US Census Bureau for population estimates.
The Fritsma Factor
6

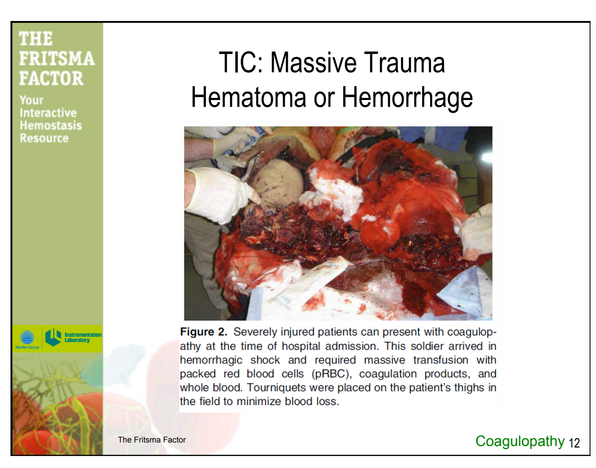

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
24-YO ♂, GSW in ED
A 24-YO male arrived in the ED with a shotgun wound causing massive abdominal trauma. He had received three units of Dextran® balanced 5% glucose-electrolyte crystalloid in transit to achieve fluid resuscitation but was hemorrhaging. ED personnel ordered and administered four RBC units. Upon the second RBC four-unit batch order the transfusion service director recommended one plasma and one pheresis platelet concentrate. After 8 RBCs, she ordered 1 more plasma and 1 more platelet, but patient was still bleeding. Labs:
PT: 20.8 s (MRI 12.9); PTT: 82.5 s (MRI 30.1)
FG: 130 mg/dL (RI 225–498); PLTs: 70,000/uL (RI 150–450,000)
The Fritsma Factor
Massive Tx Protocol
7

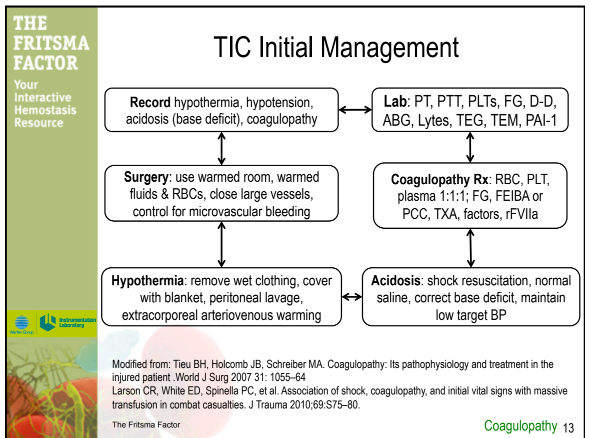

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
24-YO ♂, GSW in ED
Patient BP was 70/40, temp 32°C, pH 7.30. In surgery, major vessels were tied, but the field was obscured by microvascular bleeds. The patient survived surgery but expired in the recovery room.
Thanks to Margaret Fritsma, Mary Anne Krupsky, Michelle Brown, Birmingham, AL and Jose De Jesus, Tuscaloosa, AL for information on which this case is based.
Define massive transfusion protocol.
The Fritsma Factor
Current Massive Tx Protocol
8

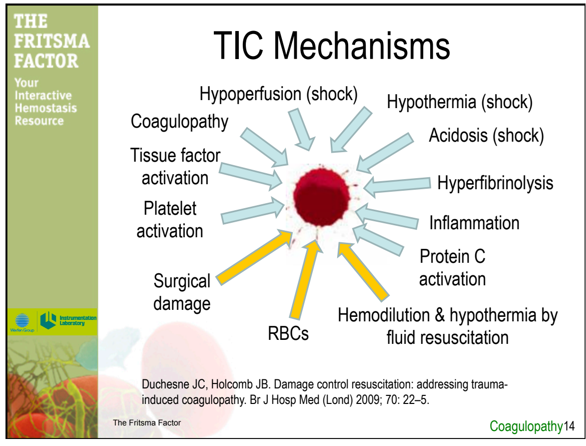

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
American Society of Anesthesiologists
2006 Practice Guidelines
• Do not use plasma to augment volume, use colloid or crystalloid expanders (5% dextrose: Dextran®)
– Plasma only if microvascular bleeding…
– And PT >1.5X "normal" or PTT >2X "normal"
• RBCs when HGB <6 g/dL
• "Usually" give platelets if <50,000/uL, unless…
– Limited blood loss is anticipated based on type of surgery
– If thrombocytopenia is associated with HIT, ITP, or TTP, where platelets may be ineffective
Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Anesthesiology 2006; 105: 198–208.
The Fritsma Factor
Massive Tx Protocol
9

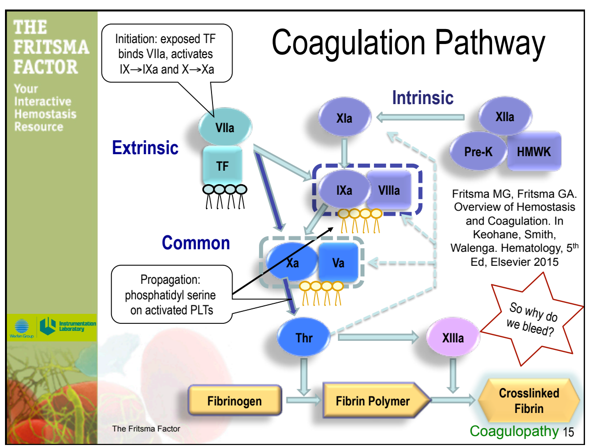

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Standard (Old) TIC Rx
• If no coagulopathy is suspected
– Ligate and treat with crystalloids and RBCs
– Discourage plasma and platelets
• If coagulopathy is suspected
– Plasma to replenish multiple coagulation factors
– Platelet concentrate for thrombocytopenia
– Coagulation factor concentrates: VIII, IX
– Replenish FG with CRYO or RiaSTAP®
– Activated PCC (FEIBA®)
– Four-factor PCC (KCentra®)
– NovoSeven® recombinant activated factor VII
Off-label
The Fritsma Factor
Massive Tx Protocol
10

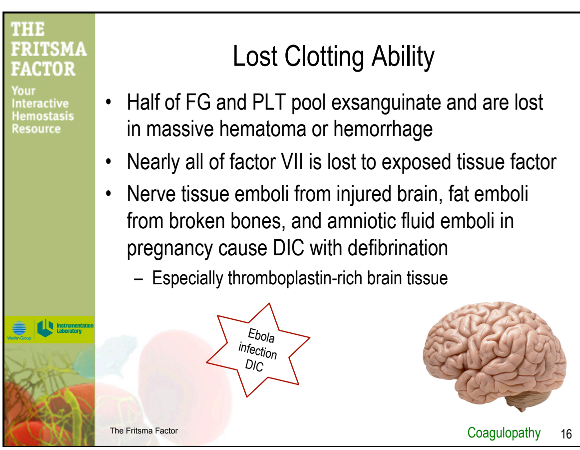

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Bottom Line At the Start (BLATS)
• Crystalloid (Dextran®) resuscitation raises blood loss, transfusion requirements, and mortality risk
• Balanced blood product (BBP) resuscitation reduces blood loss, Tx requirements, and improves survival
• Provide thawed plasma in the ER (or transport), time is critical
ARE YOU ALL RIGHT?
Holcomb JB, Pati S. Optimal trauma resuscitation with plasma as the primary resuscitative fluid: the surgeon's perspective. Am Soc Hematol Educ Program. 2013; 2013:656–9.
Duchesne JC, Holcomb JB. Damage control resuscitation: addressing trauma-induced coagulopathy. Br J Hosp Med (Lond) 2009; 70: 22–5.
The Fritsma Factor
Massive Tx Protocol
11

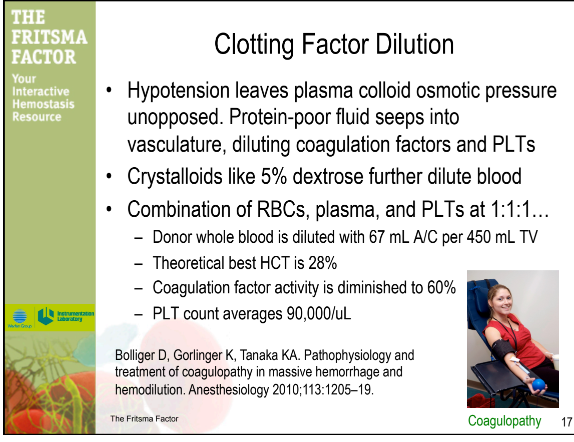

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
TIC: Massive Trauma
Hematoma or Hemorrhage
Figure 2. Severely injured patients can present with coagulopathy at the time of hospital admission. This soldier arrived in hemorrhagic shock and required massive transfusion with packed red blood cells (pRBC), coagulation products, and whole blood. Tourniquets were placed on the patient's thighs in the field to minimize blood loss.
The Fritsma Factor
Coagulopathy 12

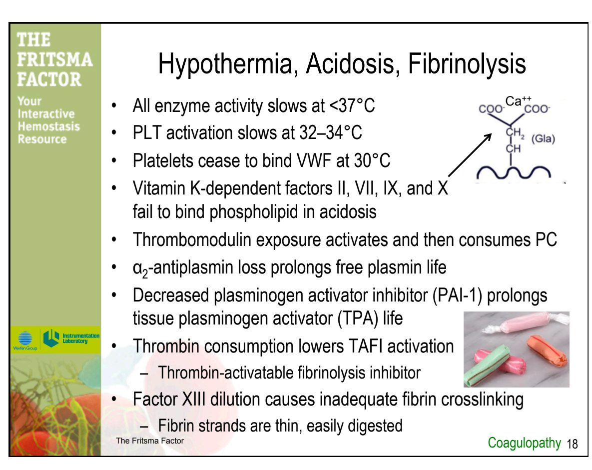

TIC Initial Management
Record hypothermia, hypotension, acidosis (base deficit), coagulopathy
Lab: PT, PTT, PLTs, FG, D-D, ABG, Lytes, TEG, TEM, PAI-1
Surgery: use warmed room, warmed fluids & RBCs, close large vessels, control for microvascular bleeding
Coagulopathy Rx: RBC, PLT, plasma 1:1:1; FG, FEIBA or PCC, TXA, factors, rFVIIa
Hypothermia: remove wet clothing, cover with blanket, peritoneal lavage, extracorporeal arteriovenous warming
Acidosis: shock resuscitation, normal saline, correct base deficit, maintain low target BP
Modified from: Tieu BH, Holcomb JB, Schreiber MA. Coagulopathy: Its pathophysiology and treatment in the injured patient .World J Surg 2007 31: 1055–64
Larson CR, White ED, Spinella PC, et al. Association of shock, coagulopathy, and initial vital signs with massive transfusion in combat casualties. J Trauma 2010;69:S75–80.
The Fritsma Factor
Coagulopathy 13

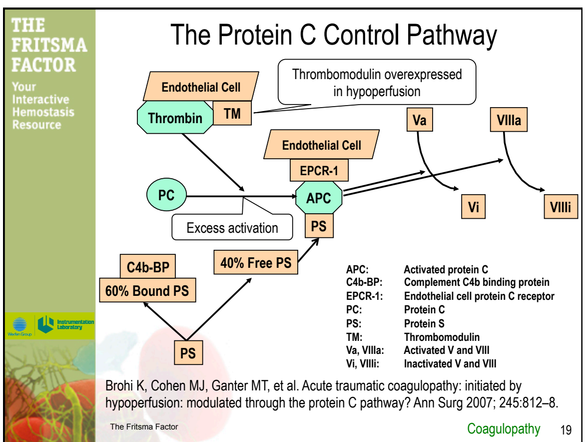

TIC Mechanisms
Hypoperfusion (shock)
Hypothermia (shock)
Coagulopathy
Acidosis (shock)
Tissue factor activation
Hyperfibrinolysis
Platelet activation
Inflammation
Protein C activation
Surgical damage
RBCs
Hemodilution & hypothermia by fluid resuscitation
Duchesne JC, Holcomb JB. Damage control resuscitation: addressing trauma-induced coagulopathy. Br J Hosp Med (Lond) 2009; 70: 22–5.
The Fritsma Factor
Coagulopathy 14

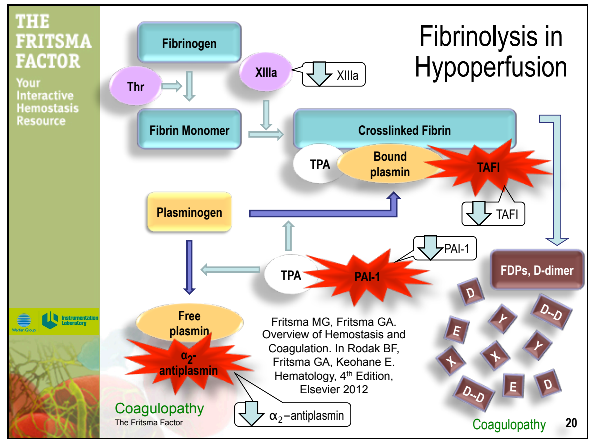

Coagulation Pathway
Initiation: exposed TF binds VIIa, activates IX→IXa and X→Xa
Extrinsic
Intrinsic
Common
VIIa
TF
XIa
XIIa
Pre-K
HMWK
IXa
VIIIa
Xa
Va
Thr
XIIIa
Propagation: phosphatidyl serine on activated PLTs
Fritsma MG, Fritsma GA. Overview of Hemostasis and Coagulation. In Keohane, Smith, Walenga. Hematology, 5th Ed, Elsevier 2015
So why do we bleed?
Fibrinogen
Fibrin Polymer
Crosslinked Fibrin
The Fritsma Factor
Coagulopathy 15


Lost Clotting Ability
Half of FG and PLT pool exsanguinate and are lost in massive hematoma or hemorrhage
Nearly all of factor VII is lost to exposed tissue factor
Nerve tissue emboli from injured brain, fat emboli from broken bones, and amniotic fluid emboli in pregnancy cause DIC with defibrination
– Especially thromboplastin-rich brain tissue
Ebola infection DIC
The Fritsma Factor
Coagulopathy 16


Clotting Factor Dilution
Hypotension leaves plasma colloid osmotic pressure unopposed. Protein-poor fluid seeps into vasculature, diluting coagulation factors and PLTs
Crystalloids like 5% dextrose further dilute blood
Combination of RBCs, plasma, and PLTs at 1:1:1…
– Donor whole blood is diluted with 67 mL A/C per 450 mL TV
– Theoretical best HCT is 28%
– Coagulation factor activity is diminished to 60%
– PLT count averages 90,000/uL
Bolliger D, Gorlinger K, Tanaka KA. Pathophysiology and treatment of coagulopathy in massive hemorrhage and hemodilution. Anesthesiology 2010;113:1205–19.
The Fritsma Factor
Coagulopathy 17


Hypothermia, Acidosis, Fibrinolysis
All enzyme activity slows at <37°C
PLT activation slows at 32–34°C
Platelets cease to bind VWF at 30°C
Vitamin K-dependent factors II, VII, IX, and X fail to bind phospholipid in acidosis
Thrombomodulin exposure activates and then consumes PC
α2-antiplasmin loss prolongs free plasmin life
Decreased plasminogen activator inhibitor (PAI-1) prolongs tissue plasminogen activator (TPA) life
Thrombin consumption lowers TAFI activation
– Thrombin-activatable fibrinolysis inhibitor
Factor XIII dilution causes inadequate fibrin crosslinking
– Fibrin strands are thin, easily digested
The Fritsma Factor
Coagulopathy 18





Injury Severity Score (ISS)

Region	Description (Examples)	Injury Score (1−6)	Highest 3 Squared
Head & neck	Cerebral contusion	3 (Serious)	9
Face	Scratches	1 (Minor)	
Chest	Sucking wound	4 (Severe)	16
Abdomen	Liver contusion Spleen rupture	2 (Moderate) 5 (Critical)	25
Extremity	Fractured femur	3 (Serious)	
External		1 (Minor)	1
Sum		ISS:	50

Maximum is 75. If injury is assigned a score of 6 (unsurvivable), the ISS is automatically 75. ISS correlates linearly with mortality, morbidity and hospital stay. See also automated revised ISS, TRISS, which incorporates respiration and BP.

Baker SP, et al. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. J Trauma 1974;14:187−96

Probability of Life-threatening Coagulopathy in Trauma

n = 58, received >10 RBCs Condition:	% Coagulopathy*
Injury severity score (ISS) >25 alone	10%
ISS >25 & systolic BP <70 mm Hg	39%
ISS >25 & body temp <34°C	49%
ISS >25 & pH <7.10	58%
ISS >25; SBP <70 mm Hg; body temp <34°C	85%
ISS >25; SBP <70 mm Hg; temp <34°C; pH <7.10	98%

*Life-threatening coagulopathy is arbitrarily defined as PT *and* PTT >2X mean of reference interval (MRI)

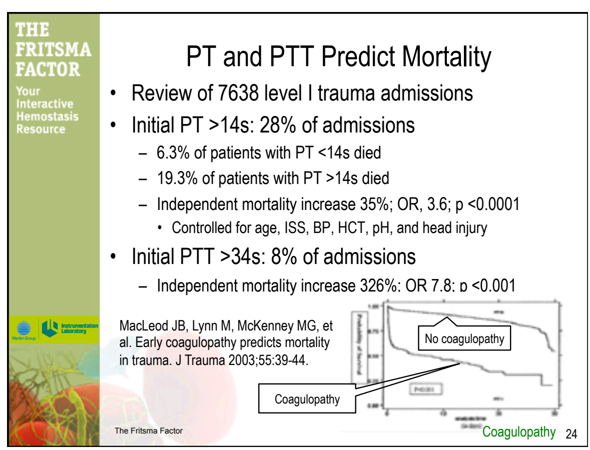
Cosgriff N, Moore EE, Sauaia A, et al. Predicting life-threatening coagulopathy in the massively transfused trauma patient: hypothermia and acidosis revisited. J Trauma 1997;42:857−62.

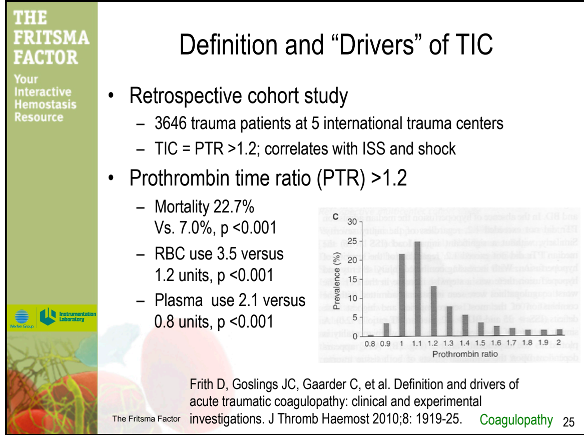
Coagulopathy in Trauma

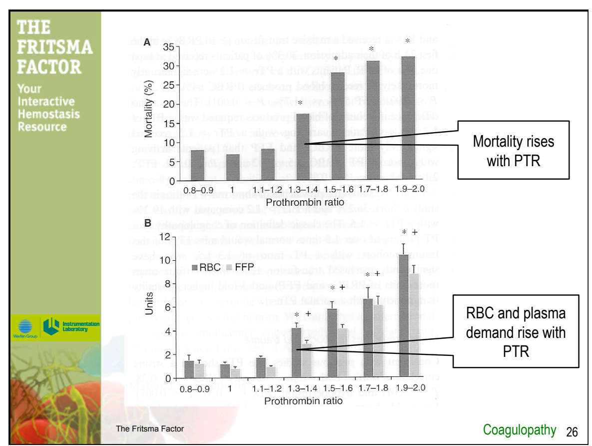
ISS & Coagulopathy n = 1088	% Coagulopathy by Lab Assay*
ISS >15; median 20	57.7%
ISS <15	10.9%
Coagulopathy at Admission	**% Mortality**
Yes (24.4%)	46%
No	10.9%
Overall mortality	19.5%

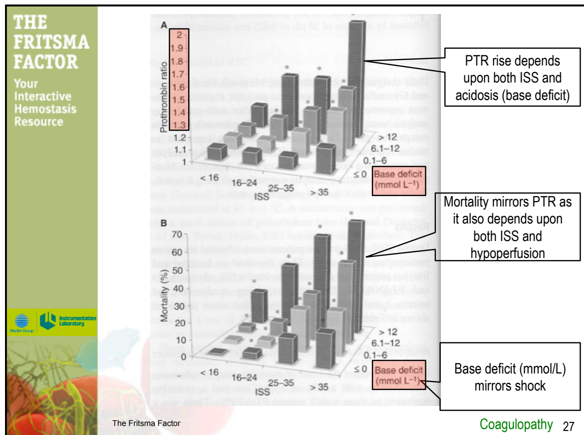
*Coagulopathy defined independent of fluid replacement as: PT >18s,16.3%; PTT >60s, 24.4%; or thrombin time >15s, 14.2%

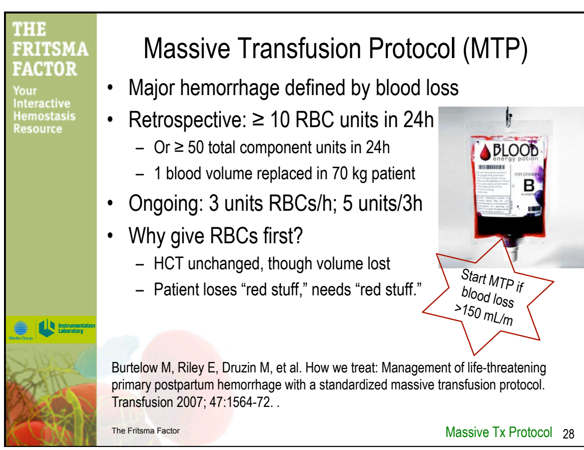
Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. J Trauma 2003; 54: 1127–30

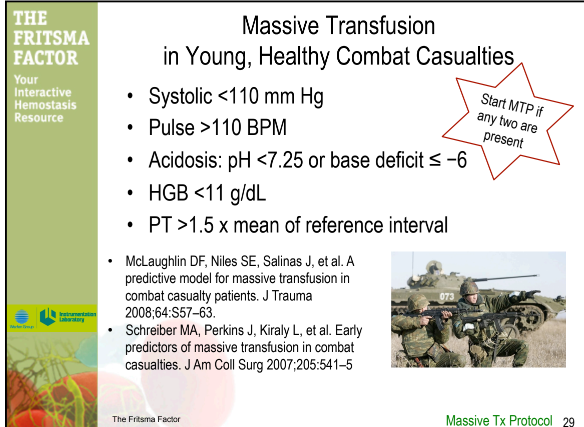


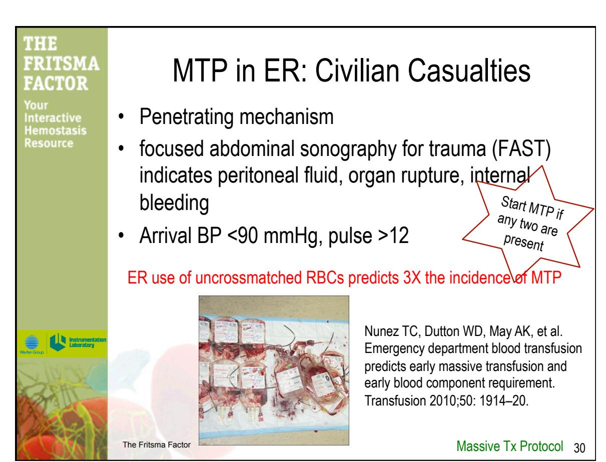

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Definition and "Drivers" of TIC
• Retrospective cohort study
– 3646 trauma patients at 5 international trauma centers
– TIC = PTR >1.2; correlates with ISS and shock
• Prothrombin time ratio (PTR) >1.2
– Mortality 22.7% Vs. 7.0%, p <0.001
– RBC use 3.5 versus 1.2 units, p <0.001
– Plasma use 2.1 versus 0.8 units, p <0.001
Prevalence (%)
Prothrombin ratio
Frith D, Goslings JC, Gaarder C, et al. Definition and drivers of acute traumatic coagulopathy: clinical and experimental investigations. J Thromb Haemost 2010;8: 1919-25.
The Fritsma Factor
Coagulopathy 25

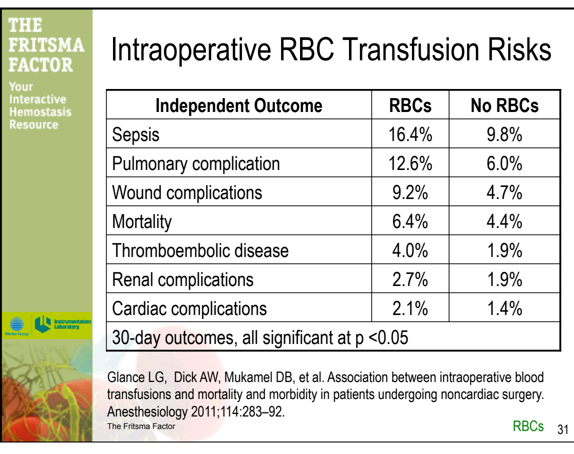

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Mortality (%)
Prothrombin ratio
Mortality rises with PTR
Units
RBC FFP
RBC and plasma demand rise with PTR
The Fritsma Factor
Coagulopathy 26


THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Prothrombin ratio
ISS
Base deficit (mmol L⁻¹)
PTR rise depends upon both ISS and acidosis (base deficit)
Mortality (%)
Mortality mirrors PTR as it also depends upon both ISS and hypoperfusion
Base deficit (mmol/L) mirrors shock
The Fritsma Factor
Coagulopathy 27


THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Massive Transfusion Protocol (MTP)
• Major hemorrhage defined by blood loss
• Retrospective: ≥ 10 RBC units in 24h
– Or ≥ 50 total component units in 24h
– 1 blood volume replaced in 70 kg patient
• Ongoing: 3 units RBCs/h; 5 units/3h
• Why give RBCs first?
– HCT unchanged, though volume lost
– Patient loses "red stuff," needs "red stuff."
BLOOD
B
Start MTP if blood loss >150 mL/m
Burtelow M, Riley E, Druzin M, et al. How we treat: Management of life-threatening primary postpartum hemorrhage with a standardized massive transfusion protocol. Transfusion 2007; 47:1564-72. .
The Fritsma Factor
Massive Tx Protocol 28

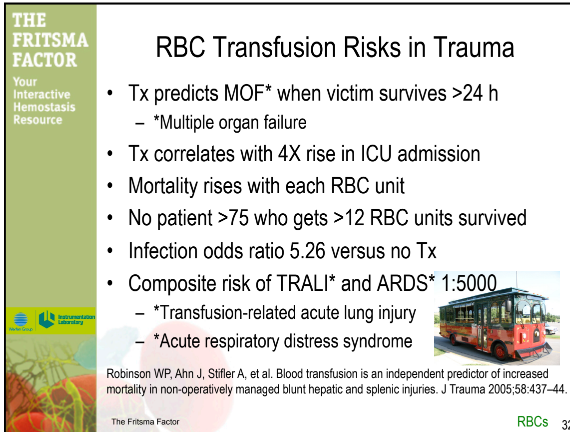

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Massive Transfusion in Young, Healthy Combat Casualties
• Systolic <110 mm Hg
• Pulse >110 BPM
• Acidosis: pH <7.25 or base deficit ≤ −6
• HGB <11 g/dL
• PT >1.5 x mean of reference interval
Start MTP if any two are present
• McLaughlin DF, Niles SE, Salinas J, et al. A predictive model for massive transfusion in combat casualty patients. J Trauma 2008;64:S57–63.
• Schreiber MA, Perkins J, Kiraly L, et al. Early predictors of massive transfusion in combat casualties. J Am Coll Surg 2007;205:541–5
The Fritsma Factor
Massive Tx Protocol 29

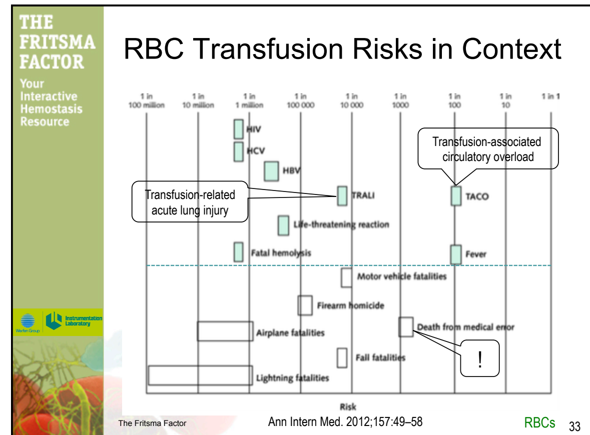

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
MTP in ER: Civilian Casualties
• Penetrating mechanism
• focused abdominal sonography for trauma (FAST) indicates peritoneal fluid, organ rupture, internal bleeding
• Arrival BP <90 mmHg, pulse >12
Start MTP if any two are present
ER use of uncrossmatched RBCs predicts 3X the incidence of MTP
Nunez TC, Dutton WD, May AK, et al. Emergency department blood transfusion predicts early massive transfusion and early blood component requirement. Transfusion 2010;50: 1914–20.
The Fritsma Factor
Massive Tx Protocol 30

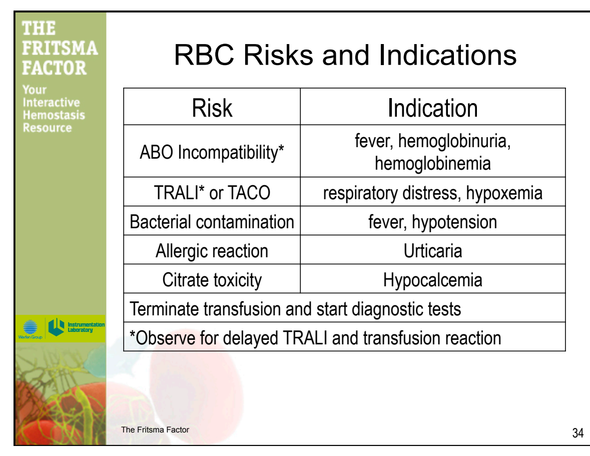


Intraoperative RBC Transfusion Risks

Independent Outcome	RBCs	No RBCs
Sepsis	16.4%	9.8%
Pulmonary complication	12.6%	6.0%
Wound complications	9.2%	4.7%
Mortality	6.4%	4.4%
Thromboembolic disease	4.0%	1.9%
Renal complications	2.7%	1.9%
Cardiac complications	2.1%	1.4%
30-day outcomes, all significant at p <0.05		

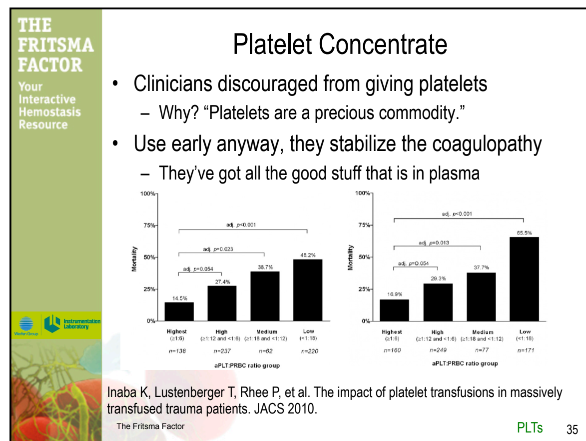


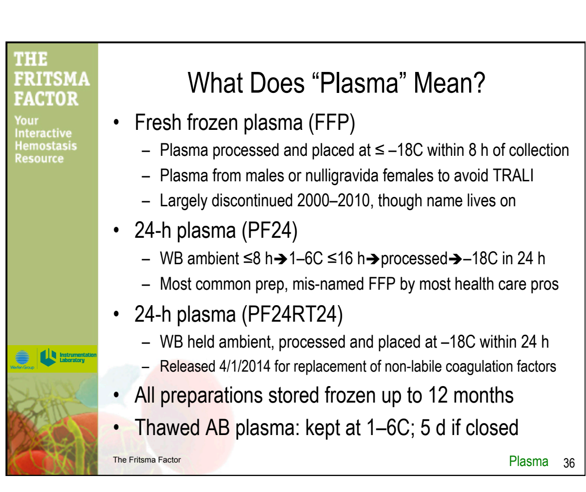




RBC Risks and Indications

Risk	Indication
ABO Incompatibility*	fever, hemoglobinuria, hemoglobinemia
TRALI* or TACO	respiratory distress, hypoxemia
Bacterial contamination	fever, hypotension
Allergic reaction	Urticaria
Citrate toxicity	Hypocalcemia
Terminate transfusion and start diagnostic tests	
*Observe for delayed TRALI and transfusion reaction	



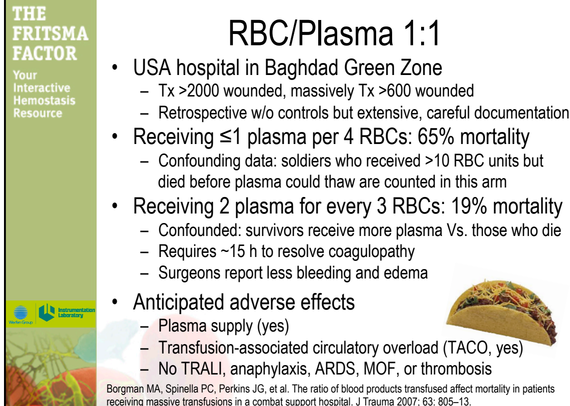


Mean Factor V, VIII and Protein S Levels in FFP, PF 24, and PF24RT24

Preparation	Factor V	Factor VIII	Protein S
FFP at thaw	85%	81%	97%
FFP 5d post-thaw	67%	43%	92%
PF24 at thaw	86%	66%	90%
PF24 5d post-thaw	59%	48%	78%
PF24RT24 at thaw	90%	86%	82%
PF24RT24 5d post-thaw	89%	86%	73%

- O'Neill EM, Rowley J, Hansson-Wicher M, et al. Effect of 24-hour whole-blood storage on plasma clotting factors. Transfusion 1999;39:488–91.
- Cardigan R, Lawrie AS, Mackie IJ, Williamson LM. The quality of fresh frozen plasma produced from whole blood stored at 4 C overnight. Transfusion 2005;45:1342–48.

The Fritsma Factor Plasma 37

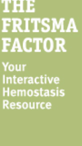


RBC/Plasma 1:1

- USA hospital in Baghdad Green Zone
  - Tx >2000 wounded, massively Tx >600 wounded
  - Retrospective w/o controls but extensive, careful documentation
- Receiving ≤1 plasma per 4 RBCs: 65% mortality
  - Confounding data: soldiers who received >10 RBC units but died before plasma could thaw are counted in this arm
- Receiving 2 plasma for every 3 RBCs: 19% mortality
  - Confounded: survivors receive more plasma Vs. those who die
  - Requires ~15 h to resolve coagulopathy
  - Surgeons report less bleeding and edema
- Anticipated adverse effects
  - Plasma supply (yes)
  - Transfusion-associated circulatory overload (TACO, yes)
  - No TRALI, anaphylaxis, ARDS, MOF, or thrombosis

Borgman MA, Spinella PC, Perkins JG, et al. The ratio of blood products transfused affect mortality in patients receiving massive transfusions in a combat support hospital. J Trauma 2007; 63: 805–13.

The Fritsma Factor Current Massive Tx Protocol 38

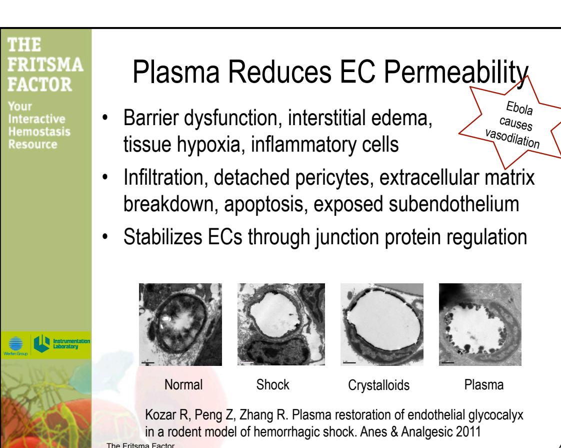


ASA Plasma Indications

- Manage preoperative or bleeding pts who require replacement of multiple coagulation factors (eg, liver disease, DIC).
- Manage patients undergoing massive transfusion who have clinically significant coagulation deficiencies.
- Manage bleeding patients taking warfarin or who need an invasive procedure before vitamin K could reverse the warfarin effect (but 4-factor PCC is better).
- Transfusion or plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP)
- Manage patients with congenital or acquired factor deficiencies for which there are no specific coagulation concentrates
  - FP24RT24 not indicated for factor VIII or protein S deficiency

Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Anesthesiology 2015;22:241–75.

The Fritsma Factor Plasma 39



Plasma Reduces EC Permeability

Ebola causes vasodilation

- Barrier dysfunction, interstitial edema, tissue hypoxia, inflammatory cells
- Infiltration, detached pericytes, extracellular matrix breakdown, apoptosis, exposed subendothelium
- Stabilizes ECs through junction protein regulation

Normal Shock Crystalloids Plasma

Kozar R, Peng Z, Zhang R. Plasma restoration of endothelial glycocalyx in a rodent model of hemorrhagic shock. Anes & Analgesic 2011

The Fritsma Factor 40

Group AB Plasma When ABO is Unknown

- Group AB from males & nulligravida females
  - Odds of AB plasma TRALI 14.5 X higher than A, B, or O
  - TRALI restrictions first applied 4/1/2014
  - AB = 2.6% of active donors before TRALI restriction
  - AB availability now cut by 33%
- AB demand raised
  - New massive Tx protocols raise plasma demand
  - Maintaining thawed plasma supply in ER
  - Thawed AB diverted to non-ABs on 5th day to avoid waste
- Solution: group A plasma

WHAT?

Zelinski MD, Johnson PM, Jenkins D, et al. Emergency use of prethawed group A plasma in trauma patients. J trauma Acute Care Surg 2013; 74: 69–75.

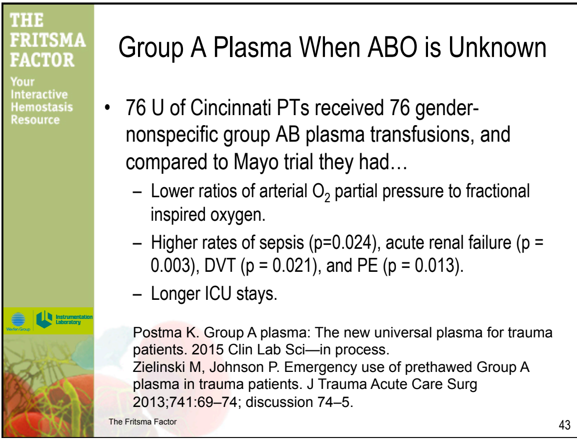
The Fritsma Factor 41

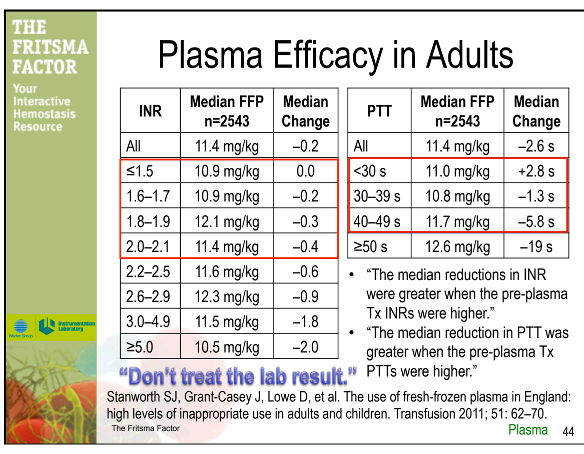
Group A Plasma When ABO is Unknown

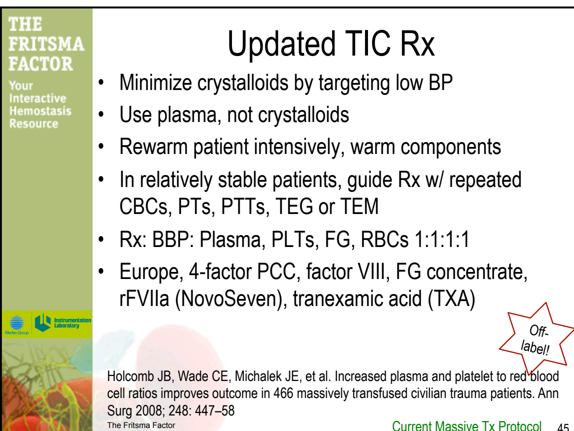
- Most recipients are A and O, compatible w/ A
- Anti-B titers low in TRALI-restricted population
- B substance in secretors neutralizes anti-B
- Pts may be receiving massive O RBCs anyway
- U Mass, 2008–13 (similar data from Mayo)
  - Emergency release of 358 A plasmas
  - 84% of recipients turned out to be A or O, compatible
  - 23 recipients were B or AB, 11 of these received O RBCs
  - No acute hemolytic transfusion reactions
  - Three weak positive post-transfusion DATs
  - Reduced AB plasma usage 97%

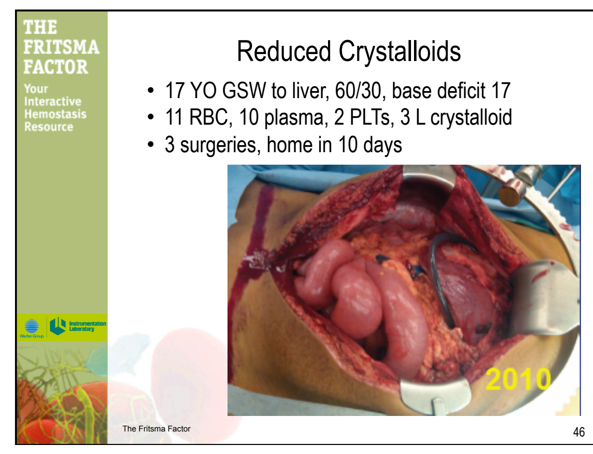
Chhibber V, Green M, Vauthrin M, et al. Is group A plasma suitable as the first option for ememrgency release transfusion? Transfusion 2014; 54: 1751–5.

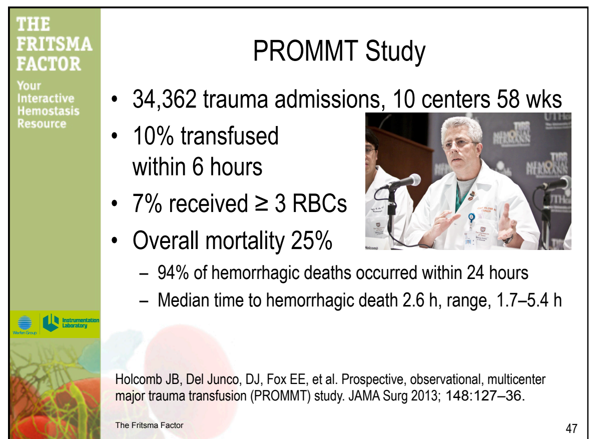
The Fritsma Factor 42

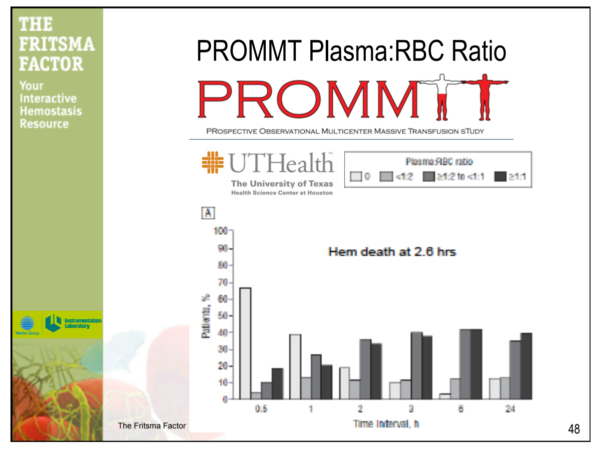

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Group A Plasma When ABO is Unknown
• 76 U of Cincinnati PTs received 76 gender-nonspecific group AB plasma transfusions, and compared to Mayo trial they had…
– Lower ratios of arterial O2 partial pressure to fractional inspired oxygen.
– Higher rates of sepsis (p=0.024), acute renal failure (p = 0.003), DVT (p = 0.021), and PE (p = 0.013).
– Longer ICU stays.
Postma K. Group A plasma: The new universal plasma for trauma patients. 2015 Clin Lab Sci—in process.
Zielinski M, Johnson P. Emergency use of prethawed Group A plasma in trauma patients. J Trauma Acute Care Surg 2013;741:69–74; discussion 74–5.
The Fritsma Factor
43

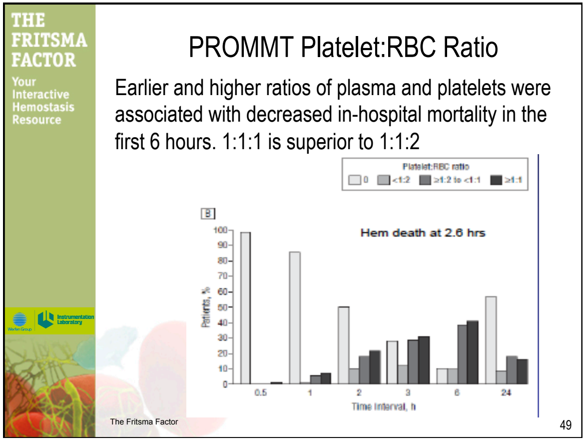

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Plasma Efficacy in Adults
INR | Median FFP n=2543 | Median Change
All | 11.4 mg/kg | –0.2
≤1.5 | 10.9 mg/kg | 0.0
1.6–1.7 | 10.9 mg/kg | –0.2
1.8–1.9 | 12.1 mg/kg | –0.3
2.0–2.1 | 11.4 mg/kg | –0.4
2.2–2.5 | 11.6 mg/kg | –0.6
2.6–2.9 | 12.3 mg/kg | –0.9
3.0–4.9 | 11.5 mg/kg | –1.8
≥5.0 | 10.5 mg/kg | –2.0
PTT | Median FFP n=2543 | Median Change
All | 11.4 mg/kg | –2.6 s
<30 s | 11.0 mg/kg | +2.8 s
30–39 s | 10.8 mg/kg | –1.3 s
40–49 s | 11.7 mg/kg | –5.8 s
≥50 s | 12.6 mg/kg | –19 s
• "The median reductions in INR were greater when the pre-plasma Tx INRs were higher."
• "The median reduction in PTT was greater when the pre-plasma Tx PTTs were higher."
"Don't treat the lab result."
Stanworth SJ, Grant-Casey J, Lowe D, et al. The use of fresh-frozen plasma in England: high levels of inappropriate use in adults and children. Transfusion 2011; 51: 62–70.
The Fritsma Factor
Plasma
44

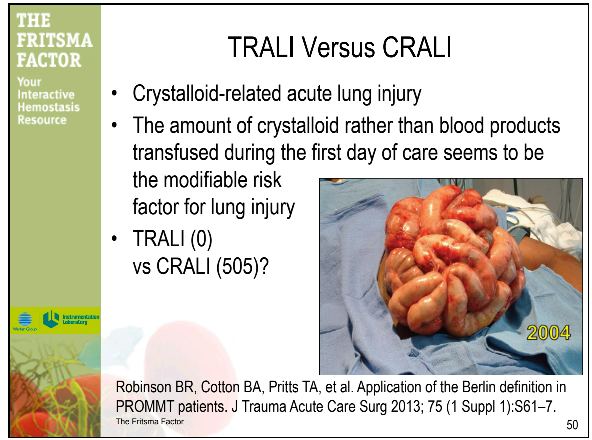

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Updated TIC Rx
• Minimize crystalloids by targeting low BP
• Use plasma, not crystalloids
• Rewarm patient intensively, warm components
• In relatively stable patients, guide Rx w/ repeated CBCs, PTs, PTTs, TEG or TEM
• Rx: BBP: Plasma, PLTs, FG, RBCs 1:1:1:1
• Europe, 4-factor PCC, factor VIII, FG concentrate, rFVIIa (NovoSeven), tranexamic acid (TXA)
Off-label!
Holcomb JB, Wade CE, Michalek JE, et al. Increased plasma and platelet to red blood cell ratios improves outcome in 466 massively transfused civilian trauma patients. Ann Surg 2008; 248: 447–58
The Fritsma Factor
Current Massive Tx Protocol
45

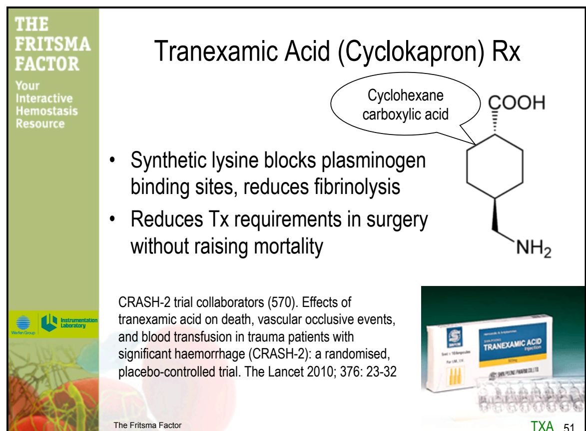

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
Reduced Crystalloids
• 17 YO GSW to liver, 60/30, base deficit 17
• 11 RBC, 10 plasma, 2 PLTs, 3 L crystalloid
• 3 surgeries, home in 10 days
2010
The Fritsma Factor
46

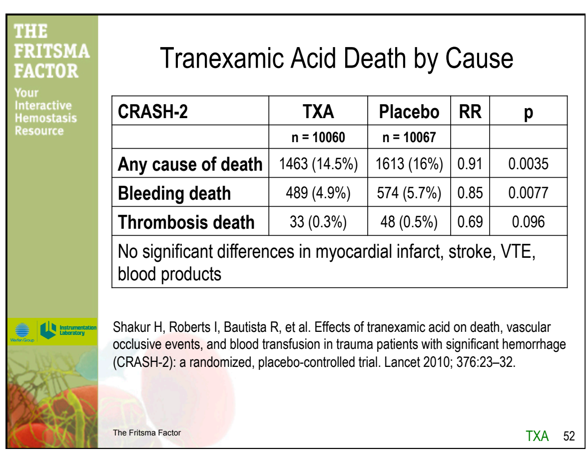

THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
PROMMT Study
• 34,362 trauma admissions, 10 centers 58 wks
• 10% transfused within 6 hours
• 7% received ≥ 3 RBCs
• Overall mortality 25%
– 94% of hemorrhagic deaths occurred within 24 hours
– Median time to hemorrhagic death 2.6 h, range, 1.7–5.4 h
Holcomb JB, Del Junco, DJ, Fox EE, et al. Prospective, observational, multicenter major trauma transfusion (PROMMT) study. JAMA Surg 2013; 148:127–36.
The Fritsma Factor
47


THE FRITSMA FACTOR
Your Interactive Hemostasis Resource
PROMMT Plasma:RBC Ratio
PROMMTT
PROSPECTIVE OBSERVATIONAL MULTICENTER MASSIVE TRANSFUSION STUDY
UTHealth
The University of Texas Health Science Center at Houston
Plasma:RBC ratio
0
<1:2
≥1:2 to <1:1
≥1:1
A
Hem death at 2.6 hrs
Patients, %
Time interval, h
0.5
1
2
3
6
24
The Fritsma Factor
48

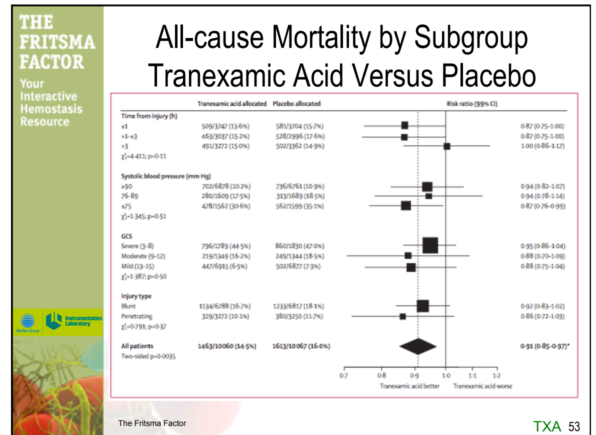


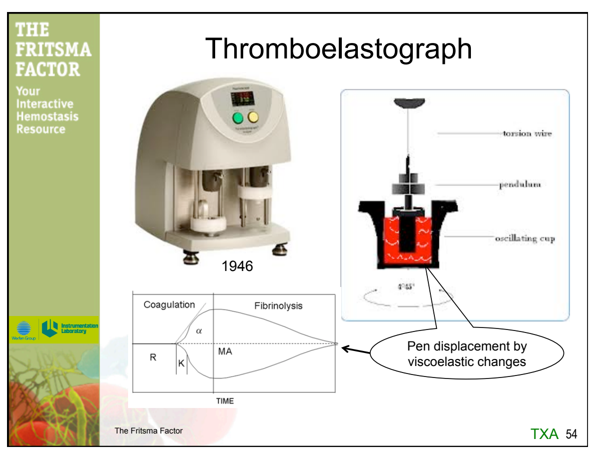


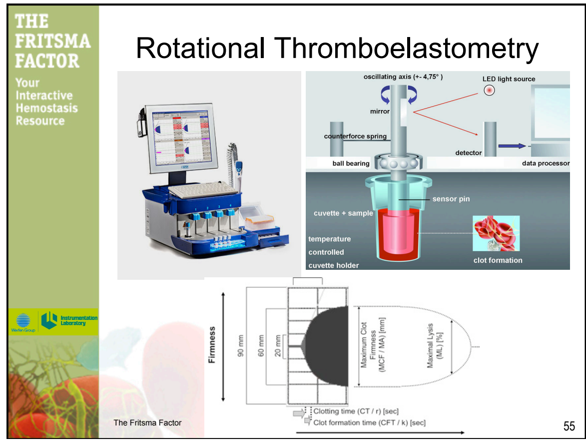


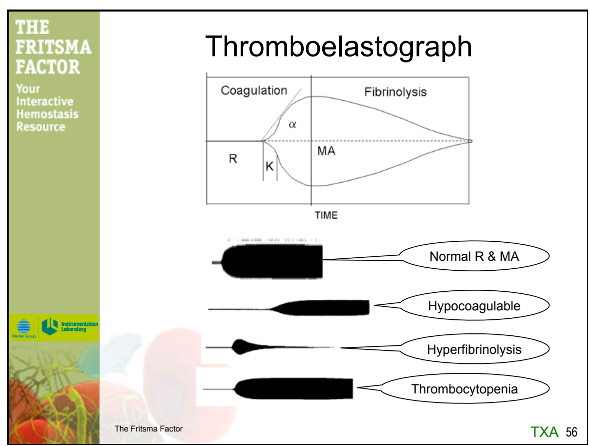


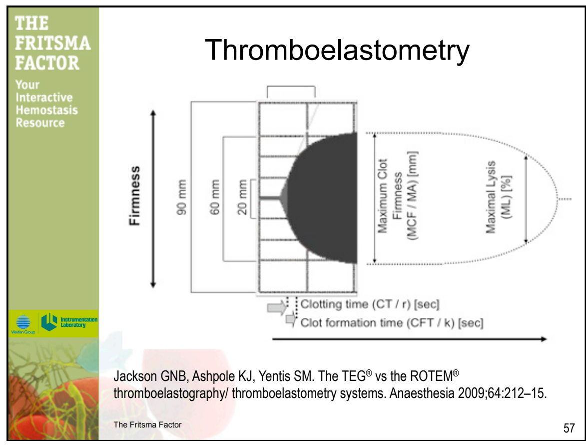
CRASH-2	TXA	Placebo	RR	p
	n = 10060	n = 10067		
Any cause of death	1463 (14.5%)	1613 (16%)	0.91	0.0035
Bleeding death	489 (4.9%)	574 (5.7%)	0.85	0.0077
Thrombosis death	33 (0.3%)	48 (0.5%)	0.69	0.096
No significant differences in myocardial infarct, stroke, VTE, blood products				

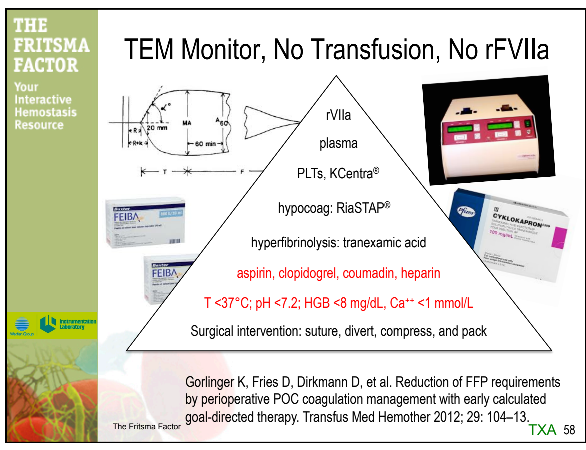


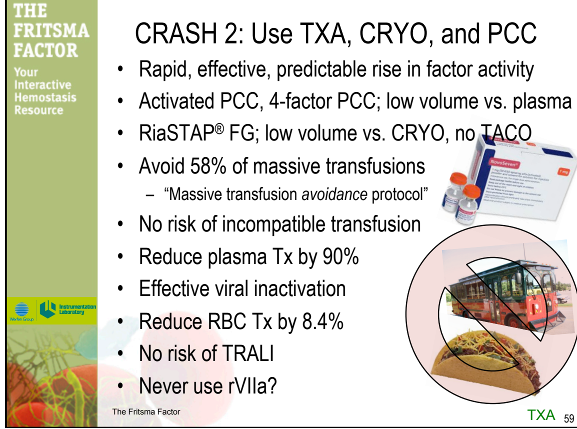


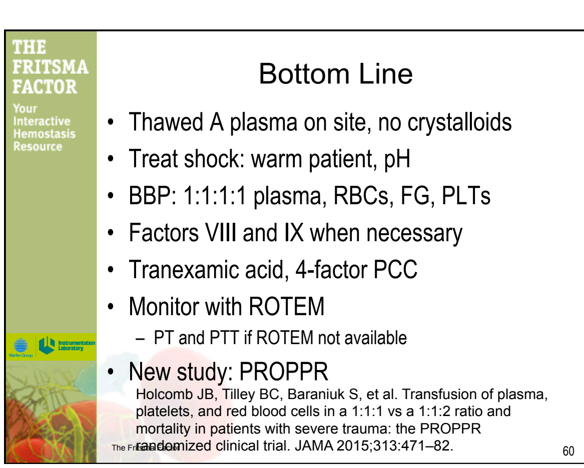

Rotational Thromboelastometry
oscillating axis (+- 4,75°)
LED light source
mirror
counterforce spring
detector
ball bearing
data processor
sensor pin
cuvette + sample
temperature
controlled
cuvette holder
clot formation
Firmness
90 mm
60 mm
20 mm
Maximum Clot Firmness (MCF / MA) [mm]
Maximal Lysis (ML) [%]
Clotting time (CT / r) [sec]
Clot formation time (CFT / k) [sec]
The Fritsma Factor
55


Thromboelastograph
Coagulation
Fibrinolysis
α
R
K
MA
TIME
Normal R & MA
Hypocoagulable
Hyperfibrinolysis
Thrombocytopenia
The Fritsma Factor
TXA 56


Thromboelastometry
Firmness
90 mm
60 mm
20 mm
Maximum Clot Firmness (MCF / MA) [mm]
Maximal Lysis (ML) [%]
Clotting time (CT / r) [sec]
Clot formation time (CFT / k) [sec]
Jackson GNB, Ashpole KJ, Yentis SM. The TEG® vs the ROTEM® thromboelastography/ thromboelastometry systems. Anaesthesia 2009;64:212–15.
The Fritsma Factor
57


TEM Monitor, No Transfusion, No rFVIIa
rVIIa
plasma
PLTs, KCentra®
hypocoag: RiaSTAP®
hyperfibrinolysis: tranexamic acid
aspirin, clopidogrel, coumadin, heparin
T <37°C; pH <7.2; HGB <8 mg/dL, Ca⁺⁺ <1 mmol/L
Surgical intervention: suture, divert, compress, and pack
FEIBA
CYKLOKAPRON
Gorlinger K, Fries D, Dirkmann D, et al. Reduction of FFP requirements by perioperative POC coagulation management with early calculated goal-directed therapy. Transfus Med Hemother 2012; 29: 104–13.
The Fritsma Factor
TXA 58


CRASH 2: Use TXA, CRYO, and PCC
Rapid, effective, predictable rise in factor activity
Activated PCC, 4-factor PCC; low volume vs. plasma
RiaSTAP® FG; low volume vs. CRYO, no TACO
Avoid 58% of massive transfusions
"Massive transfusion avoidance protocol"
No risk of incompatible transfusion
Reduce plasma Tx by 90%
Effective viral inactivation
Reduce RBC Tx by 8.4%
No risk of TRALI
Never use rVIIa?
The Fritsma Factor
TXA 59


Bottom Line
Thawed A plasma on site, no crystalloids
Treat shock: warm patient, pH
BBP: 1:1:1:1 plasma, RBCs, FG, PLTs
Factors VIII and IX when necessary
Tranexamic acid, 4-factor PCC
Monitor with ROTEM
PT and PTT if ROTEM not available
New study: PROPPR
Holcomb JB, Tilley BC, Baraniuk S, et al. 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. JAMA 2015;313:471–82.
60