MANAGEMENT OF COAGULOPATHY AFTER TRAUMA OR MAJOR SURGERY

19th ANNUAL CONTROVERSIES AND PROBLEMS IN SURGERY

Thabo Mothabeng

General Surgery: 1 Military Hospital

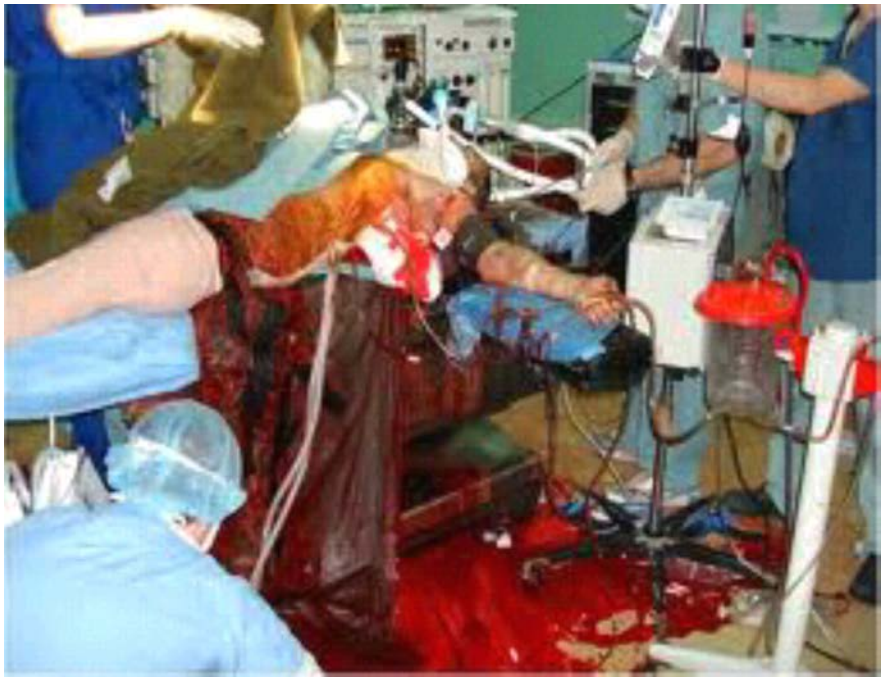
sa military health service

Department:
Defence
REPUBLIC OF SOUTH AFRICA

ONE OF THE MOST FRUSTRATING SITUATIONS ever encountered by the operating surgeon is an open wound in a patient whose blood will not clot and cannot be made to clot. By far the most extreme example is a bleeding diathesis complicating laparotomy. This event is an all-too-common occurrence in the patient who has sustained a major intraabdominal injury or who has a disease process or operation which has been attended by a massive hemorrhage. The coagulopathy can seldom be reversed satisfactorily. Thus, the usual outcome is continued bleeding and thereby death through exsanguination.

HH Stone et al. Ann Surg. May 1983; 197(5): 532–535.

Coagulopathy of Trauma



The blood loss is usually underestimated!

What is this Coagulopathy?

- **Various terminology**
  - Trauma Induced Coagulopathy (TIC)
  - Acute Coagulopathy of Trauma Shock (ACoTS)
  - Acute Traumatic Coagulopathy (ATC)
- **Acute Coagulopathy**
  - Bloods ability to clot is impaired
  - Increased fibrinolysis
  - There may be thrombotic states
  - Prolonged or excessive bleeding

Acute Coagulopathy of Trauma

- Complicates trauma and major surgery
  - Hypoperfusion is crucial
- Control of bleeding is difficult when coagulopathy is established
- Immediate/ Early Onset
  - One in four trauma patients
  - Four fold increase in mortality

Characteristics of Coagulopathy

- Immediate effect; before hemodilution
- Proportional to injury
- Hypoperfusion initiates
- Hypothermia and acidemia augment
- Clot strength reduced (Coagulopathy)
- Clot formation minimally delayed
- Fibrin polymerization impaired (Fibrinolysis)
- Platelet dysfunction augments (?Delayed)

Association with ISS

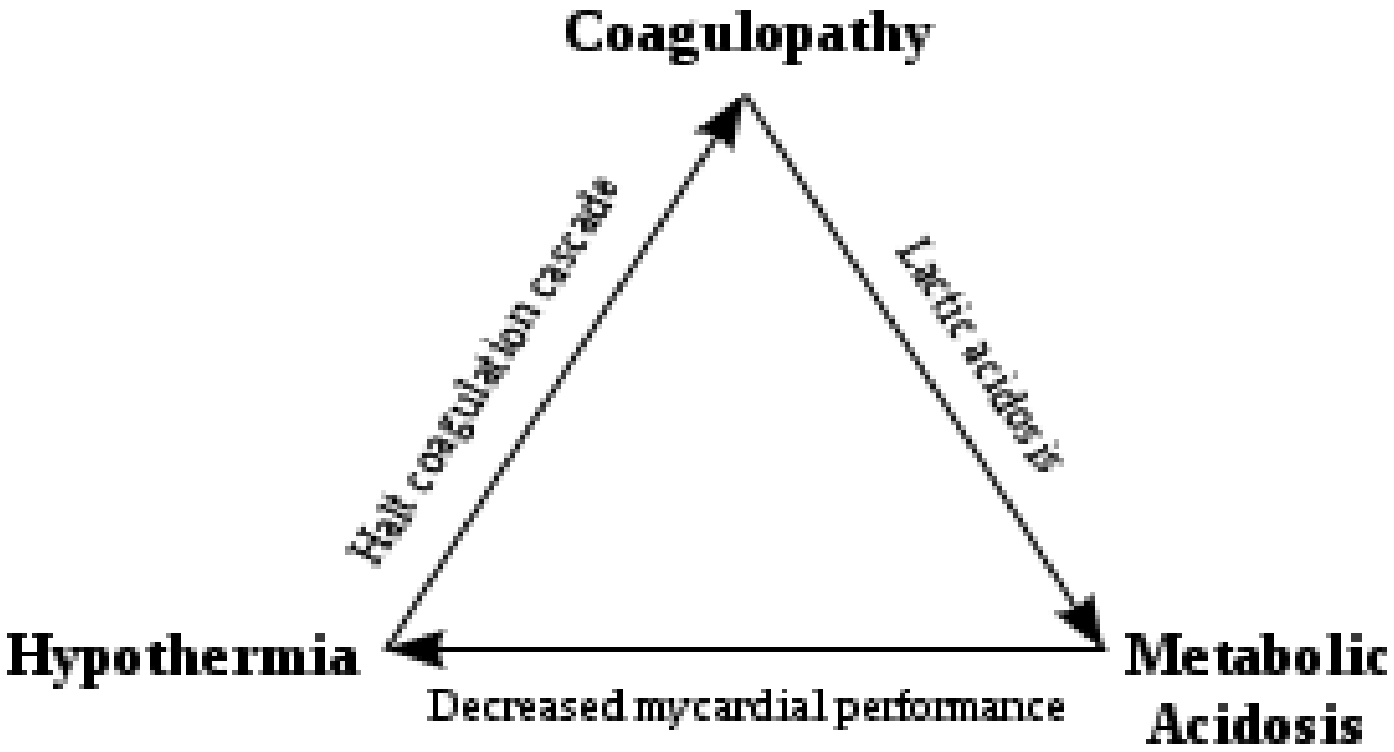
Injury Severity Score	Incidence of ACoTS
15 - 29	21%
30 - 44	41%
45 - 59	59%
60 - 75	79%

May. J Trauma 2003; 54

Key Initiators

1. Tissue damage (Endothelial damage)
2. Hypoperfusion (Shock)
3. Hemodilution
4. Hypothermia
5. Acidosis
6. Inflammation

LETHAL TRIAD OF TRAUMA



Hypothermia

- Reduced function of all factors
- Activity reduced by 50% at T^{o} *less than 33^{o}C*
- Impaired platelet aggregation

Johnston. J Trauma 1994; 37

- Fibrinolysis is stimulated.
- Rohrer et al found that aPTT

37 Degrees	34 degrees	31 degree
36seconds	39	46

- Decreases activation of platelets

Acidosis

- Reduced activity and activation of coagulation factors

Meng. J Trauma 2003

- Increased degradation of fibrinogen
- Impaired function of plasma proteases
- Corrected by administration of buffer solutions
  - ✓**This does not correct coagulopathy**

Shock

- Prime driver of early coagulopathy
  - Direct tissue trauma
  - Systemic hypoperfusion
- Prolonged clotting times

BASE DEFICIT	<6MMOL/L	>6MMOL/L
% PROLONGED CLOTTING TIMES	2%	20%

Hemodilution

- Direct loss of coagulation factors
- Haemorrhage quickly reduce
  - Fibrinogen (10g)
  - Platelets (15ml)
- Losses are then replaced with fluids
  - Crystalloids or colloids
  - Causing **dilutional coagulopathy**
- **Paradigm shift in resuscitation!**

THE “BLOODY VICIOUS CYCLE”

- Injury severity score > 25
- pH<7.10 + Systolic BP<70 mmHg
- Core temperature <34^{o}C

WHEN ALL 3 PRESENT: INCIDENCE OF COAGULOPATHY = 98%

Underlying Diseases and Drugs

- Coagulation defects e.g. von Willebrand disease
- Liver disease
  - Thrombopoietin and haemostatic proteins
  - Reduced Vit K dependent coagulation factors (II, VII, IX and X)
  - Inhibited platelet aggregation.
- Renal disease
  - Impaired platelet function
- Oral anticoagulants

Vitamin K Antagonists

- Increased incidence of use: 2.3% (2002) to 12.8% (2006)
- Related to 50% mortality in young patients
- Prothrombin concentrate complex (PCC) & Vit K.

CA Dossett. Arch Surg 2011

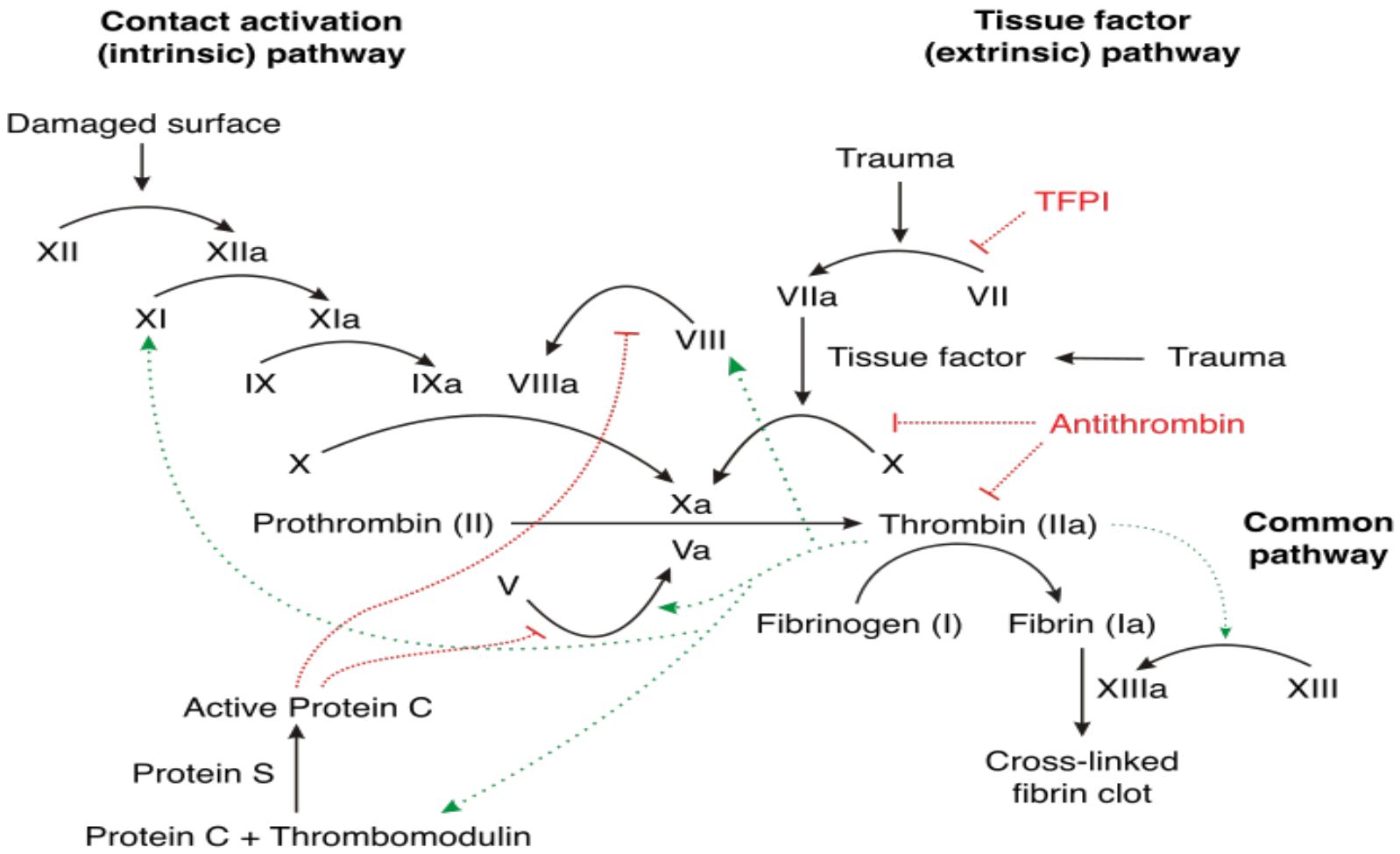
GH Guyatt. Chest 2012

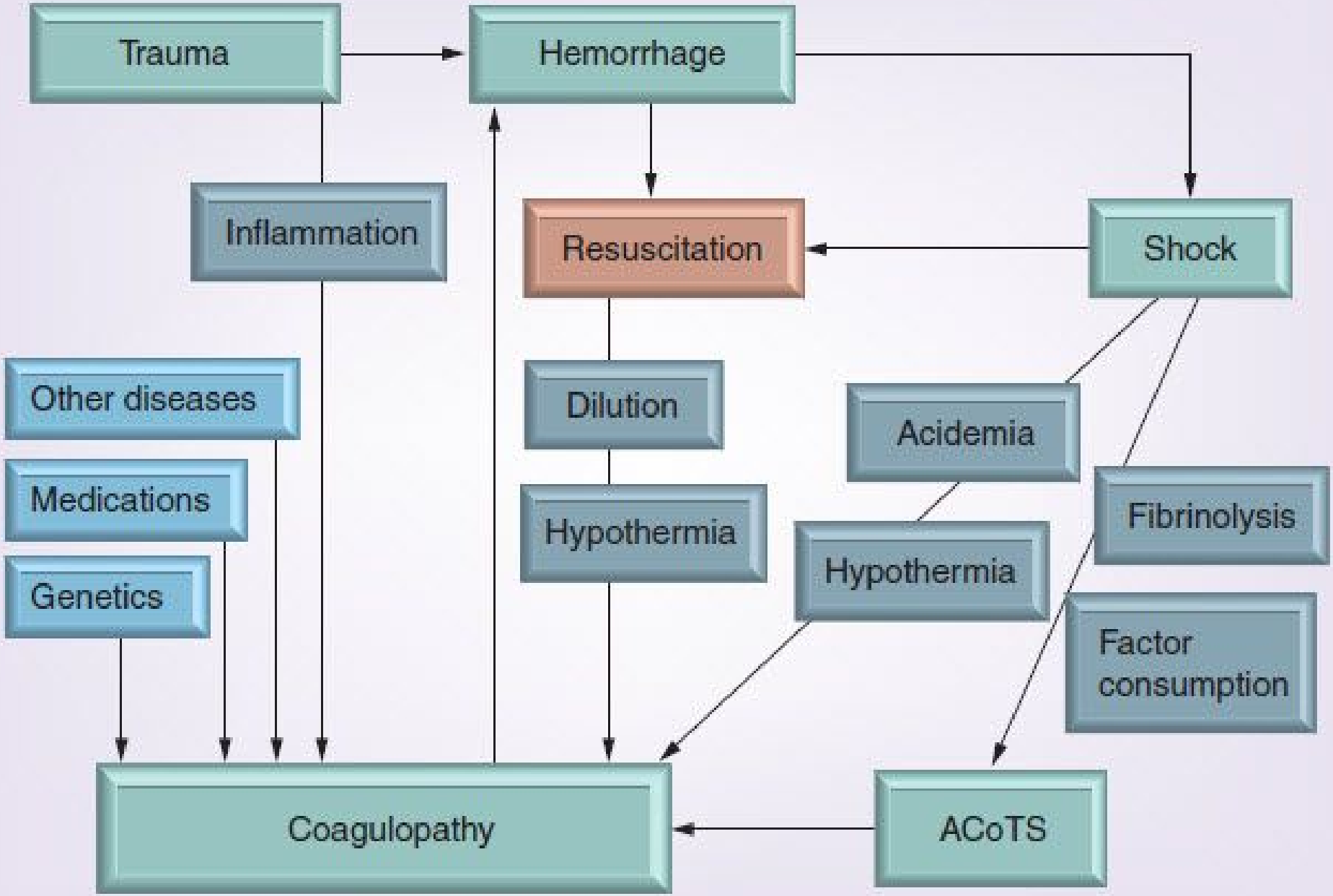
D Keeling. Br J Haematol 2011

- High doses of PCC reverse rivaroxaban, not dabigatran

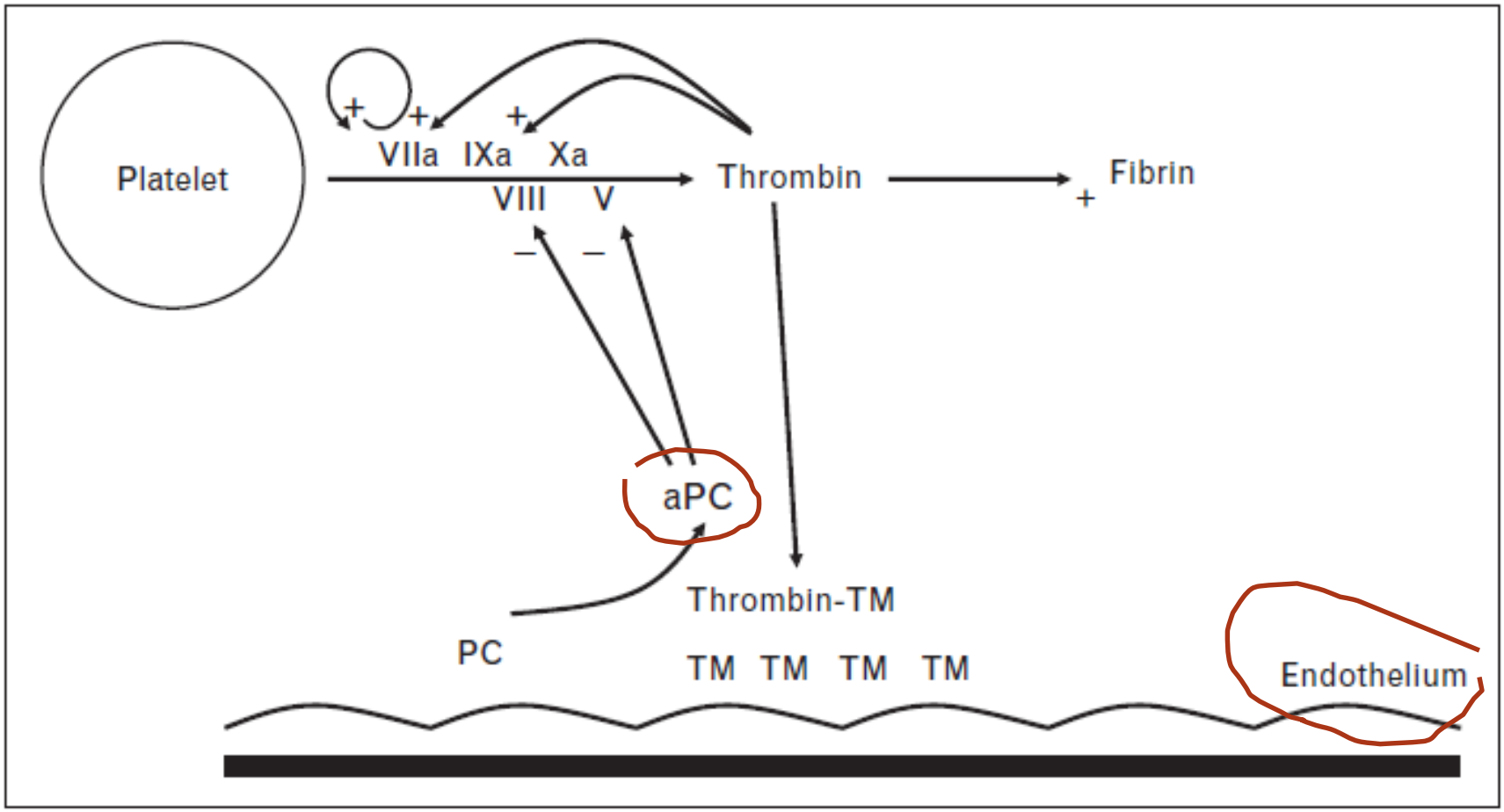
S Kaatz. Am J Hematol 2012

Pathophysiology

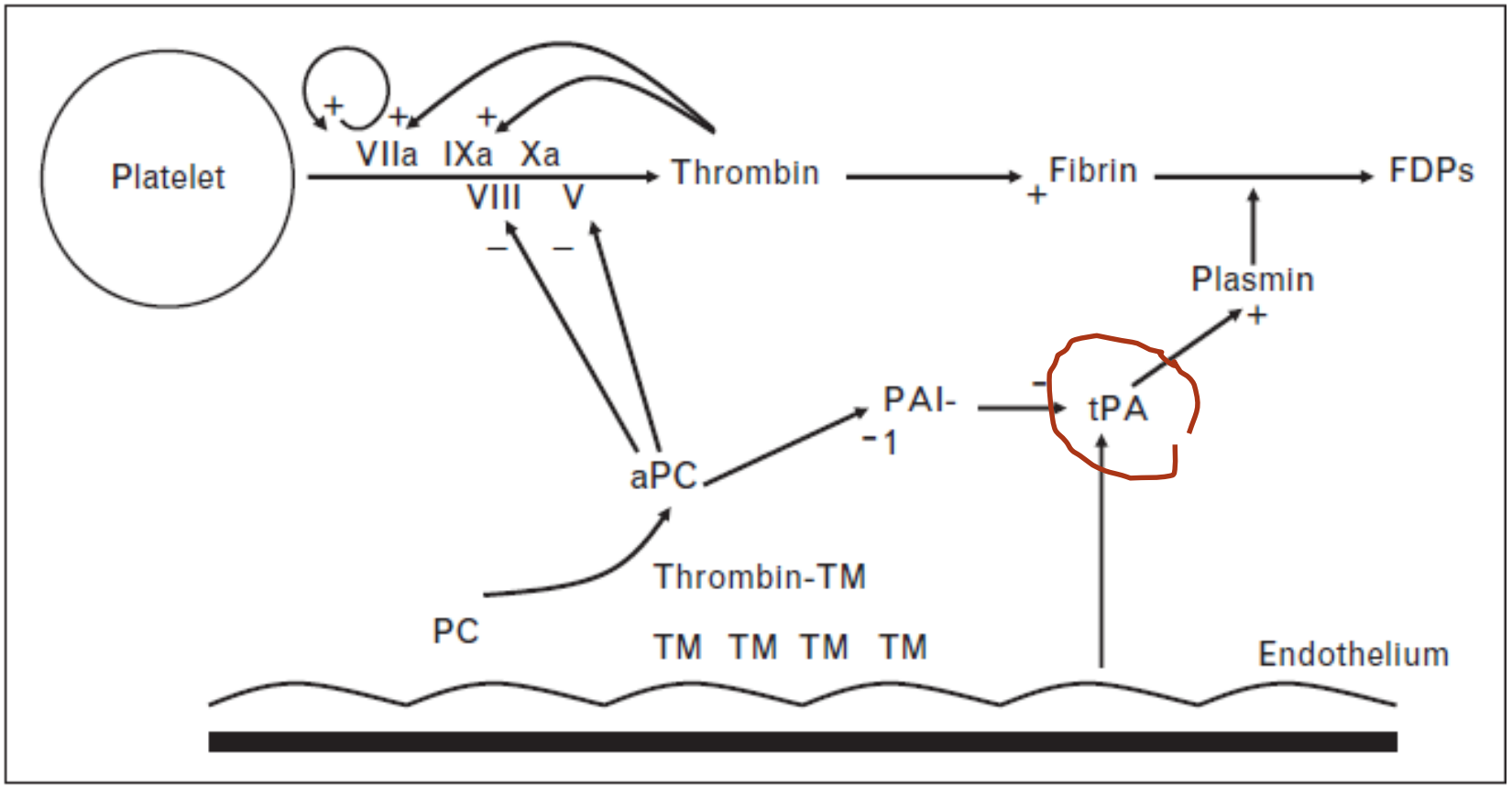




Pathophysiology



Fibrinolysis



Classical Coagulation Tests

- Platelet count
- Haematocrit
- INR
- Prothrombin time
- Activated partial thromboplastin time
- Fibrinogen
- Platelet function analysis

Classical Coagulation Tests

- No consensus on what values
- Test first 20 seconds of clot mechanism
- No correlation with bleeding or clotting factor activity
- Plasma based test not whole blood (in vivo)
- May not detect fibrinolysis
- Takes 45 to 75 minutes
  - Schochl H, Scand J Trauma Resusc Emerg Med. 2012;20:15.

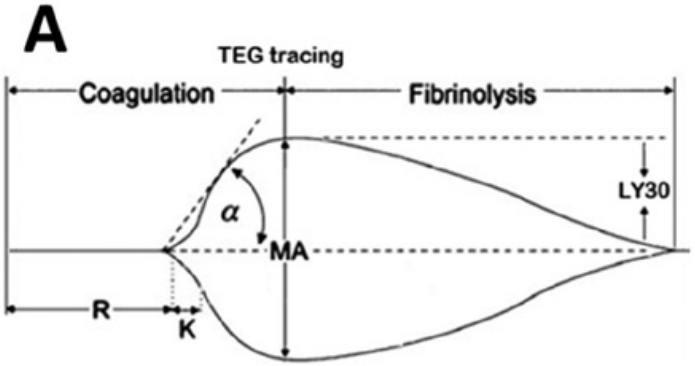
“Closer to the Ideal”

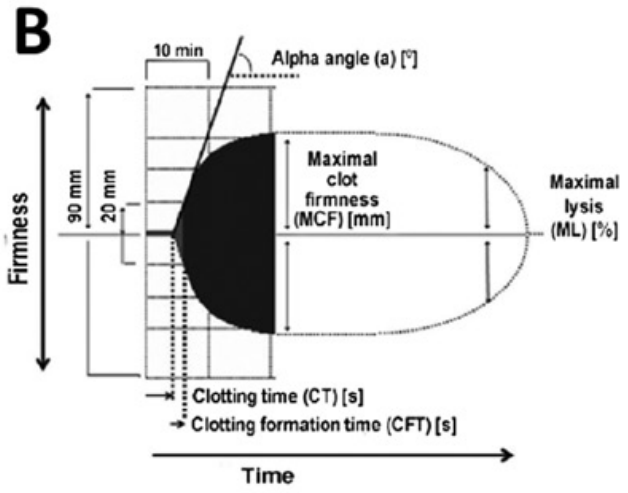
- Thromboelastography (TEG)
- Rotational thromboelastography (ROTEM)
  - Replacing TEG
  - Information in 5 to 10 minutes
  - Measure of entire clotting mechanism (in vivo haemostasis)
  - 64% accuracy vs. 10% of CCT
  - Predict need for massive transfusion

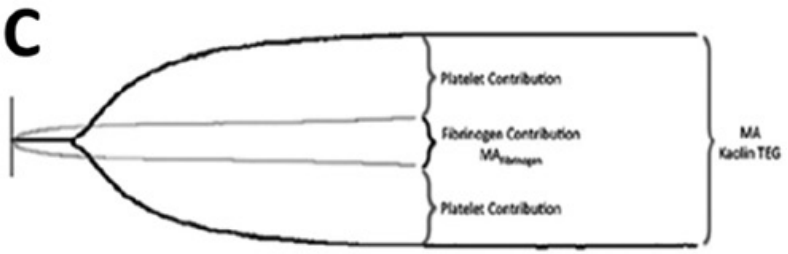
Schochl H, 2012.

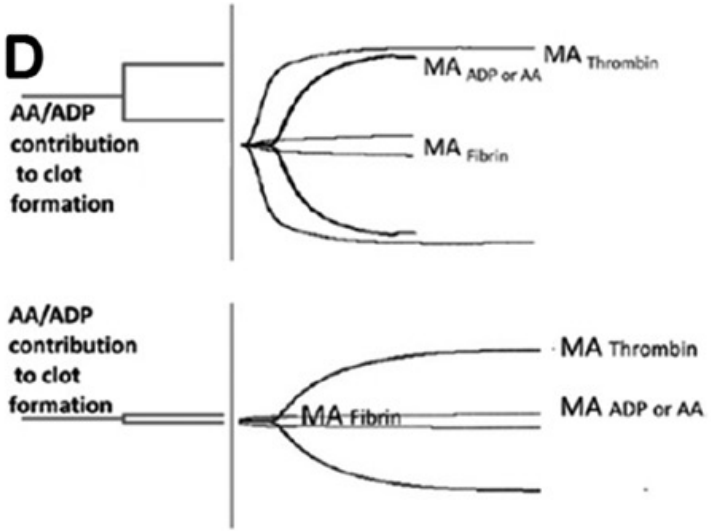
Davenport R, 2011

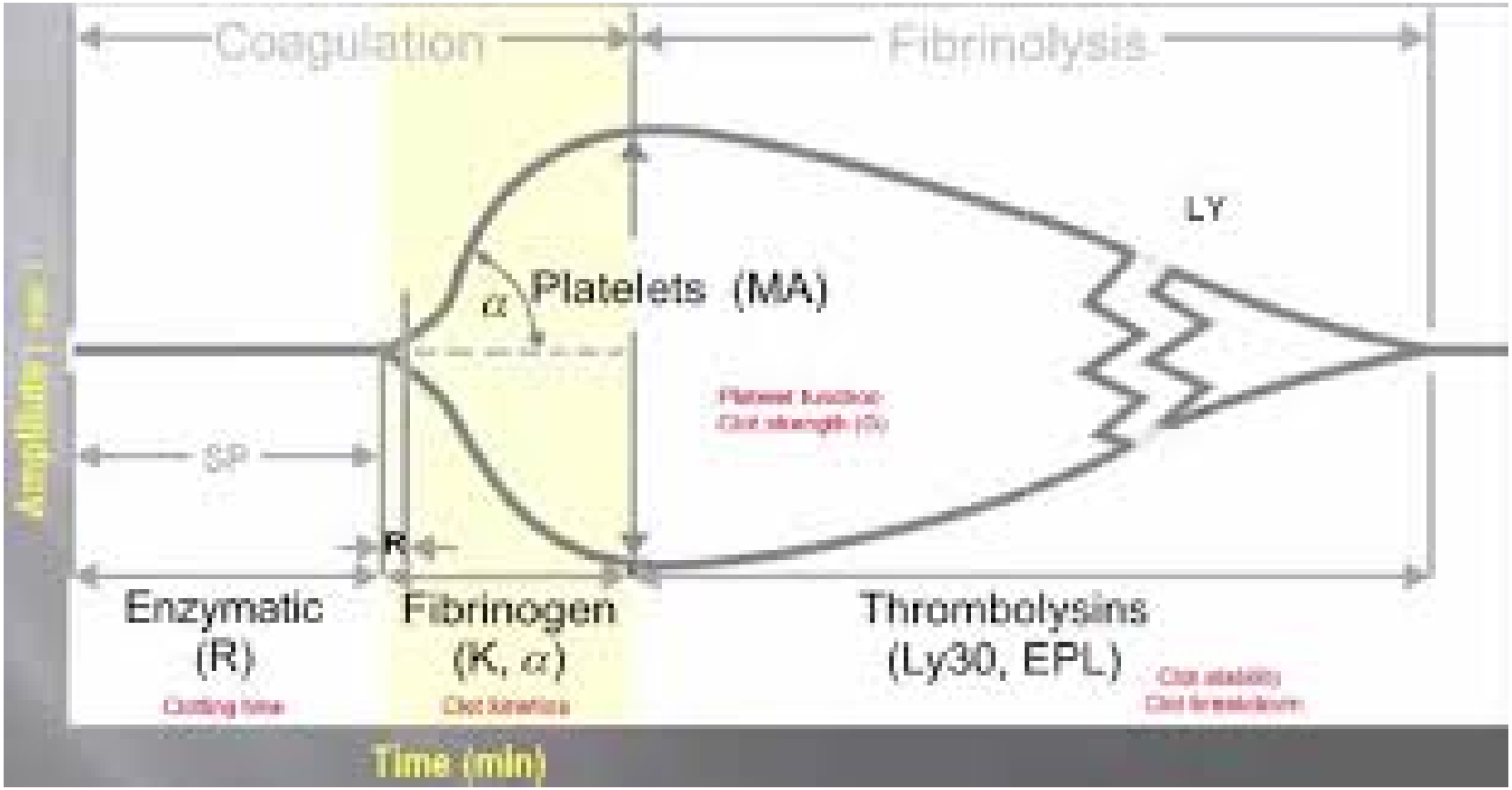
Viscoelastic Haemostatic Assay










Coagulation
Fibrinolysis
LY
α
Platelets (MA)
SP
R
Enzymatic
(R)
Fibrinogen
(K, α)
Thrombolysins
(Ly30, EPL)
Time (min)

Viscoelastic Haemostatic Assay

- Measures 5 parameters
  - **R time:**
    - Coagulation factor activity
  - **K time:**
    - Speed of clot formation
  - **Alpha angle:**
    - Fibrin formation
  - **Maximal Amplitude (MA):**
    - Platelet function
  - **Whole blood lysis**:

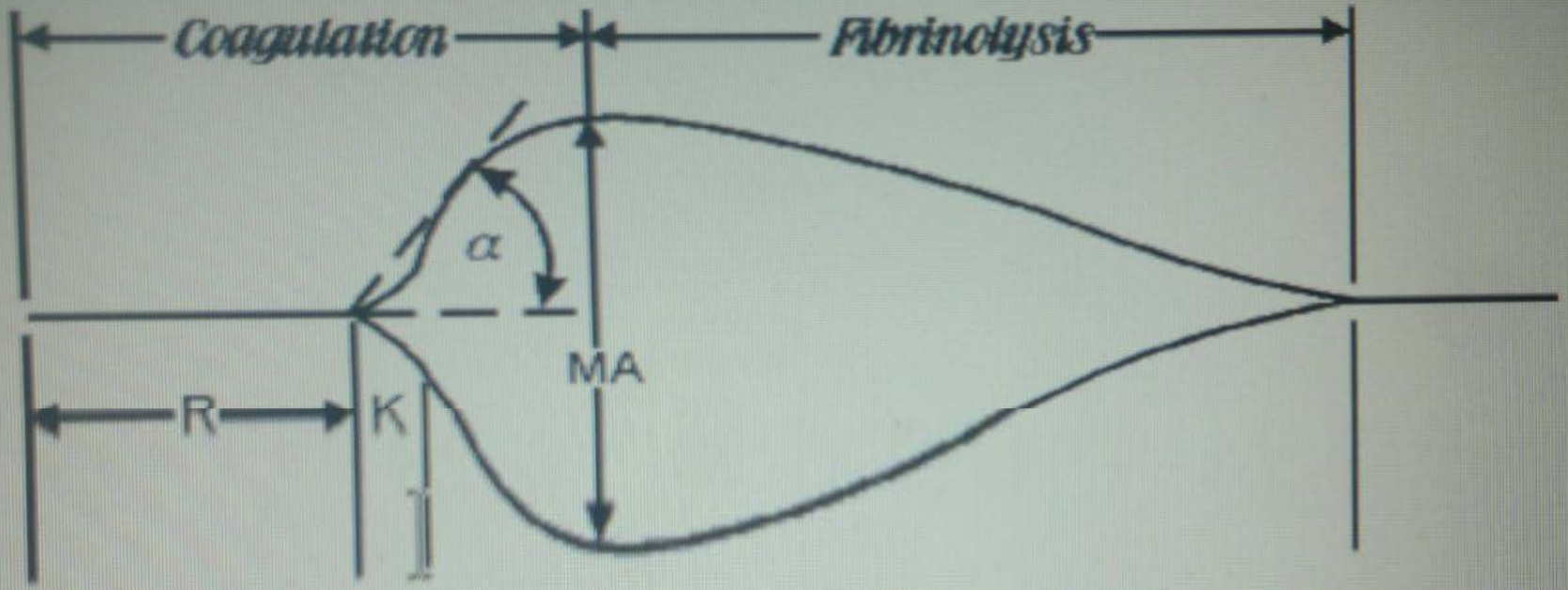


Figure 4. Thromboelastograph (TEG) tracing. The reaction time (R) represents the time to onset of clot formation. K time is a measure of the speed to reach a certain level of clot strength. α angle represents the rate of clot formation. The maximum amplitude (MA) measures the clot strength. Reprinted with permission from Kiraly, J Trauma 2006;61:57–64.

Management: Key Steps

- Permissive hypotension
- Blood and blood products
- Temperature control and Rewarming
- Correction of acidosis
- Calcium homeostasis
- Pharmacological treatment
  - Tranexamic acid
  - Antifibrinolytic
  - Prothrombin complex concentrate (PCC)

Predicting massive transfusion

- ❑ INR Greater than 1.2
- ❑ Base deficit Less than -6 mmol/L
- ❑ Systolic blood pressure Less than 90 mmHg
- ❑ Injury severity score Greater than 15
- ❑ Haemoglobin Less than 11 g/dL
- ❑ FAST exam Positive for haemorrhage
- ❑ Blood pH Less than 7.25
- ❑ Body temperature Less 35.5 celsius
- ❑ Heart rate Greater than 120 bpm

End points of resuscitation

- VHA directed management
- Give FFP, cryoprecipitate and platelets as indicated
- Massive Transfusion Protocol
- Targets
  - INR < 1.5
  - Fibrinogen > 1 gm/L
  - Platelets > 50 x 10^9/L

Fibrinogen

- Affected early and most of all factors
- Depleted in many bleeding patients
- Poor outcome, reversed by administration

Rourke. J Thrombo Haemost 2012; 10

Tranexemic Acid

Standard of care in most trauma units

Benefit when administered early

H Shakur. Lancet 2010; 376

Recombinant Factor VIIa

- Boffard K et al

	BLUNT	PENETRATING
NUMBER	143	134
PLACEBO	74	64
rFVIIa	69	70
REDUCTION RBC UNIT	REDUCED: 2.6UNIT	REDUCED: 1UNIT
MASSIVE TRANSFUSION	REDUCED BY 33%	REDUCED BY 19%

Recombinant FVIIa

- Binds directly to surface of activated platelets
- Enhances
  - Enhances thrombin generation
  - Fibrin clot formation
  - Producing a stable clot

Prothrombin Complex Concentrate

- PCC or a complex of factors , II, Ⅶ, Ⅸ, Ⅹ
- Off label use in trauma
- Reduce transfusion requirements
- Reversal of oral anticoagulants

Combination of fibrinogen and PCC:

- Fibrinogen levels are the first to decline haemorrhage
- Use of PCC can
  - Reduce risk of TRALI
  - Reduce risk of viral infections.
  - Reduce blood loss
  - Shorten time to coagulation
- Maintain fibrinogen level of > 1.5 g/L

Leir. J Trauma 2008

Calcium homeostasis

- Necessary for fibrin clot stabilisation.
- Hypocalcaemia (< 0.9 mmol/ L) should be treated
- Hypocalcaemia is aggravated by rapid infusion of blood products
- Chelation of calcium by the anticoagulant citrate
- Low levels associated with higher mortality and increased need for blood transfusion.

Cherain, WJS 2014

Thank You!