Significance:

Haemorrhage is a leading cause of early and late death from trauma and some may be preventable.

Roughly 10% of human trauma patients are coagulopathic on admission.

Human trauma patients which are hypocoaguable on admission to hospital have 4x the likelihood of death when compared to non-coagulopathic patients.

Traditional resuscitation may contribute to worsening of coagulopathy, so patients presenting with the condition need to be prioritized for damage control resuscitation.

There may be a role for the use of anti-fibrinolytic drugs in selected patients. There is evidence of benefit in humans, but not yet in veterinary patients.

Pathophysiology

Initiators (major):

Severe tissue injury
Hypoperfusion

Contributing components:

Systemic Inflammation
Hypothermia
Metabolic acidosis
haemodilution

Manifestation:

Hypocoaguable and hyperfibrinolytic state

Veterinary Literature

Mischke 2004 (The Veterinary Journal)¹
30 traumatized dogs with shock evaluated within 24 hours of trauma and before fluid therapy. There were reductions in platelet count, individual clotting factors, and prolongation of PT and aPTT

Abelson et al 2013 (JVECCS)²
30 traumatized dogs with ATT >5 before any intervention. Found hypercoaguability rather than hypocoaguability.

Holowaychuk 2014 (JVECCS)³
42 traumatized dogs with severe blunt trauma evaluated within 12 hours. Coagulopathic dogs were more likely to receive blood products, and more likely to die
Prolonged aPTT was associated with highest risk of death

Pathophysiology (three hypotheses):

1. **DIC hypothesis**: ATC is a variation of DIC with an initially hypocoaguable, hyperfibrinolytic phenotype (caused by massive activation of plasminogen by t-PA). The patient later becomes
hypercoaguable as fibrinolysis is reduced by greater expression of plasminogen activator inhibitor relative to t-PA

2. **Excessive activation of protein C**: Extensive tissue injury leads to massive thrombin generation which in turn results in excessive binding of thrombin to thrombomodulin and activation of protein C. APC inactivates factors Vi, and V. Fibrinolysis is enhanced because APC inhibits plasminogen activator inhibitors.

3. **The neuro-hormonal hypothesis**: Sympathetic nervous system initiated catecholamine release leads to glycolcalyx damage (shedding) and subsequently massive activation and dispersal of the pro-and anticoagulant anticoagulants.

**Diagnosis:**

1. Underlying hypoperfusion (MAP < 60, SBP< 80, BD< -6, lactate > 5) + severe tissue injury.
2. Haemorrhage (severe).
3. aPTT or PT >150% normal (unreliable because of three things: a) clotting factor deficiency may not be a player (need >70% reduction to increase), these tests may not be correlated with increased bleeding risk, and the tests are done at standard pH and Temp so don’t take into account in vivo changes).
4. Reduced amplitude clot strength (G, Ma MCF) on viscoelastic testing.

**Management:**

1. Rapid haemostasis is the key goal. Provide external counter-pressure wherever possible. 20mm HG pressure of abdominal wrap has been effective in reducing re-bleeding in experimental models. 
2. Damage control resuscitation: target low/normal SBP (80mmHg) MAP (>60mmHG) Higher pressures targeted when head trauma is a component SBP 100mmHg MAP >80mmHG to maintain cerebral perfusion pressure.

Use the most physiologically appropriate fluid. Where possible, an exsanguinating patient could be resuscitated using a massive transfusion protocol.

Use aliquots of fluid and resuscitate to adequate BP, and resolution of the clinical signs of shock.

**Massive transfusion**

* 5ml/kg HTS
* 20ml/kg crystalloid
* 10ml/kg colloid

3. **Manage coagulation**

Early use of anti-fibrinolytics (within 3 hrs) should be considered. Tranexamic acid dose is 10-15mg/kg IV, followed by 1-5mg/kg/hr CRImay be considered.

Anti-fibrinolytics: EACA/TXA bind to the lysine binding site of plasminogen and prevent its activation.

FFP 10-15ml/kg target PT/aPTT less than 150% normal

Manage hypothermia

*Blood transfusion:*
Massive transfusion requires protocol to be effectively initiated and performed
Fresh whole blood is an attractive choice as it contains appropriate components and less likelihood of storage lesion.

Otherwise component therapy 1 FFP: 2pRBC
Or 1:1.
There is not yet consensus on the correct ratio for blood product administration. Platelet rich plasma, and cryoprecipitate are also potential options but not available.

Target PCV 21-24

Damage control surgery:

Haemostasis (pack or tie)
Source control
Surgical time < 60min where possible.

Interesting points, which came up during reading:

In splenectomised dogs, acute hemorrhage (30% total estimated blood volume) caused a rapid and moderate drop in mean Hct to 17% below baseline within 15 minutes post-hemorrhage. Large-volume fluid resuscitation (3:1) resulted in a further Hct drop to 50% below baseline, whereas small-volume resuscitation (1:1) resulted in a decrease in Hct to only 24% below baseline.

In 2003, Mapstone et al conducted a systematic review of fluid resuscitation in 44 animal models of hemorrhagic shock. Regardless of the hemorrhage model used (eg, aortic injury, organ incision, tail resection, other vascular injuries), the data collected from Mapstone et al demonstrated that hypotensive resuscitation reduced the risk of death in all trials investigating this strategy. Prolonged hypotension is much more deleterious than brief periods. There was high mortality in a swine model of haemorrhage and air blast when hypotensive resuscitation (SBP 80mmHg) was implemented for 8 h.

Data supports hypotensive resuscitation to sustain life until early surgical intervention, if haemorrhage does not spontaneously resolve. The difficulty is in predicting which patients require the more aggressive approach. A simple strategy is to take to surgery the patients whom relapse into shock after initial resuscitation. Hypotensive resuscitation could be considered contra-indicated in patients with CNS injury especially where CPP must be maintained. These patients should have a SBP of 100mmHg targeted.

Unlike isotonic crystalloids, experimental animal models have shown HTS may exert positive immunomodulatory effects primarily attributable to alterations of neutrophil-endothelial interactions. Other reported benefits of HTS include reduced endothelial cell swelling, improved regional blood flow and microcirculation, improved cardiovascular function, and reduced edema formation due to less overall fluid requirements.


Also: