MVA

Sept 2018

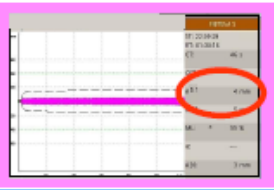
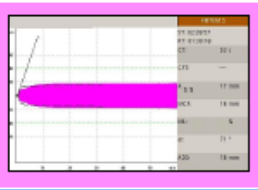
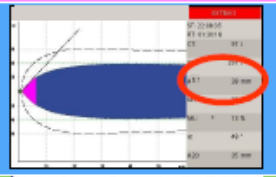
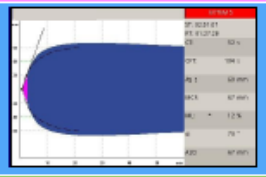
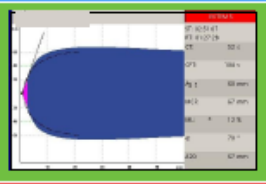
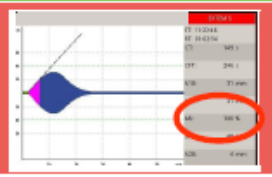
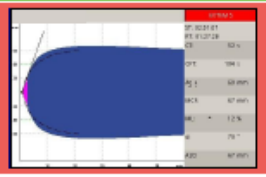
Thanks to Dr Ben Piper from Dept of Anaesthesia in Royal Darwin Hospital for sharing this.

Disclaimer / Pre-amble

- These cases have been de-identified to protect the identity of the patient and the treating teams.
- These are all real cases and real ROTEMs. The individuals involved in these difficult cases have agreed to anonymously share these with us – thank you for your generosity.
- Successful management of the bleeding patient involves much more than just administration of blood products.
- The primary aim of these cases is to teach the use ROTEM guided blood product therapy. We have deliberately not included a lot of detail about some of the other aspects of management which might detract from this focus.

KEMH ROTEM Algorithm for Critical Bleeding

Key Points: This algorithm should be used in conjunction with the KEMH Blood Product Guidelines for Major Obstetric Haemorrhage. Only treat abnormal values if active bleeding or at high risk of bleeding. Repeat ROTEM analysis 10 mins after intervention to assess response.

	ABNORMAL ROTEM	CRITERIA	DIAGNOSIS	INTERVENTION	CORRECTED ROTEM
FIBRINOGEN		**FIBTEM A5≤10mm**	**Low fibrinogen**	**Cryoprecipitate OR Fibrinogen concentrate** (see dosing guide) **AND Tranexamic acid 1 g**	
PLATELETS		**EXTEM A5 ≤35mm** and FIBTEM A5 ≥10mm	**Low platelets**	**Platelets: 1 adult dose** (correlate with platelet count)	
		EXTEM A5 ≤25mm and FIBTEM A5 ≤10mm	**Low platelets** and **Low fibrinogen**	**Platelets and fibrinogen** (correlate with platelet count)	
FACTORS		**EXTEM CT 80-140s** and FIBTEM A5 ≤10mm	**Low fibrinogen**	Correct **fibrinogen** and reassess	
		EXTEM CT >140s and FIBTEM A5 ≤10mm	**Low fibrinogen and Low coagulation factors**	**FFP 1-2U + Fibrinogen as indicated** (Consider Prothrombinex-see below)	
FIBRINOLYSIS		Early Diagnosis **EXTEM A5≤35mm** or **FIBTEM CT >600s**	**High likelihood of excess fibrinolysis**	**Tranexamic acid 1g** Consider repeat dose if has lost over 1 blood volume since initial dose	
		Late Diagnosis **EXTEM or FIBTEM ML ≥5%**	**Excess fibrinolysis**		

Fibrinogen Dosing Guide

FIBTEM A5 Target: ≥12mm

FIBTEM A5	Increase required	Cryoprecipitate	Fibrinogen Concentrate
9-10mm	2-3 mm	1-2 doses	2g*
7-8mm	4-5 mm	1-2 doses	3g*
4-6mm	6-8 mm	2 doses	4g
<4mm	≥9mm	2 doses	5g

*Outside of currently approved guidelines, must be discussed with haematologist

Fibrinogen Concentrate

Guidelines For Use

- Consultant anaesthetist or haematologist approval required.
- Patients must be experiencing life threatening haemorrhage.
- Fibrinogen concentrate may be indicated instead of, or in addition to, cryoprecipitate if the FIBTEM A5 is 6mm or below, OR there is a high suspicion of coagulopathy in a life threatening haemorrhage.
- Use at higher FIBTEM values may be appropriate in patients refusing cryoprecipitate.

Administration

- Reconstitute 1g in 50ml warm sterile water (use prepared kit in fluid warmer).
- Swirl gently and do not shake (to avoid foaming).
- Administer each 1g via syringe driver over 2-4 mins if life-threatening haemorrhage or over 10 mins if not.

Cryoprecipitate

1. 1 dose is equivalent to 10 whole blood units or 5 apheresis units.
2. May be supplied as whole blood units or as apheresis units (or a combination) 1 apheresis unit = 2 whole blood units.
3. Availability time: generally available within 10 minutes of request being made

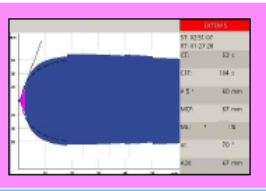
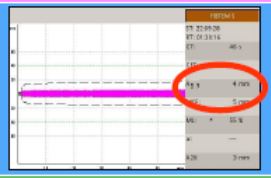
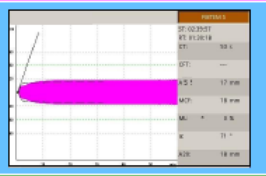
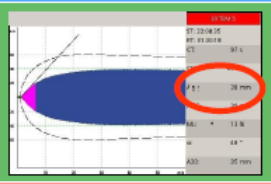
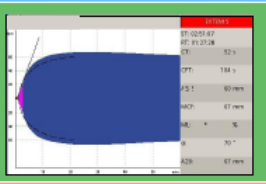
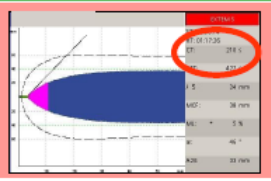
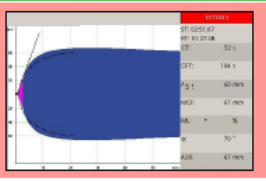
Prothrombinex

1. Haematologist approval required
2. Consider as an alternative to FFP for patients with coagulation factor deficiency (e.g. prolonged EXTEM CT see above) in the following circumstances:
   - Circulatory overload
   - Rapid correction in extreme coagulopathy

Endorsed by the Department of Anaesthesia and Pain Medicine and the Hospital Transfusion Committee on 31/05/2017

SCGH ROTEM Algorithm for Critical Bleeding

Key Points: This algorithm should be used in conjunction with the SCGH Critical Bleeding Protocol. Only treat abnormal values if active bleeding or at high risk of bleeding. Repeat ROTEM analysis 10 mins after intervention to assess response.

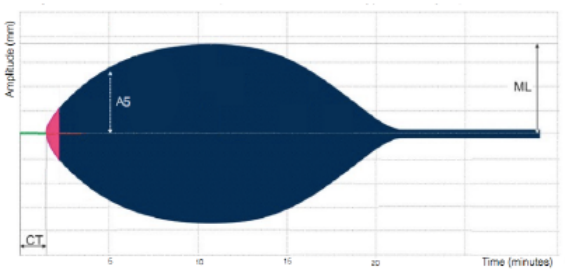
	ABNORMAL ROTEM	CRITERIA	DIAGNOSIS	INTERVENTION	CORRECTED ROTEM
FIBRINOLYSIS		Early Diagnosis **EXTEM A5≤35mm** or **FIBTEM CT >600s**	**High likelihood of excess fibrinolysis**	**Tranexamic acid 1g** Consider repeat dose if has lost over 1 blood volume since initial dose	
		Late Diagnosis **EXTEM or FIBTEM ML ≥5%**	**Excess fibrinolysis**		
FIBRINOGEN		**FIBTEM A5≤10mm**	**Low fibrinogen**	**Cryoprecipitate** (see dosing guide)	
PLATELETS		**EXTEM A5 ≤35mm** and FIBTEM A5 >10mm	**Low platelets**	**Platelets: 1 adult dose** (correlate with platelet count)	
		EXTEM A5 ≤25mm and FIBTEM A5 ≤10mm	**Low platelets** and **Low fibrinogen**	**Platelets and fibrinogen** (correlate with platelet count)	
FACTORS		**EXTEM CT 80-140s** and FIBTEM A5 ≤10mm	**Low fibrinogen**	Correct **fibrinogen** and reassess	
		EXTEM CT >80s but FIBTEM A5 >10mm	**Low coagulation factors**	**FFP 1-4U** or **Prothrombinex 10 U/kg** (+ fibrinogen if indicated)	
		EXTEM CT >140s and FIBTEM A5 ≤10mm	**Low fibrinogen and Low coagulation factors**		

Fibrinogen Dosing Guide

FIBTEM A5 Target: ≥12mm

FIBTEM A5	Increase required	Cryoprecipitate*
9-10mm	2-3 mm	10 Units
7-8mm	4-5 mm	15 Units
4-6mm	6-8 mm	20 Units
<4mm	≥9mm	20-25 Units

*Cryoprecipitate dosing is for standard adult units
(Cryo 5 units = Fibtem A5 increase of approx 2mm)



Prothrombinex

1. Warfarin Reversal: Indicated for urgent reversal of warfarin in critical bleeding, usual dose 25-50U/kg (+/- FFP) discuss with haematologist.

2. Consider as an alternative to FFP for patients with coagulation factor deficiency (e.g. prolonged EXTEM CT see above) in the following circumstances:
- Circulatory overload
- Rapid correction in extreme coagulopathy
- Consider lower dose 10U/kg (round to nearest 500U).

Endorsed by the Department of Anaesthesia and Pain Medicine and the Haematology department January 2017 Adapted from KEMH hospital algorithm with permission

FSH ROTEM Algorithm for Critical Bleeding

This algorithm should be used in conjunction with the FSH Major Haemorrhage Protocol
Treat abnormal values only if there is active bleeding or the patients is at high risk of bleeding.
Repeat ROTEM analysis 10 mins after any intervention to assess response.

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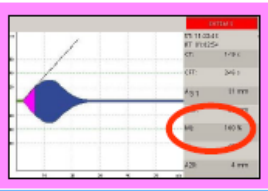
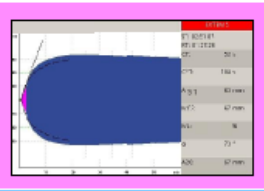
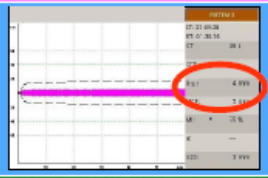
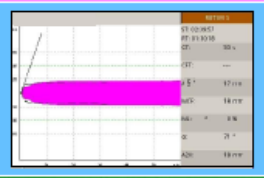
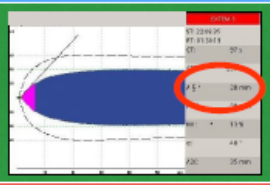
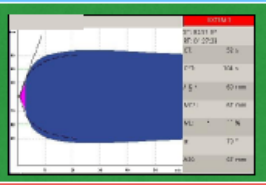
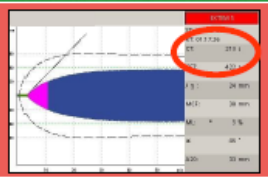
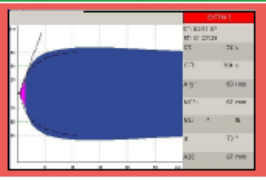
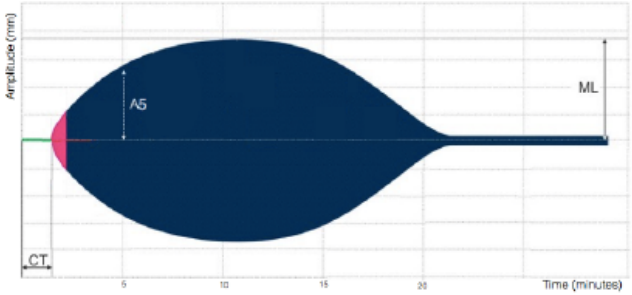
FIBRINOLYSIS		Trauma (within 3hrs) OR Post partum haemorrhage Flat trace OR Maximal lysis >5%	→ Hyperfibrinolysis	Tranexamic acid 1g	
FIBRINOGEN		FIBTEM A5 ≤10mm	Hypofibrinogenaemia	Cryoprecipitate	
PLATELETS		EXTEM A5 ≤35mm with normal fibrinogen*	Thrombocytopaenia	Platelets	
FACTORS		EXTEM CT 90-140sec with normal fibrinogen** OR EXTEM CT >140sec	Low coagulation factors	Fresh Frozen Plasma 2-4u OR Prothrombinex 25IU/kg	

Cryoprecipitate Dosing Guide

FIBTEM A5	Non-obstetric	Obstetric
7-10	1 dose	2 doses
<6	2 doses	3 doses

One dose = five apheresis units = Fibtem A5 increase of approximately 4mm

*If EXTEM ≤25 and FIBTEM A5 ≤10 consider replacing both factors
**Fibrinogen replacement in the context of hypofibrinogenaemia may overcome a minor prolongation of clotting time



Key components	
EXTEM CT Clotting Time	Thrombin generation
EXTEM A5 Amplitude at 5 minutes	Fibrinogen and platelet concentration and function
FIBTEM A5 Amplitude at 5 minutes	Fibrinogen concentration and function
ML % Maximal lysis	Degree of fibrinolysis over temogram

Version 1.2. Endorsed by the Department of Anaesthesia and Pain Medicine and the FSH Transfusion Services Committee on 10/11/16. Adapted from the King Edward Memorial Hospital ROTEM algorithm.

GENERAL SURGICAL / OBSTETRIC HAEMORRHAGE ROTEM TRANSFUSION ALGORITHM (2017)

Maintain: Temp >36 C, pH >7.2, iCalcium >1 mmol/L, Platelets >70, Hb >70 g/L
Only consider APTT and INR in the presence of heparin and warfarin.

Adjust dose of blood products for patients <50kg after consulting senior clinician

Repeat ROTEM test 10 mins after EACH intervention

IS THERE CLINICALLY SIGNIFICANT BLEEDING?

YES

High risk of Fibrinolysis? Consider Tranexamic Acid now

ROTEM Result in 6 min

NO

Observe

FIBRINOLYSIS

EARLY DIAGNOSIS:
IS EXTEM A5 < 35 mm?

OR LATE DIAGNOSIS:
Leave test running for up to 60 min
IS EXTEM ML ≥ 5%?
Clot should be stable for 1 hour, not tapering > 5 %

YES → Hyperfibrinolysis → **Tranexamic Acid 1 gram**
Consider repeat dose if patient has lost over 1 blood volume since initial dose
Adjust subsequent dose for renal dysfunction

NO → PROCEED WITH ALGORITHM

FIBRINOGEN

IS FIBTEM A5 < 10 mm?

YES → Low Fibrinogen → **Cryoprecipitate 5 Units Apheresis**
OR
IF FIBTEM A5 < 8 mm may need > 5U of Cryo See "Dosage Schedule"
Ensure platelets also available in case needed
RETEST

NO

PLATELETS

IS FIBTEM A5 ≥ 10 mm?
AND
IS EXTEM A5 < 35 mm?

YES → Poor Platelet Contribution → **1 Pool Platelets**
If chronic renal dysfunction also consider DDAVP 0.3 mcg/kg
Ensure FFP "ready to thaw" in case needed
RETEST

NO

FACTORS

IS FIBTEM A5 ≥ 10 mm?
AND
IS EXTEM CT >90 sec?

YES → Low Coagulation Factors → **FFP 2-4 units**
OR
Prothrombinex 10 U/kg
If volume overloaded
RETEST

NO

NORMAL

STILL BLEEDING? Make stronger clot:

- Give Cryo to FIBTEM A10 > 15 mm
- Give platelets to EXTEM A10 > 50mm or consider Platelet Function testing (in hours)
- Consider FFP to shorten clotting time to EXTEM CT < 80 sec

IF STILL BLEEDING:

- Consider SURGICAL/OBSTETRIC PROBLEM and discuss with surgeon/obstetrician and blood bank/haematologist (rFVIIa)
- Re check temperature, pH, iCalcium, platelets and haemoglobin
- Consider other contributors to bleeding
  - platelet inhibiters (do Multiplate Platelet Function test)
  - Consider VWD, warfarin (INR), clexane etc.

When clinically possible always complete the algorithm in a stepwise manner and check the ROTEM between steps as indicated. This reduces unnecessary transfusion especially of FFP.

Please stick this label in the patients progress notes

ROTEM ANALYSIS AND TREATMENT PLAN

Nurse or JMO to circle algorithm used then insert results from ROTEM Next circle range (action red range) and use algorithm to create a plan.

Date: / / Time:

ALGORITHM USED (circle one):

CARDIAC/VASCULAR or GENERAL/OBSTETRIC

- For CARDIAC/VASCULAR start here and do all:

INTEM CT = ... Below 205 / 205 & Above

HEPTEM CT = ... Below 205 / 205 & Above

- For GENERAL/OBSTETRIC start here(this section only):

EXTEM A5 = ... Below 35 / 35-40 / Above 40

FIBTEM A5 = ... Below 10 / 10-15 / Above 15

EXTEM CT =..... Below 80 / 80-90 / Above 90

EXTEM ML =.....Below 5 / 5 & Above

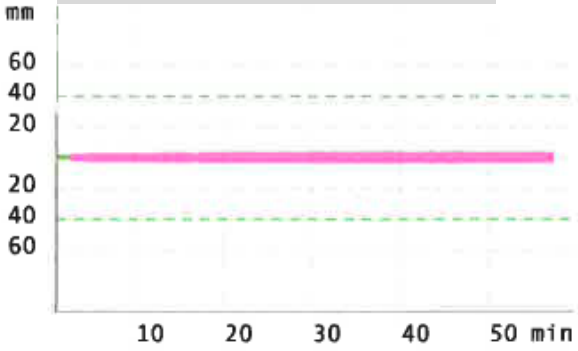
Management Plan: .....

Please stick this label in the patients progress notes

History

- MVA
- Patient randomised to PATCH trial (TXA or placebo)
- Initial ROTEM as follows

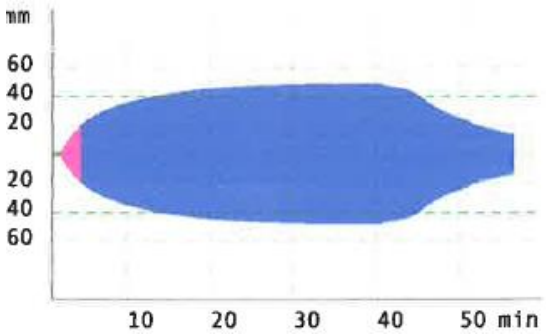
FIBTEM



FIBTEM C [defa
2326562

RT:	00:56:32	
CT	116	s
A5	3	mm
A10	3	mm
MCF	3	mm
ML	:* 0	%
CFT		s
α		°

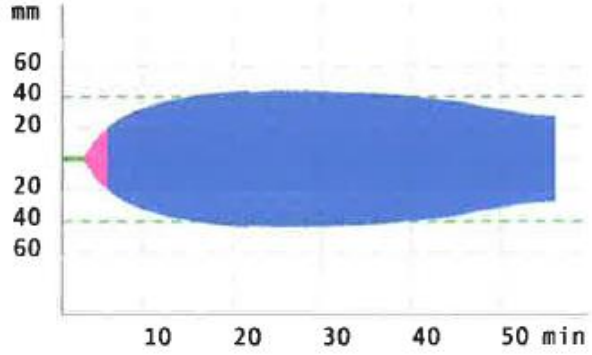
EXTEM



EXTEM C [defau
2326562

RT:	00:55:51	
CT	88	s
A5	29	mm
A10	38	mm
MCF	48	mm
ML	:* 72	%
CFT	146	s
α	66	°

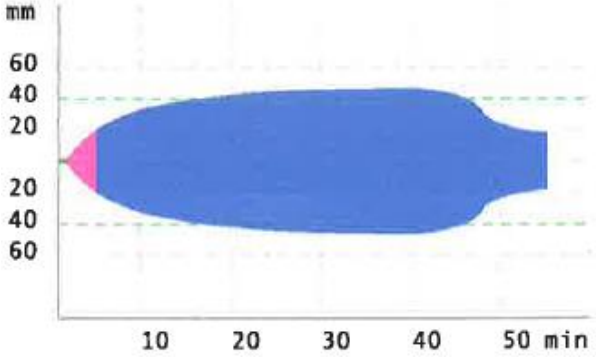
INTEM



INTEM C [c
2326562

RT:	00:55:22	
CT	180	
A5	29	
A10	38	
MCF	44	
ML	:* 37	
CFT	156	
α	66	

APTEM



APTEM C [defau
2326562

RT:	00:54:22	
CT	76	s
A5	26	mm
A10	35	mm
MCF	46	mm
ML	:* 61	%
CFT	195	s
α	58	°

FIBTEM A5 = 3mm, EXTEM CT = 88s, EXTEM A5 = 29mm
EXTEM ML = 72% APTEM ML = 61%

Now interprete the initial ROTEM

What treatments would you give?
Use the FSH algorithm or better your hospital's if it has one.

Of note the ML is 61% on APTEM - hmmm?

FSH ROTEM Algorithm for Critical Bleeding

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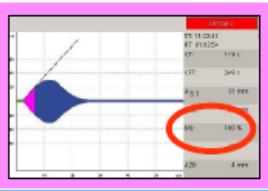
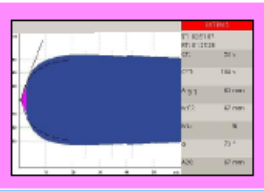
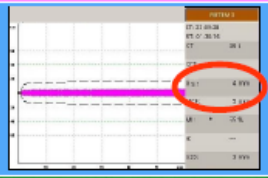
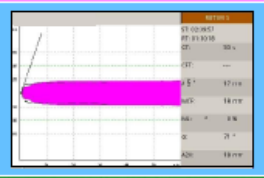
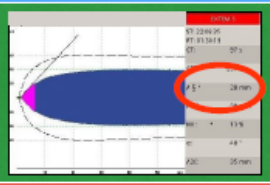
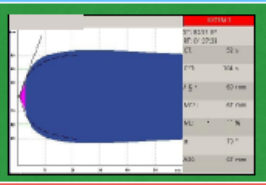
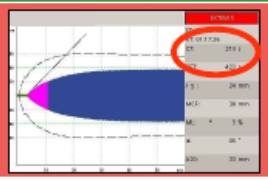
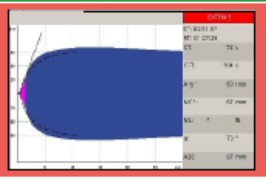
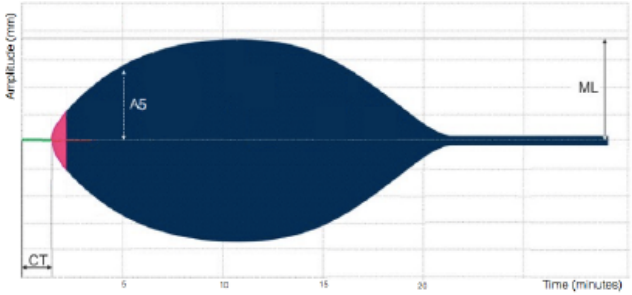
FIBRINOLYSIS		Trauma (within 3hrs) OR Post partum haemorrhage Flat trace OR Maximal lysis >5%	→ Hyperfibrinolysis	Tranexamic acid 1g	
FIBRINOGEN		FIBTEM A5 ≤10mm	Hypofibrinogenaemia	Cryoprecipitate	
PLATELETS		EXTEM A5 ≤35mm with normal fibrinogen*	Thrombocytopaenia	Platelets	
FACTORS		EXTEM CT 90-140sec with normal fibrinogen** OR EXTEM CT >140sec	Low coagulation factors	Fresh Frozen Plasma 2-4u OR Prothrombinex 25IU/kg	

Cryoprecipitate Dosing Guide

FIBTEM A5	Non-obstetric	Obstetric
7-10	1 dose	2 doses
<6	2 doses	3 doses

One dose = five apheresis units = Fibtem A5 increase of approximately 4mm

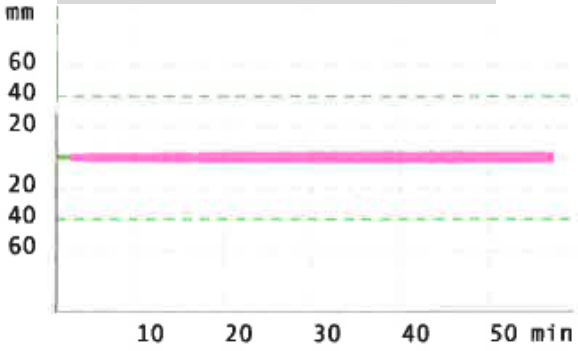
*If EXTEM ≤25 and FIBTEM A5 ≤10 consider replacing both factors
**Fibrinogen replacement in the context of hypofibrinogenaemia may overcome a minor prolongation of clotting time



Key components	
EXTEM CT Clotting Time	Thrombin generation
EXTEM A5 Amplitude at 5 minutes	Fibrinogen and platelet concentration and function
FIBTEM A5 Amplitude at 5 minutes	Fibrinogen concentration and function
ML % Maximal lysis	Degree of fibrinolysis over temogram

Version 1.2. Endorsed by the Department of Anaesthesia and Pain Medicine and the FSH Transfusion Services Committee on 10/11/16. Adapted from the King Edward Memorial Hospital ROTEM algorithm.

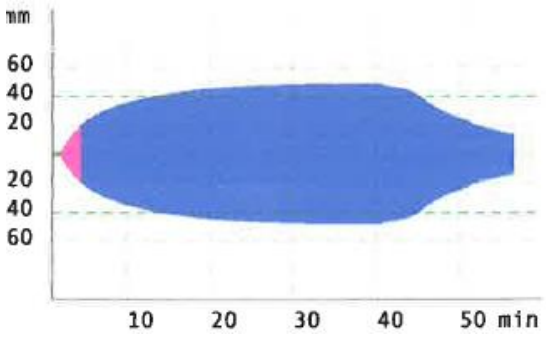
FIBTEM



FIBTEM C [defa
2326562

RT:	00:56:32	
CT	: 116	s
A5	: 3	mm
A10	: 3	mm
MCF	: 3	mm
ML	:* 0	%
CFT	:	s
α	:	°

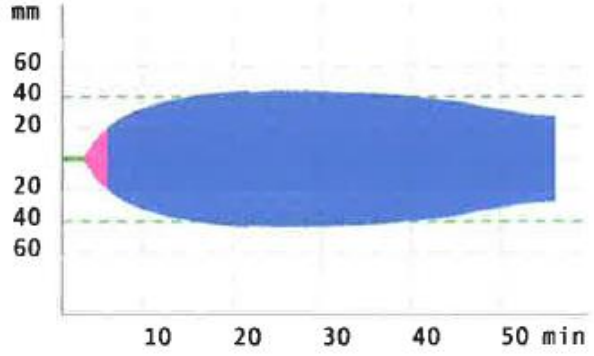
EXTEM



EXTEM C [defau
2326562

RT:	00:55:51	
CT	: 88	s
A5	: 29	mm
A10	: 38	mm
MCF	: 48	mm
ML	:* 72	%
CFT	: 146	s
α	: 66	°

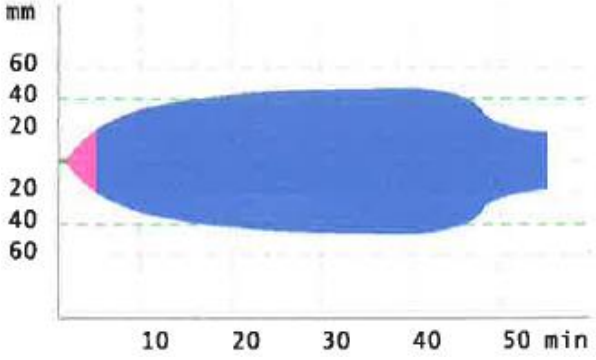
INTEM



INTEM C [c
2326562

RT:	00:55:22	
CT	: 180	
A5	: 29	
A10	: 38	
MCF	: 44	
ML	:* 37	
CFT	: 156	
α	: 66	

APTEM



APTEM C [defau
2326562

RT:	00:54:22	
CT	: 76	s
A5	: 26	mm
A10	: 35	mm
MCF	: 46	mm
ML	:* 61	%
CFT	: 195	s
α	: 58	°

INTERPRETATION

ROTEM ONE

<u>Treatment if following FSH algorithm:</u>

FIBRINOLYSIS: Extem ML = 72% give TXA 1g

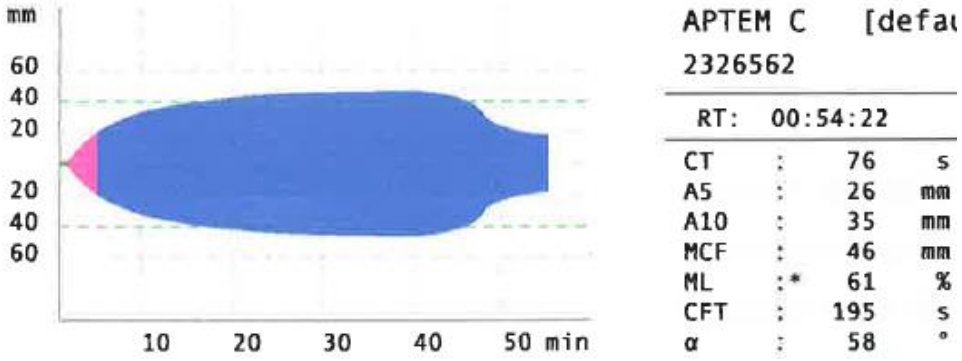
FIBRINOGEN: Fibtem A5 = 3mm – <u>very low</u> give a large dose of fibrinogen – e.g. 2-3 adult doses of cryoprecipitate (20-30 units of whole blood cryo OR 10-15 units of apheresis cryo) OR fibrinogen concentrate 4-6g

PLATELETS: Extem A5 = 29mm – low because of low fibtem. No platelets needed at this stage

FACTORS: Extem CT = 88s – slightly long because of low fibrinogen. No FFP needed at this stage

Do the EXTEM / INTEM / APTEM show fibrinolysis or is it something else?
Why does the APTEM also show fibrinolysis (eg an ML of 61%?
Doesn't the APTEM have TXA in it to inhibit this?

APTEM

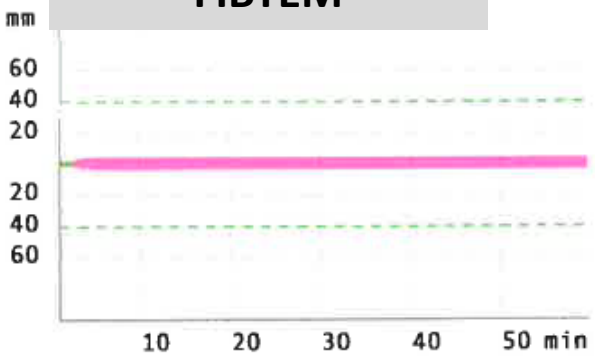


- We asked a few clever people for their opinion and the answer is we don't know for sure.
- Is it artefact / test error (the curve is concave not tapered …?)
- Is it fibrinolysis that was severe enough that the TXA in the APTEM was insufficient to inhibit all of the fibrinolytic enzymes
- Is it platelet mediated clot retraction (doesn't really fit usually much milder)
- The safest course of action is to assume it's real fibrinolysis and give more TXA
- If you have a comment or suggestion please let us know!

Treatment

- They are treated with TXA 1g and 10units of cryoprecipitate
- Another ROTEM is done

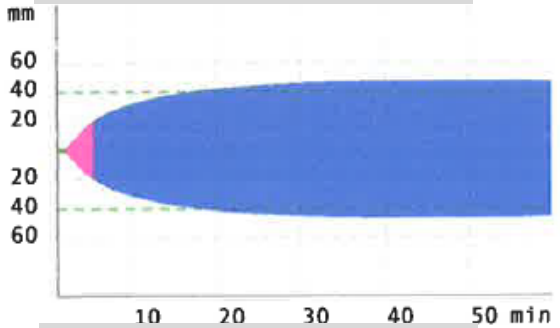
FIBTEM



FIBTEM C [defa
2326561

RT:	01:14:36	
CT	: 121	s
A5	: 4	mm
A10	: 4	mm
MCF	: 4	mm
ML	:* 2	%
CFT	:	s
α	:	°

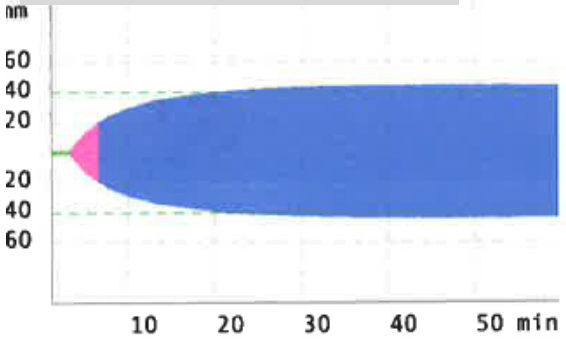
EXTEM



EXTEM C [defau
2326561

RT:	01:13:55	
CT	: 88	s
A5	: 26	mm
A10	: 35	mm
MCF	: 47	mm
ML	:* 4	%
CFT	: 196	s
α	: 57	°

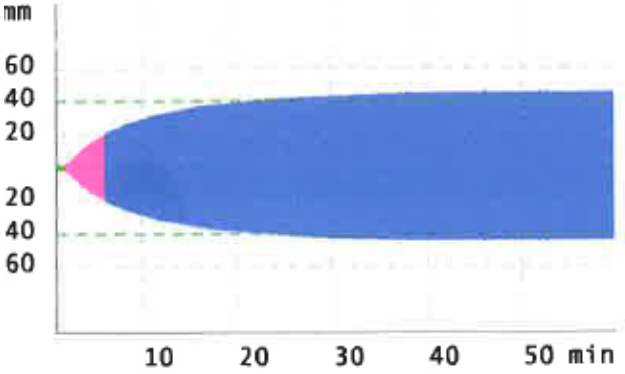
INTEM



INTEM C [defa
2326561

RT:	01:13:26	
CT	: 157	s
A5	: 25	mm
A10	: 34	mm
MCF	: 44	mm
ML	:* 5	%
CFT	: 202	s
α	: 59	°

APTEM



APTEM C [d
2326561

RT:	01:12:25	
CT	: 77	
A5	: 23	
A10	: 32	
MCF	: 45	
ML	:* 1	
CFT	: 246	
α	: 52	

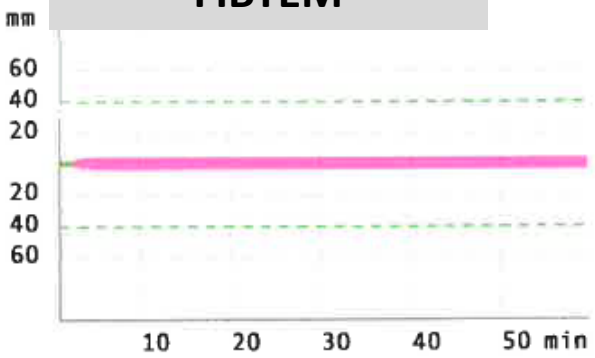
ROTEM TWO

FIBTEM A5 = 4mm, EXTEM CT = 88s, EXTEM A5 = 26mm
EXTEM ML = 4% APTEM ML = 1%

Now interprete the second ROTEM

What treatments would you give?
Use the FSH algorithm or better your hospital's if it has one.

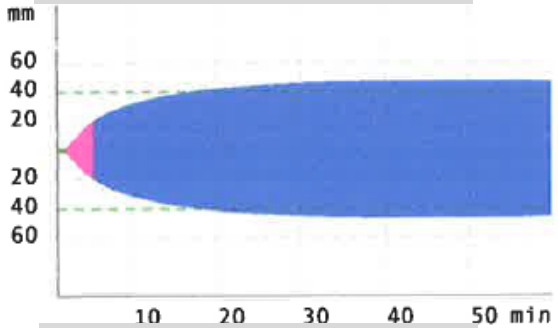
FIBTEM



FIBTEM C [defa
2326561

RT:	01:14:36	
CT	: 121	s
A5	: 4	mm
A10	: 4	mm
MCF	: 4	mm
ML	:* 2	%
CFT	:	s
α	:	°

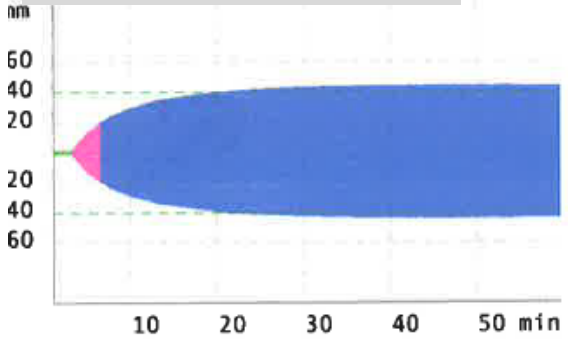
EXTEM



EXTEM C [defau
2326561

RT:	01:13:55	
CT	: 88	s
A5	: 26	mm
A10	: 35	mm
MCF	: 47	mm
ML	:* 4	%
CFT	: 196	s
α	: 57	°

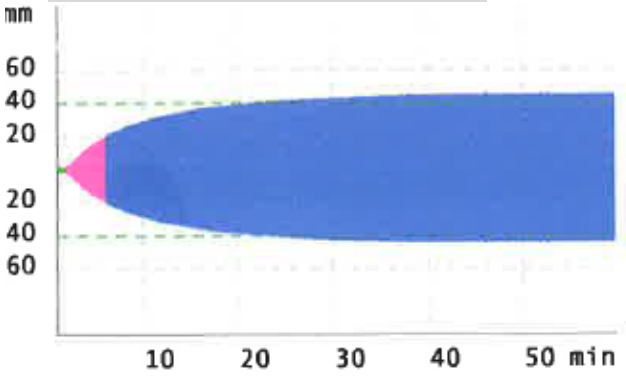
INTEM



INTEM C [defa
2326561

RT:	01:13:26	
CT	: 157	s
A5	: 25	mm
A10	: 34	mm
MCF	: 44	mm
ML	:* 5	%
CFT	: 202	s
α	: 59	°

APTEM



APTEM C [d
2326561

RT:	01:12:25	
CT	: 77	
A5	: 23	
A10	: 32	
MCF	: 45	
ML	:* 1	
CFT	: 246	
α	: 52	

ROTEM TWO

INTERPRETATION

<u>Treatment if following FSH algorithm:</u>

FIBRINOLYSIS: No evidence of fibrinolysis now

FIBRINOGEN: Fibtem A5 = 4mm – <u>still very low</u> despite the 10units of cryo! 10units is nowhere near enough fibrinogen when the fibtem A5 is 3mm and even more so if there is a lot of ongoing bleeding. Give a large dose of fibrinogen – e.g. 2-3 adult doses of cryoprecipitate (20-30 units of whole blood cryo OR 10-15 units of apheresis cryo) OR fibrinogen concentrate 4-6g

PLATELETS: Extem A5 = 26mm – probably mainly due to low fibtem. However it is close to 25mm and likely that platelets will be needed soon or if they are immediately available and the patient is still severely compromised then I would give some now.

FACTORS: Extem CT = 88s – slightly long because of low fibrinogen – will probably fully correct if adequate dose of cryo / fibrinogen is given. No FFP needed at this stage.

Unfortunately we don’t have any more clinical information on the patient, but there is plenty to learn from these two ROTEMs.

Take Home Points

1. Very low fibrinogen levels (eg fibtem A5<6mm) need large doses of fibrinogen to correct the deficit. Give an appropriately large dose of fibrinogen based on the first ROTEM result (20-30u cryo or 5-6g Fib conc) – using this approach you can potentially correct their coagulopathy within 30-45min. If you just give small doses and recheck you can take hours to catch up or if they continue to bleed rapidly you may actually even fall behind….
2. When you routinely use viscoelastic testing in haemorrhage you realise that as in this case fibrinolysis and low fibrinogen are the most common haemostatic defects to develop in hypovolaemic haemorrhagic shock.

Thanks again to Dr Ben Piper from the Dept of Anaesthesia Royal Darwin Hospital NT for sharing this case.