Hemostatic Resuscitation in Trauma Patients

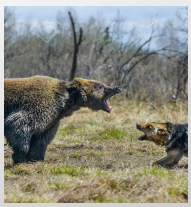
CANADA WEST
VETERINARY SPECIALISTS

Carsten Bandt, DVM, DACVECC
Canada West Veterinary Specialists

Outline

- Trauma and Hemorrhage
- Transfusion indications
- Acute traumatic coagulopathy
- Hemostatic resuscitation
- Antifibrinolytics
- Massive Transfusion Protocols

Canadian Trauma Cases



Rationale

- **Hemorrhage leading cause of death following traumatic injury with coagulopathy and exsanguination causing:**
  - > than 80% of deaths in the operating room (OR)
  - 50% of deaths in the first 24 hours after injury
- The high mortality rate is due to the hemorrhagic shock that is a result of the "lethal triad" of acidosis, coagulopathy and hypothermia.

Why transfuse?

- Post-traumatic hemorrhage remains one of leading causes of human deaths (Ertmer, 2011; Kauvar, 2006)
- 40-70% of human trauma-related deaths occur within minutes to 6 hours post-injury (Spinella, 2009)
  - Massive hemorrhage
  - Head trauma

Blood Loss

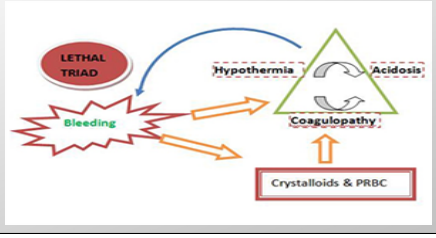
Category 1:
15% of the TBV has been lost; no treatment required;
Category 2:
15% - 30% of TBV has been lost; usually requires IV fluid. Patient signs and symptoms include fatigue, lightheadedness, paleness;
Category 3:
30% - 40% of TBV has been lost; IV fluid and blood transfusion required. Patient signs and symptoms include irritability, confused, weak, fatigue, paleness
Category 4:
More than 40% loss of TBV. Requires aggressive emergency treatment with IV fluids and blood transfusion. This is a life-threatening condition in which treatment must be immediately started to replace blood and fluids, as well as stop the hemorrhaging.

Why transfuse?

- Shock = O_2 debt due to impaired delivery, utilization, or both with resultant anaerobic metabolism and organ dysfunction
- Optimization of O_2 debt dependent on DO_2 = Q x CaO_2
- CaO_2 (mL O_2/dL) = [(Hgb x 1.34 x SaO_2) + (PaO_2 x 0.003)]
- During resuscitation
  - Balance between maximal oxygen content (HCT = 100%) and minimal blood viscosity (HCT = 0%)
  - Oxygen carrying capacity of allogeneic erythrocytes impaired due to storage changes

Peracci, Kashuk, Moore, 2013

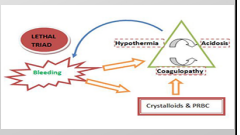
Iatrogenic coagulopathy?



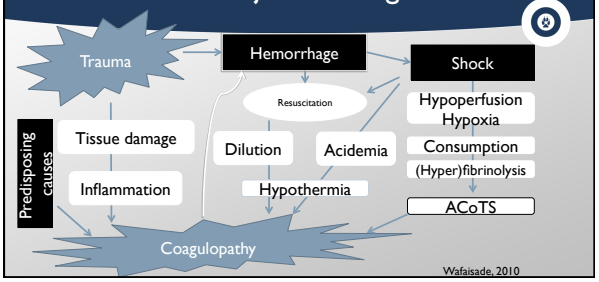
Iatrogenic coagulopathy?

Resuscitation-associated coagulopathy
→ hypothermia, acidosis, coagulopathy
(Pieracci, 2013)

Clotting factor depletion due to hemorrhage and consumption
Iatrogenic coagulopathy (Cohen, 2012)
- Surgery → hypothermia
- Large volume, cool fluids → dilution and hypothermia
- pRBCs→ dilution
- Sick patients → acidotic



More than just a triangle…



Wafaisade, 2010

Acute traumatic coagulopathy

- Acronyms (ATC, ACoTS, TIC)
- Immediate hypercoagulable → hypocoagulable → hypercoagulable
- Mechanism poorly defined and controversial
- 25-34% human trauma patients present hypocoagulopathic (Hebert, 1999 and Brohi, 2008)
- 4-fold increase risk of MODS and death in those that present with coagulopathy (Brohi, 2008)
- ATC positively correlated with Injury Severity Score (Brohi, 2008)
- Patients with ATC have higher ISS, transfusion requirements, mortality (Johansson, 2011)

Severity of injury

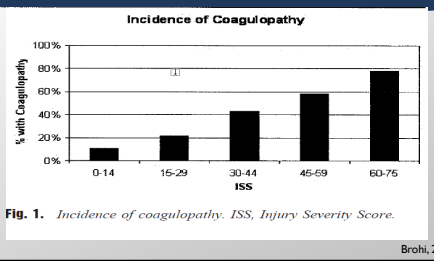


Fig. 1. *Incidence of coagulopathy. ISS, Injury Severity Score.*

Brohi, 2003

Mortality

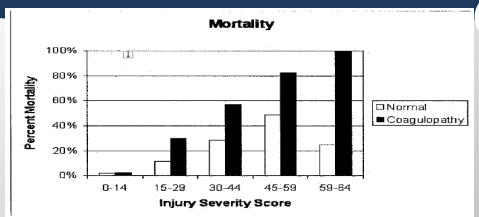


Fig. 2. *Mortality.*

Brohi, 2003

Acute traumatic coagulopathy

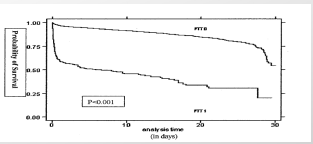


Fig 2: Kaplan-Meier survival estimates by PTT. PTT0, normal; PTT1, abnormal PTT

- **20,000+ patients:**
- Hgb, platelet count, base deficit, PT, PTT
- Odds ratio for death
  3.6 abnormal PT
  7.81 abnormal PTT
- Limitations:
  - Retrospective
  - Mortality all-cause
  - Other medications

MacLeod, 2011

Acute traumatic coagulopathy

- **30 dogs with 24 hours of trauma**
  -Long bone fractures, thoracic and/or abdominal trauma
  -Significantly decreased ($p<0.01$)
  -Platelet count
  -Individual coagulation factors
    -VIII:C, IX, XI, XII reduced in line with albumin
    -V most severe (76% of dogs)
    -Inhibitors of blood coagulation (antithrombin, protein C)
    -Plasminogen
- Soluble fibrin and fibrin degradation products (FDPs) both significantly elevated

Mischke, 2005

Acute traumatic coagulopathy

- **Prospective, 41 dogs with blunt and penetrating trauma:**
  -Lactate, platelet count, antithrombin, D-dimer, protein C, antiplasmin, plasminogen, TEG

Results:

Non-survivors and those with most severe injuries hypocoagulable
ATC positively correlated with incidence of transfusion requirements
Incidence of body cavity hemorrhage and need for transfusion correlated with:
↓ plt count,
↓ markers of TEG clot strength,
↓ antithrombin and protein C, ↑ aPTT

Holowaychuk, 2011

Acute traumatic coagulopathy

- **Hypoperfusion and acute traumatic coagulopathy in severely traumatized canine patients**
  - Based on *G* values as measured by TEG , 10/30 dogs (33%) showed evidence of hypercoagulability. Hypocoagulability as determined by prothrombin time, activated partial thromboplastin time, or TEG was not shown in any of the 30 dogs.

Abelson, 2013

Acute traumatic coagulopathy

Evaluation of acute traumatic coagulopathy in dogs and cats following blunt force trauma:

- 18 dogs and19 cats within 8 hours of presentation without prior.
- ATC was diagnosed in 1 dog and 1 cat on presentation.
- Hypercoagulability was documented in 4/18 (22%) of dogs and 1/19 (5.3%) of cats
- Dogs: Prolongation of PT (P = 0.018), aPTT (P = 0.013) and decrease in maximum amplitude (MA) (P = 0.027) were significantly associated with injury severity as measured by the animal trauma triage (ATT) score
- Cats: PT, aPTT, MA, and clot strength (G) were not associated with injury severity.

- **ATC is rare in minimally injured dogs and cats following blunt trauma.**
- **In dogs, ATT score is significantly associated with PT, aPTT, and MA, suggesting an increased risk of ATC in more severely injured animals. ATT score does not appear to predict coagulopathies in cats.**

Gottlieb, 2017

Role of hypoperfusion

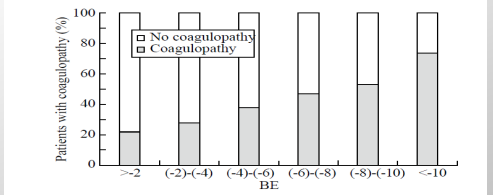
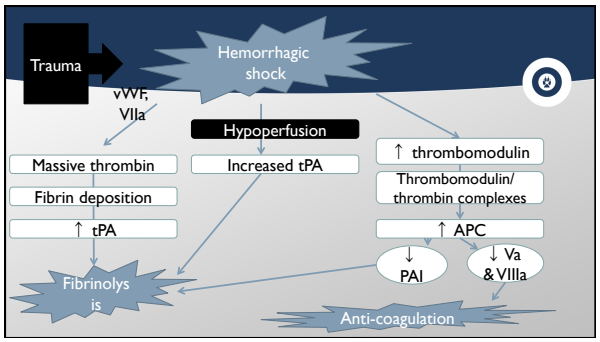


Figure 4. Incidence of ATC as a function of BE on ER arrival.

Maegele, 2010



Risk factors for coagulopathy

1. Severity of injury
2. Severity of abdominal injury
3. Base excess
4. Body temperature ≤ 95°F
5. Presence of shock
6. Prehospital colloids:crystalloids ≥ 1:2
7. Prehospital IVF ≥ 3000 mL

Wafaisade 2010

Why do we care…

Presence of ATC may confound resuscitative efforts and increase mortality

- Exacerbating blood loss
- Increasing transfusion requirements
- Prolonging hypoperfusion

Massive Transfusion

Definitions:

- ≥ 10 U pRBCs between ER and ICU admission (Maegele, 2010)
- 3 U/h (Savage, 2013)

Patient blood volume in 24 hours (Jutkowitz, 2002)

Prognosis worse with massive transfusion
100% mortality (3/3) dogs (Jutkowitz, 2002)

Massive Transfusion

Veterinary Definitions:

- Blood volume in 24 hour
- 1.5 ml/kg/min over 20 minutes
- Replacement of 150% of patient's blood volume irrespective of time
- Replacement of ½ the patient's blood volume in 3 hours

Prognosis worse with massive transfusion
100% mortality (3/3) dogs (Jutkowitz, 2002)

Risk of Massive Transfusions

- **Problems secondary to volume resuscitation**
- **Dilutional problems**
- **Problems related to transfusion of large volume of stored blood**
- **Late complications**

Problems Secondary to Volume Resuscitation

Inadequate resuscitation:

-Hypoperfusion leads to lactic acidosis, systemic inflammatory response syndrome (SIRS), disseminated intravascular coagulation and multiorgan dysfunction

Overzealous resuscitation:

- Transfusion Associated Circulatory Overload (Pulmonary edema, AKI, compartment syndrome)

Dilutional problems

Dilutional coagulopathy:

- During haemorrhagic shock, there is fluid shift from the interstitial to the intravascular compartment that leads to dilution of the coagulation factors.
- Worsened if lost blood is replaced with coagulation factor deficient fluids.

Problems related to transfusion of large volume of stored blood

1. Citrate toxicity
2. Hyperkalemia
3. Hypothermia
4. Hypomagnesemia
5. Acidosis

Problems related to transfusion of large volume of stored blood

Citrate toxicity:

- 80 ml of citrate phosphate dextrose adenine solution present in each blood bag contains approximately 3 g citrate
- A healthy 30 kg dog can metabolise this load in 5 min
- Hypoperfusion or hypothermia associated can decrease this rate of metabolism leading to citrate toxicity
- Citrate can then lead to hypocalcaemia, hypomagnesemia and worsen the acidosis.
- Hypocalcaemia can lead to myocardial depression that manifests earlier than hypocalcaemic coagulopathy.Hypotension not responding to fluids could be a sign of this complication.

Problems related to transfusion of large volume of stored blood

Hyperkalemia:

- Rare but can develop in some blood products.
- Cardiac effects of hyperkalaemia are accentuated by hypocalcaemia.

Problems related to transfusion of large volume of stored blood

Hypothermia:

- Due to infusion of cold fluids and blood and blood products, opening of cavities and decreased heat production.
- Worsens citrate metabolism and drug clearance and more importantly, contributes to the development of coagulopathy.
- Coagulopathy due to hypothermia is not reflected in laboratory tests as the samples are warmed during processing

Problems related to transfusion of large volume of stored blood

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Hypomagnesemia:

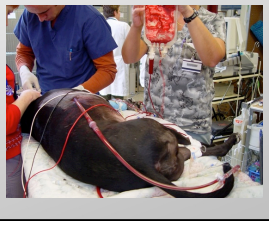
- Citrate also binds to magnesium and can lead to hypomagnesaemia which can further accentuate effects of hypocalcaemia.
- Infusion of large amounts of magnesium poor fluid can also contribute to hypomagnesemia.

Problems related to transfusion of large volume of stored blood

Acidosis:

- 2 week old PRBCs have a pH below 7.0, and each unit has an acid load of approximately 6 mEq.
- Acidosis directly reduces activity of both extrinsic and intrinsic coagulation pathways.
- A pH decrease from 7.4 to 7.0 reduces the activity of FVIIa and FVIIa/TF by over 90% and 60% respectively

Can we predict need for massive transfusion?



Massive transfusion

Early identification to guide therapeutic intervention and prognosis:

1. Trauma Associated Severe Hemorrhage (TASH) score (Yucel, 2006)
2. PROMMTT Study – Massive Transfusion Score (Callcut, 2012)
3. CAT – Critical Administration Threshold (Savage, 2012)

Variables	Variable	Points	Score
	<7	8	
	<9	6	
HemoGlobin (mg/dl)	<10	4	
	<11	3	
	<12	2	
	<-10	4	
Base excess (mmol/L)	<-6	3	
	<-2	1	
Sytolic blood pressure (mmHg)	<100 <120	4 1	
Heart rate (beats/min)	>120	2	
Free intraabdominal fluid (e.g.by FAST)		3	
Clinically instable pelvic fracture		6	
Open or dislocated femur fracture		3	
Male gender		1	
TASH (sum of score points)=			

Probability for mass transfusion	
TASH	P
1-8	<5%
9	6%
10	8%
11	11%
12	14%
13	18%
14	23%
15	29%
16	35%
17	43%
18	50%
19	57%
20	65%
21	71%
22	77%
23	82%
24+	>85%

Figure 5. TASH-score. The TASH-score of 18 equals to a 50% risk for massive transfusion (MT) after severe multiple injuries.

Maegele, 2010

PROMMTT (Callcut, 2012)

Variables
- Prothrombin time
- Systolic blood pressure
- Hemoglobin
- Base deficit
- FAST +
- Heart rate
- Temperature
- Penetrating injury

Score = 1/variable
Results:
- PT most predictive (OR 2.5)
- MTS < 2
  - Unlikely MT (NPP 89%)
- MTS ≥ 2
  - 85% sensitive for predicting MT
    - MT 33% with MTS > 2
    - MT 11% with MTS < 2

Redefining massive transfusion

CAT – critical administration threshold
- # units pRBCs in 60 minutes
- 3 U/h

Prior MT definitions
- Retrospective
- Arbitrary
- Prone to survivor bias

Mortality
CAT+ → 3.6 X more likely to die than CAT-

Damage Control Resuscitation

Component therapy:

Ratio pRBC:FFP (Harrigan, 1989)
- >5:1 increased mortality
- >8:1 overt coagulopathy

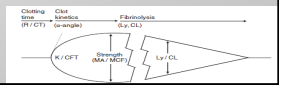
1:1 ratio (Pieracci, 2013)
- Anemic (HCT 27%)
- Factor deficient (65% activity)

Current opinions
- 1:2 to 1:3 pRBC:FFP for resuscitation (Pieracci, 2013)
- 1 U platelets/10 U pRBC or evidence of platelet dysfunction on TEG (Pieracci, 2013)
- 1:1:1 pRBC:FFP:platelets

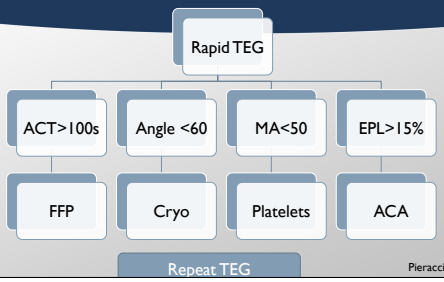
Damage Control Resuscitation

Fresh whole blood
- Improved survival in combat surgery (Nessen, 2013)

Goal-directed resuscitation bundles (Johanssen, 2013)
- 1:1:1 → RBC:FFP:platelets
- Antifibrinolytics
- Cryoprecipitate
- Fibrinogen concentrate
- Based on TEG



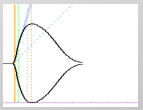
Goal directed resuscitation



Pieracci, 2013

Antifibrinolytics

- Aminocaproic acid and tranexamic acid
- CRASH-2 Trial (Shakur, 2010)
  - Tranexamic acid reduced risk of death due to bleeding (14.5% vs. 16%)
  - Penetrating blunt injuries
  - No significant increase in thromobosis
  - Most effective w/i 3 hrs
- Human guidelines:
- use based on viscoelastic analysis



Pieracci, 2013

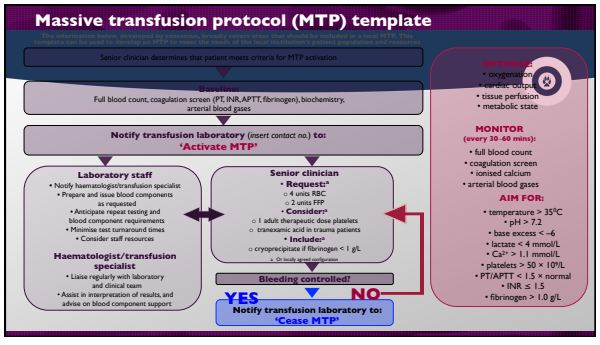
Damage control surgery

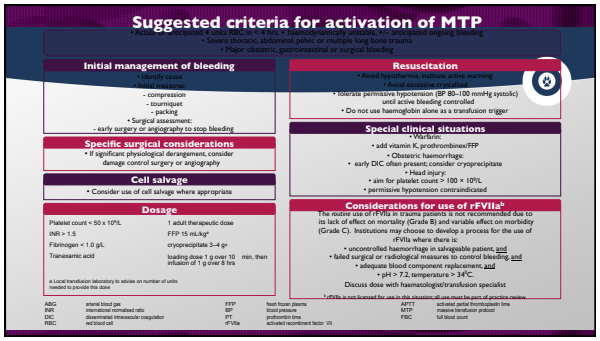
- Abbreviated surgery (< 60 minutes)
- Control hemorrhage
- Control contamination
- Approach
  - 1st surgery: abbreviated control
  - ICU care to correct acidosis, hypothermia, coagulopathy
  - Definitive repair
- Complications: compartment syndrome, sepsis, MODS

- DCR with DCL (Duchesne, 2010)
  - Greater survival (73.6% vs. 64.8%)
  - Shorter ICU stay (11 d vs. 20 d)
  - No difference intraop transfusion

Massive Transfusion Protocol

- Massive transfusion Protocols(MTP)





Massive Transfusion Protocols

- MTPs are designed to interrupt the lethal triad of acidosis, hypothermia and coagulopathy that develops with massive transfusion
- MTP describes the process of management of blood transfusion requirements in major bleeding episodes
- Assisting the interactions of the treating clinicians and the blood bank and ensuring judicious use of blood and blood components

Massive Transfusion Protocol (MTP)

- Massive transfusion protocols are activated by a clinician in response to massive bleeding.
- MTPs have a predefined ratio of RBCs, FFP/ cryoprecipitate and platelets units in each pack (e.g. 1:1:1 or 2:1:1 ratio) for transfusion.

Massive Transfusion Protocols

- Early involvement of Criticalist
- Early use of warming of patients
- Use of blood warmers to avoid further hypothermia
- Standardized Blood gases and Coagulation rechecks post transfusion

Summary

- Uncontrolled hemorrhage leading cause of potentially preventable death in humans
- Inherent coagulopathy due to trauma which can be exacerbated with historical resuscitation strategies
- Permissive hypotension may be beneficial
- Early resuscitation with component therapy or whole blood
- Early surgical intervention with uncontrolled hemorrhage

Questions?

Unwashed red Cell Autotransfusion

Unwashed salvaged blood contains:

Inflammatory mediators, fibrin split products[1], complement fractions, interleukins, tumour necrosis factor α, and fat particles[1],

Acute Traumatic Coagulopathy

Disseminated intravascular coagulation or acute coagulopathy of trauma shock early after trauma? An observational study

Pär I Johansson[1*], Anne Marie Sørensen[2,3], Anders Perner[4], Karen Lise Welling[5], Michael Wanscher[6], Claus F Larsen[5] and Sisse R Ostrowski[1]

Theories

- Disseminated intravascular coagulopathy with a fibrinolytic phenotype (Gando, 2011; Johansson, 2011))
- Shock → tissue hypoperfusion → activated protein C → systemic anticoagulation → hyperfibrinolysis (Brohi, 2008; Frith, 2010; Kashuk, 2010; Johansson, 2011)
- Marked sympathoadrenal response leading to catecholamine-induced endothelial damage (Ostrowski, 2011; Johansson, 2010)

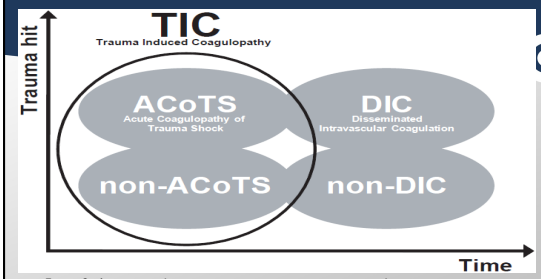


Figure 2: Association between assessment time-point, trauma hit, and type of coagulopathy in trauma patients Johansson, 2011

Thank you!

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