Bleeding & Clotting

“The Bleeding Truth”

A/Prof David Roxby
SA Pathology Transfusion Service
South Australia

National Blood Symposium
Patient Blood Management

PBM = Good clinical medicine
An approach to safe, quality patient care... BUT one size doesn’t fit all

- Aim to **optimise**, **conserve** and **manage the patient’s own blood** to minimise or avoid exposure to allogeneic blood
- Changing from a **product** focus to a **patient** focus
- Patient specific **team approach**
- Results in **improved patient outcomes**

It will be nice to **only transfuse what is needed**, based on level 1 data, finally **balancing risk and benefit** in data-driven fashion **for the benefit of our patients**.

J Holcomb Critical Care 2010;14:162
Patient Blood Management Principles

Anaemia
Iron deficiency

Blood loss & bleeding

Transfusion

Planned, multi-modal team approach to blood conservation & transfusion, involving patient, combination of strategies

Courtesy of A Thomson
Haemorrhage

- Bleeding is a major cause of in-hospital mortality following:
  - Cardiovascular surgery/procedures
  - Organ transplantation
  - Orthopaedic surgery
  - Obstetrics
  - Trauma

- Haemorrhage:
  - Causes 30-40% of trauma mortality
  - Leading cause of death in first hour of arrival\(^1\)
  - Responsible for more than 80% of OT deaths\(^2\)
  - Accounts for nearly 50% of deaths in first 24 h\(^2\)

- Control commonly thwarted by coagulopathy \([25-30\%]\)\(^3,\ 4\)

GOOD THINGS
- Retrieval
- Scoop & Run
- Stay and Play
- Triage
- Hypotensive resuscitation
- Trauma management teams
- Diagnosis
  - Imaging
  - Invasive
- Damage control surgery versus definitively “fixing” the problem
- Organ supportive therapy

BAD THINGS
- Pre-existing disorders
- Increasing Shock
- Trauma to vital organs
- Trauma ⇒ Coagulopathy
- SIR ⇒ MOF
- Sepsis
- Blood storage lesion
- Compounding medical disorders (Myocardial, Respiratory, Renal)

Survival
0%

Resuscitation

Time

Mortality

Courtesy of J Isbister
<table>
<thead>
<tr>
<th>CLEAR FLUIDS</th>
<th>RED CELLS</th>
<th>HAEMOSTASIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalloid v Colloid</td>
<td>Fresh v LD v Aged</td>
<td>FFP, Cryo, Plts, rVIIa</td>
</tr>
<tr>
<td><strong>What is the importance of Blood/Plasma Viscosity?</strong></td>
<td><strong>Are the stored red cell transfusions restoring O₂ delivery to the tissues and ↑ O₂ Consumption</strong></td>
<td><strong>What is the quality of stored platelet concentrates?</strong></td>
</tr>
<tr>
<td><strong>What is the importance of Colloid Oncotic Pressure?</strong></td>
<td><strong>Do the stored red cell transfusions have a causal connection with the development of MOF and Sepsis (ie TRIM &amp; Storage Lesions)?</strong></td>
<td><strong>When should FFP, Cryo and Platelets be given?</strong></td>
</tr>
<tr>
<td><strong>What is the best electrolyte composition?</strong></td>
<td></td>
<td><strong>What is the role of haemostatic agents?</strong></td>
</tr>
</tbody>
</table>

Local v Systemic

Courtesy of J Isbister
Clinical & Laboratory Issues

Identify haemostatic imbalance

- Before surgery
  - Is there a bleeding history or coagulopathy?
- During surgery
  - What is the cause of bleeding?
    - Plt function
    - Excess fibrinolysis
    - Factor deficiency Vs residual anticoagulant
  - What coagulopathy is developing?
- After surgery
  - If patient is bleeding, is it due to
    - Surgical problems?
    - Excess heparin?
    - Coagulopathy?
Can We Predict Who Will Bleed?

There Is a Difference Between Who Is at Risk and Who Will Bleed

- Who is likely to bleed or clot too much?
- How do we optimize the patient’s physiology?
- Which local haemostatic agents are effective?
- Which systemic haemostatic agents are effective?

Patients at Risk for Surgical Bleeding

Certain patients are at higher risk for surgical bleeding including:

- Patients taking:
  - Anticoagulant therapy - warfarin
  - Anti-platelet therapy – clopidogrel

- Patients undergoing
  - Repeat surgical procedures
  - Oncologic surgery
  - Aortic surgery
  - Cardiac surgery
  - Neurologic procedures or neurosurgery
  - Radical prostatectomy

- Dialysis patients

- Trauma patients
Haemorrhage

- Surgical or vascular component
- Corrected by surgical intervention or embolisation
- Coagulopathy component: more difficult to control due to several interrelated mechanisms
  - Consumption of coagulation factors & platelets
  - Dilution of coagulation factors
  - Metabolic (e.g., hypothermia, acidosis)
  - Inflammatory process due to tissue injury
  - Drugs (aspirin, clopidogrel, warfarin)
Haemorrhage/Transfusion in Elective Surgery

- Tissue trauma is controlled
- Initiation of transfusion is rapid
- Normovolemia is maintained
- Normothermia is maintained
- Monitoring of haemostasis is ongoing
- Coagulopathy is a late event
Transfusion in Elective Surgery

Pre-Op Assessment of Bleeding Risk
- Assessment of surgical risk
- Structured bleeding history - defining any bleeding diathesis
- Estimated quality & duration of haemostatic support required
- Consultation across specialties

Intra-Op Approach to Bleeding
- Key relationships & lines of communication
- Appreciation of significance of haemodilution
- Early Rx of coagulopathy
- Application of Haemostatic Resuscitation principles similar to massive blood transfusion in trauma
Tissue trauma is massive & uncontrolled
Initiation of transfusion may be late
Hypovolemia & shock are present
Temperature is not controlled => hypothermia
Monitoring of haemostasis is late
Coagulopathy occurs early
Complications of Massive Transfusion
Lethal Triad: Hypothermia, Acidosis, Coagulopathy

Adverse Outcomes

- Systemic inflammatory response syndrome
- Multi-organ failure
- Sepsis
- TRALI/ARDS
- Mortality
**Definition:** Failure of blood to clot normally in response to tissue injury from trauma, surgery or routine invasive procedures.
**Risk factors for coagulopathy**

- 4 Major independent risk factors:
  - Injury Severity Score: ISS > 25
  - pH: < 7.10
  - Systolic Blood Pressure < 70 mmHg
  - Hypothermia: < 34°C

- All risk factors: 98%
- None of these risk factors - 1%

*Cosgriff et al. J Trauma 1997; 42: 857–61*
Challenges inherent to the management of bleeding

- Represents a significant clinical challenge
  - trauma, surgical, medical & obstetric scenarios
- High mortality
- Poor planning
- Poor communication
- Infrequent or inappropriate laboratory monitoring
- Massive transfusion
  - Inappropriate use of blood products
- Significant delay in ordering/administering plasma/fgn
- Failure to prevent hypothermia & low use of fluid warmers
Bleeding Management

- Treating team
- Lab services
- Blood products supplying service
Communication
Strategies to Minimise Blood Requirements

- Pre-operative bleeding risk assessment
  - Bleeding history
  - Drugs
- Anaemia management
  - Fe therapy
  - EPO

- Maintain haemostasis
- Oxygen support
- Maintain normovolaemia
- Temperature
- Anti-fibrinolytics (TXA)
- Red cell salvage
- Drain salvage - re-infusion systems
- Goal directed therapy
- POCT
Alternatives in Bleeding Management

- **Blind therapy**
  - According to estimated blood loss
  - 1:1:1 formula driven (RC:FFP:Plts)

- **Individualised therapy**
  - Routine lab results directed therapy [time delays]
  - PoC directed therapy – algorithm based
    - Specific coagulation factor concentrates
Goals and End Points

- If physiologic derangements can be minimized with better haemorrhage control and resuscitation early in care, likely that rates of later complications and mortality will decrease and outcomes improve
  - Minimize delays in receiving products
  - Correct products in appropriate volumes [ratios] and order to maintain reasonable concentrations of all factors
**Transfusion Guidelines - Clinical Aims**

- Maintain temp > 35°C
- pH > 7.2
- Base excess < -6
- Ionised calcium > 1.1 mmol/L
- Hb > 70 g/L
- Plt count > 50 x 10⁹/L
- PT < 1.5 x normal
- INR < 1.5
- aPTT < 1.5 x normal
- Fibrinogen > 1.0 g/L (APH/PPH > 2.0 g/L)

Avoid hypothermia, metabolic acidosis, electrolyte disturbance & haemodilution
**Effect of Hypothermia**

**Effect on Platelets**
- Temp 33-35°C results in reversible function defect
- Alteration in function of GP receptor proteins – vWF and plt GP1b/IX stop functioning

**Effect on Coagulation Cascade**
- Slows enzymatic reactions of the coagulation cascade
  - ↓ activity by ~10% / 1°C fall
- Decreases hepatic synthesis of coagulation factors
- Increases fibrinolytic activity
Clinically... Hypothermia

- Impairs thrombin generation
- **CLOTTING STOPS!**
- When occurs in conjunction with metabolic acidosis, mortality can be as high as 90%

Hypothermia impairs thrombin generation and formation of platelet plugs and fibrin clots, and at the same time increases the clot lysis resulting in coagulopathy and uncontrolled bleeding
pH

- Activity reduced at pH~7.1 for:
  - FVIIa, VII/TF complex, Xa/Va complex

- Global clotting factor enzyme activity decreased by 90% at pH~7.1

- Thrombin activity decreased by 70%
Moving Toward Normal Haemostasis

Moving Toward Normal Haemostasis

Topical Haemostatics
- Purified Factors
- FFP
- Cryo
- PLTs

Aminocaproic acid
- Tranexamic acid

Procoagulant

Antifibrinolytic Activity
- t-PA
- SK
- UPA

Anticoagulant Activity
- Heparin
- Warfarin
- LMWH

FFP=fresh frozen plasma; Cryo=cryoprecipitate; PLTs=platelets; SK=streptokinase; UPA=urinary-type plasminogen activator; LMWH=low-molecular-weight heparin.

Therapeutic Goals

- Judicious use of blood components to correct coagulopathy
  - Treat early
  - Treat adequately
  - ‘Too little, Too late’
  - ‘Not too wet nor too dry’

- Early goal-directed coagulation management
  - Surgical bleeding ↔ coagulopathy

- Goal
  - Prevent/minimize coagulopathy
  - Avoid unnecessary transfusions
  - Minimize end organ dysfunction
Goals in Transfusion Therapy

- Move from Unstable to Stable
  - Restore circulating blood volume

- Restore Oxygen carrying capacity of the blood ($DO_2$)
  - Fluid overload/underload
  - Defective RC function
  - Impaired Hb function
  - ARDS

- Avoid coagulopathy
  - Restore/maintain haemostasis
Bleeding Management

- Red Cells
  - Donor RCs
  - Scavenged RCs
- Blood components
  - Fresh Frozen Plasma (FFP)
  - Platelets
  - Cryoprecipitate [Fibrinogen]
  - PCCs (FII, [FVII], FIX, FX)
  - [rFVIIa]
- Drugs
  - Anti-fibrinolytic agents - Tranexamic acid
Red Cells

- Why give these?
  - Restore DO₂
  - Maintain blood architecture / rheology
  - Maintain contribution to haemostasis

- Why not
  - Immunomodulation
  - Infection risk
  - Independent predictor of mortality?
Haemostatic Resuscitation: RC

- Haemoglobin level ≥ 80 g/L
- O2 delivery (DO2)
- RCs promote marginalization of platelets - concentrate along endothelium & remain almost seven times that of the average blood concentration
- Hct correlates with BT
  - In rabbits, BT ↑ when the Hct < 35%
  - In humans, the BT ↑ 60% when HCT ↓ 15%
- Hct to sustain haemostasis in the bleeding patient is unknown

Red Cells

Last update: 2012
18 trials - 6264 pts

No difference in adverse events in restrictive regimes compared to liberal regimes.

Target (70-80 g/L)
The Ideal Haemostatic Agent

- Will work within minutes
- Will clot inappropriate haemorrhage
- Will not clot working vessels
- Will not have side effects
- Will be easy to store and use
- Will be inexpensive
**Coagulation factors**

- **Prior to 1990 (approximately)**
  - Fresh, stored or modified whole blood
  - Labile coagulation factors not a problem

- **Since 1990**
  - Use of packed red cells (30-60 mL of plasma)
  - Coagulation factors have become an issue
Coagulation factors

• Prior to 1990 (approximately)
  □ Fresh, stored or modified whole blood
  □ Labile coagulation factors not a problem

• Since 1990
  □ Use of packed red cells (30-60 mL of plasma)
  □ Coagulation factors have become an issue
# Clotting Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Molecular Weight</th>
<th>Plasma Concentration (µg/ml)</th>
<th>Required for Hemostasis (% of normal concentration)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen</td>
<td>330,000</td>
<td>3000</td>
<td>30</td>
</tr>
<tr>
<td>Prothrombin</td>
<td>72,000</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>Factor V</td>
<td>300,000</td>
<td>10</td>
<td>10-15</td>
</tr>
<tr>
<td>Factor VII</td>
<td>50,000</td>
<td>0.5</td>
<td>5-10</td>
</tr>
<tr>
<td>Factor VIII</td>
<td>300,000</td>
<td>0.1</td>
<td>10-40</td>
</tr>
<tr>
<td>Factor IX</td>
<td>56,000</td>
<td>5</td>
<td>10-40</td>
</tr>
<tr>
<td>Factor X</td>
<td>56,000</td>
<td>10</td>
<td>10-15</td>
</tr>
<tr>
<td>Factor XI</td>
<td>160,000</td>
<td>5</td>
<td>20-30</td>
</tr>
<tr>
<td>Factor XIII</td>
<td>320,000</td>
<td>30</td>
<td>1-5</td>
</tr>
<tr>
<td>Factor XII</td>
<td>76,000</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>Prekallikrein</td>
<td>82,000</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>HMWK</td>
<td>108,000</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>
What's the Problem?

- Constant changes in treatment recommendations
- Variation in clinical practice
- Lack of good evidence to guide practice
  - Lack of randomised controlled trials
- Assumptions
  - Abnormalities of PT/INR correlate with risk of bleeding from procedure
  - FFP use can correct abnormal PT/INR & reduce or eliminate risk of bleeding
- Inappropriate use of labile blood components
  - Exposing patients to risk with poor evidence for benefit
  - Inappropriate use of FFP to normalise INR

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Fig. 1. Relationship between coagulation screening test (PT/INR) values and in-vivo coagulation factor concentrations (adapted with permission from Dzik33). The response of PT/INR to plasma transfusion is non-linear. Relatively small increments of coagulation factors from 10% to 25% decrease INR from 3.0 to 2.2. However, the similar increase of coagulation factors at INR of 1.3 minimally shortens the INR value. PT = prothrombin time, INR = international normalised ratio.
# Summary of Dilutional Coagulopathy

<table>
<thead>
<tr>
<th>Blood Volumes Lost</th>
<th>% BV Exchanged</th>
<th>% Residual Coag Factors</th>
<th>PT/aPTT (x normal)</th>
<th>Fgn</th>
<th>Plts (x10⁹/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td>70</td>
<td>30</td>
<td>&lt;1.5</td>
<td>&gt;1.0</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Two</td>
<td>85</td>
<td>15</td>
<td>&gt;1.5</td>
<td>&lt;1.0</td>
<td>50</td>
</tr>
<tr>
<td>Three</td>
<td>≥95</td>
<td>5</td>
<td>&gt;1.8</td>
<td>&lt;0.5</td>
<td>&lt;50</td>
</tr>
</tbody>
</table>
Haemostatic Resuscitation: FFP

- Remains controversial when and in what dose plasma should be transfused to massively bleeding patients
- Optimal ratio of FFP:RCs remains to be established
  - FFP:RC ratio >1:2 is associated with improved survival compared to one <1:2
  - Goal directed management
Fresh Frozen Plasma (FFP)

- Recommendations / Guidelines
  - Patient Blood Management 2011
    - FFP:RBC > 1:2
    - “Evidence base is poor”
    - “Survivor bias”
    - No PoCT recommended
Is There an Optimal Ratio of FFP:RC?

<table>
<thead>
<tr>
<th>Pro 1:1 – 1:2</th>
<th>Indifferent</th>
<th>Con 1:1</th>
</tr>
</thead>
</table>
Haemostatic Resuscitation: Plts

- Platelets pivotal for haemostasis: low Plts increases mortality
- The highest survival was established in patients who received both a high Plt:RC and a high FFP:RC ratio

Fibrinogen

- Primary Haemostasis – mediator for platelet aggregation
- Ligand between activated platelets
- GP receptor IIb/IIIa has a high affinity of Fgn

Secondary Haemostasis
- Precursor for fibrin » clot strength
- Most common clotting factor, usually first to fall to critically low levels
- Reduced Fgn associated with increased bleeding
- Reduced Fgn on arrival increases risk of death after trauma
- Hyperfibrinolysis key part of the acute traumatic coagulopathy
- Extremely low Fgn levels are seen in massive PPH
- Impaired polymerisation

Colloids
- Fibrin degradation products
- FXIII deficiency
**Sequence of Critical Clotting Factor Concentrations**

- Most common clotting factor
- Usually the first clotting factor to fall to critically low levels

<table>
<thead>
<tr>
<th>Coagulation Factors</th>
<th>Critical Level</th>
<th>Blood Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen</td>
<td>&lt;1g/l</td>
<td>142% (117-169)</td>
</tr>
<tr>
<td>Prothrombin</td>
<td>20%</td>
<td>201% (160-244)</td>
</tr>
<tr>
<td>Factor V</td>
<td>25%</td>
<td>229% (167-300)</td>
</tr>
<tr>
<td>Factor VII</td>
<td>20%</td>
<td>236% (198-277)</td>
</tr>
<tr>
<td>Platelets</td>
<td>50 x 10⁹/L</td>
<td>230% (169-294)</td>
</tr>
</tbody>
</table>
Fibrinogen

- **PBM**
  - Fibrinogen < 1.0g/L – “indicative of critical derangement”
  - “current guidelines recommend... keeping fibrinogen above 1.0g/L”

“..insufficient evidence to identify... a fibrinogen level... to trigger a blood component transfusion”

Other guidelines (and authors) recommend fibrinogen > 1.5 or 2.0 g/L
Cryoprecipitate

- Fgn, FVIII, vWF, FXIII, fibrinectin
- Stored frozen @<-20ºC
- Dose: 2ml/kg body weight
  - WB: 378 ± 125 mg/unit (vol: 37 ± 2 mL) (Std Dose: 10 bags)
  - Apheresis: 856 ± 298 mg/unit (vol: 54-66 mL) (Std Dose: 5 bags)
  - Dose on mls/Kg not total gms
- Thawed cryoprecipitate self life 6 hrs
- Each unit ~ increases [Fgn] by 0.2 -0.4g/L
- Accurate dosing difficult
- Use when fibrinogen < 1.0 g/L despite FFP
- 1500mL of FFP = 300mL of cryoprecipitate = ~4g fgn
Fibrinogen and Clinical Benefit

Fibrinogen concentrate in bleeding patients (Review)

Wikkelsø A, Lunde J, Johansen M, Stensballe J, Wetterslev J, Möller AM, Afshari A

- August 2013
- Six RCTs of elective surgery
- Fibrinogen Concentrate reduces the risk of allogenic transfusion (RR 0.47)
- No effect on other outcomes
- Trials: “Low quality,... high risk of bias,... underpowered.”
- Excluded 14 retrospective cohort studies
Peri-operative Coagulation Monitoring

- Rational diagnostic basis for pro- & anti-thrombotic interventions in patients undergoing emergency & elective surgery
- Main goal of peri-operative monitoring of haemostasis is to:
  - increase safety of patients undergoing surgical procedures
Importance of Coagulation Monitoring

- Diagnose potential causes of haemorrhage
- Predict risk of bleeding
- *Guide appropriate haemostatic therapy*
  - Blood products associated with increased
    - LOS
    - Infections & sepsis
    - MOF
    - Morbidity & mortality
    - TRALI
    - TACO
- Standard coagulation assays
  - Often provide a specific biochemical diagnosis
  - No assurance that this correlates to the clinical picture
Rational Haemostatic Function & End Points

Identify Cause & Stop The Bleeding
- Surgery
- Physical measures
- Embolisation
- Minimise delay in receiving products

Adequate Haemostatic Function
- Std coags or PoCT (ROTEM/TEG)
- Correct blood products in appropriate volumes
- Anti-fibrinolytics
How to Optimally Monitor & Assess Haemostatic Function

- Require information on all aspects of haemostasis
- Knowledge of rate & amount of thrombin production
- PT & aPTT only report initial generation of thrombin based on first appearance of clot
- Events that occur after initial thrombin generation are also critical but ARE NOT assessed by PT & aPTT:
  - Changes in fibrin assembly, structure and mechanical properties
  - Platelet activation
  - Fibrinolysis
A good model should be simple enough to improve clarity, but....
Coagulation Pathway

The classic coagulation 'cascade' does not explain how blood clots in vivo.
Coagulation

There really are ‘Intrinsic’ & Extrinsic Pathways

- Not redundant – operate on different cell surfaces

- ‘Extrinsic’ or TF pathway works on the initiating cell
- ‘Intrinsic’ pathway works on platelet surface
Normal Haemostasis Is a Balance

Bleeding to Death

• Trauma
• Major Surgery
• Haemophilia

Clotting to Death

• Stroke
• MI
• Thrombosis

- Blood coagulation
- Anticoagulation
- Fibrinolysis
- Anti-fibrinolysis
- Vascular tone and blood flow
- Endothelial cells and platelets

The Ideal ‘Global’ Assay?

- Allow assessment of an individual’s haemostatic state
- Based on plasma or cell model of coagulation
  - Endpoint: clot formation or thrombin generation
  - Incorporate platelet/membrane components
  - Include fibrinolysis
- Good correlation with clinical outcomes
  - Thrombosis and bleeding risk
  - Sensitive to various anticoagulants
- Rapid, inexpensive
- Easy to use in routine lab or clinical setting

“All experimental systems, whether in vitro, ex vivo or in vivo are, in their own way, artificial, with limitations both known and unknown” Allen et al J Thromb Haem 2:402 2004
Standard Coagulation Tests

- The commonly used clinical coagulation tests only reflect the adequacy of the coagulation factor levels in the pathway being tested.

- Each test only assays *a part* of the components required for haemostasis.
Coagulation Monitoring

- No appropriate tests available for use in complex surgery or critical bleeding
- Routine coagulation testing – limited for massive bleeding

**Standard testing [PT/INR, aPTT, Fgn, Plts]:**
- Not good predictors of transfusion requirements
- Indirect correlation with clinical picture
- Poor predictive value for bleeding
  - PT/INR – developed to monitor warfarin therapy
  - aPTT – developed to monitor heparin therapy
  - Fibrinogen (Clauss Method) may be over estimated by up to 30% in presence of infused colloids or starches
Standard Coagulation Tests

- Stop measuring at first stage of coagulation, when the clot first forms
- Platelet poor plasma tests - measures plasma haemostasis not patient haemostasis, which is in whole blood
- Important role of RCs, plts and phospholipids in coagulation not taken into account
Plasma Clotting Analyses

Shortcomings

- Traditional plasma coagulation analyses return only information of clot formation start
Viscoelastic Coagulation Methods

- Growing evidence that rotational thromboelastometry (ROTEM) or thromboelastography (TEG) are superior to conventional assays
- Real-time measurement of visco-elastic properties of clot kinetics
- Potential to guide coagulation therapy according to actual needs
  - Reduce risk of over or under transfusion – algorithm guided replacement
  - Cohort studies
    - Reduced transfusion requirements
    - Reduced transfusion related adverse events
    - Improved outcomes
- Used in various clinical settings – liver transplant, cardiac surgery, obstetrics & trauma
- High negative predictive value
  - normal results → bleeding highly unlikely due to significant coagulopathy
The Technology

- Advantages
  - Assesses broader picture of haemostasis
  - Identifies mechanisms of massive intra-operative blood loss & trauma-associated coagulopathy
  - Clotting is induced under low sheer conditions (similar to rheologic properties in venous system *in vivo*)
  - Improved TAT for clinical therapy

- Disadvantage
  - Endothelial component not involved
  - Activators result in generation of thrombin and may mask effect of anti-platelet agents
Viscoelastometry

- Functional assay
- Global assessment (from initiation of coagulation through clot lysis)
- Multiple end-points
- Reflect ability to monitor thrombin burst
- Functional fibrinogen
  - Function
  - How much used in clot
- Factor Deficiencies
- Platelet Function
- Clot Strength
- Fibrinolysis
Hemorrhage and traumatic coagulopathy are major causes of early death in multiply injured patients. Thrombelastography (TEG) seems to be a fast and accurate coagulation test in trauma care...to detect an acute traumatic coagulopathy and especially primary fibrinolysis....
Thrombelastography (TEG) or thromboelastometry (ROTEM) to monitor haemotherapy versus usual care in patients with massive transfusion (Review)

Afshari A, Wikkelso A, Brok J, Moller AM, Wetterslev J

“No beneficial effect on patient’s survival [no RCTs]”

BUT

“Positive results on reducing bleeding and proportion of patients requiring transfusion (platelets and plasma)”

2011
POC Improves Outcome


- 152 – randomized to 100 Pts with complex surgery and adverse bleeding randomized to POC (RoTEM plus Multiplate) Vs conventional therapy
- Primary Outcome: RC Usage 4.9 u (conventional) Vs 2.6 POC p<0.001
- Secondary outcomes all less in POC:
  - FFP, Plt ,Mech Vent time, LOS, 6 month mortality

Anesth 2012; 117: 531-47
Use of PoCT

- Time efficient
- Clinically efficacious
- Cost effective
- Pathophysiology driven therapy
- Guiding selective blood component/anti-fibrinolytic use
- Reduce inappropriate transfusions
- Decreases variability in treatment
**Therapeutic Considerations**

**Timing & Sequence of Interventions**
- Correct pH & temp
- Explore traumatic/surgical source of bleeding
- Avoid excessive dilution with colloids/crystalloids
- First line substitution with Fgn
- Facilitate thrombin generation with PCC or FFP
- Plt transfusion

- Basic conditions
  - $T > 34 \, ^\circ C$, pH 7.2, $Ca^{++} > 1$mmol/L, $Hb > 80$g/L

- Surgical control (compression, pelvic compression, packing)

- Anti-fibrinolytics
  - Aspirin, oral anticoagulants, heparin

- PCC or FFP

- Platelets

- rFVIIa

- FXIII
Summary

- Establish a multi-disciplinary approach
- Consider blood conservation strategies
- Blood transfusions are not benign - must be used in an individualised goal directed manner in all patients
- Coagulopathy is an intricate multi-cellular & multi-factorial process
- PT & aPTT used as surrogate markers
- Problems with conventional assays
  - Time lapse for reporting result
  - Insufficient identification of the haemostatic defect
Conclusion

- Change in philosophy required
  - From sending std coags or PoCT only when there is obvious bleeding
  - Towards concept of routinely monitoring high risk patients throughout resuscitation/surgery

- PoCT results in:
  - Fewer transfusions
  - Improved outcomes

- Informs clinical practice
- Identifies patients at risk
- Allows early identification & treatment of evolving coagulopathy
- No longer acceptable to manage bleeding patients on the basis of clinical judgement & probabilities – invariably leads to increased transfusions
THANK YOU