

A thick blue wavy line that starts on the left, dips down, and then rises towards the right, spanning the width of the slide.

Extending the Shelf Life of Thawed Cryoprecipitate

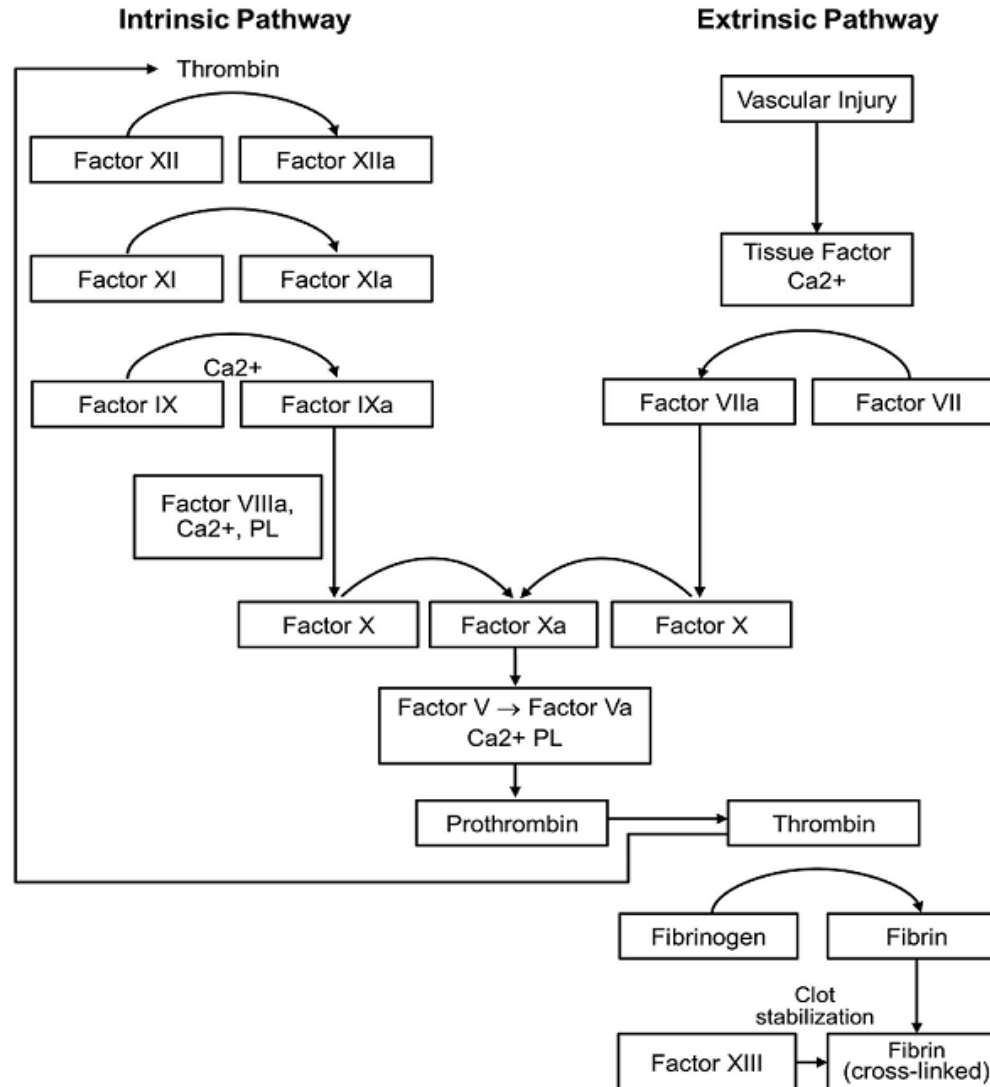
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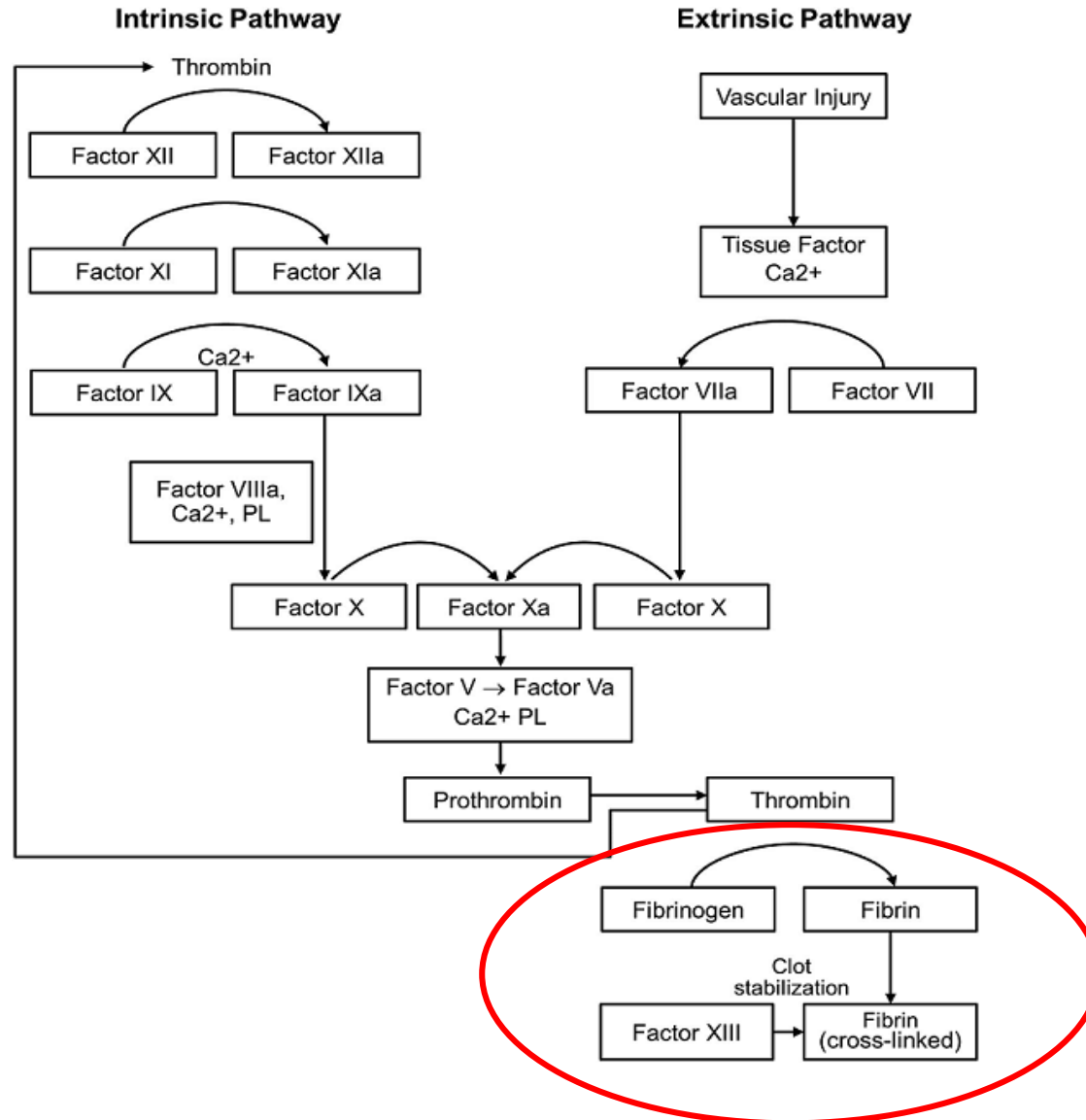
Coagulation

- Mechanism by which blood forms a clot
- Part of haemostasis (process that stops bleeding)
- Complex cascade of reactions
 - Cross linked fibrin
- Strengthens the initial platelet plug

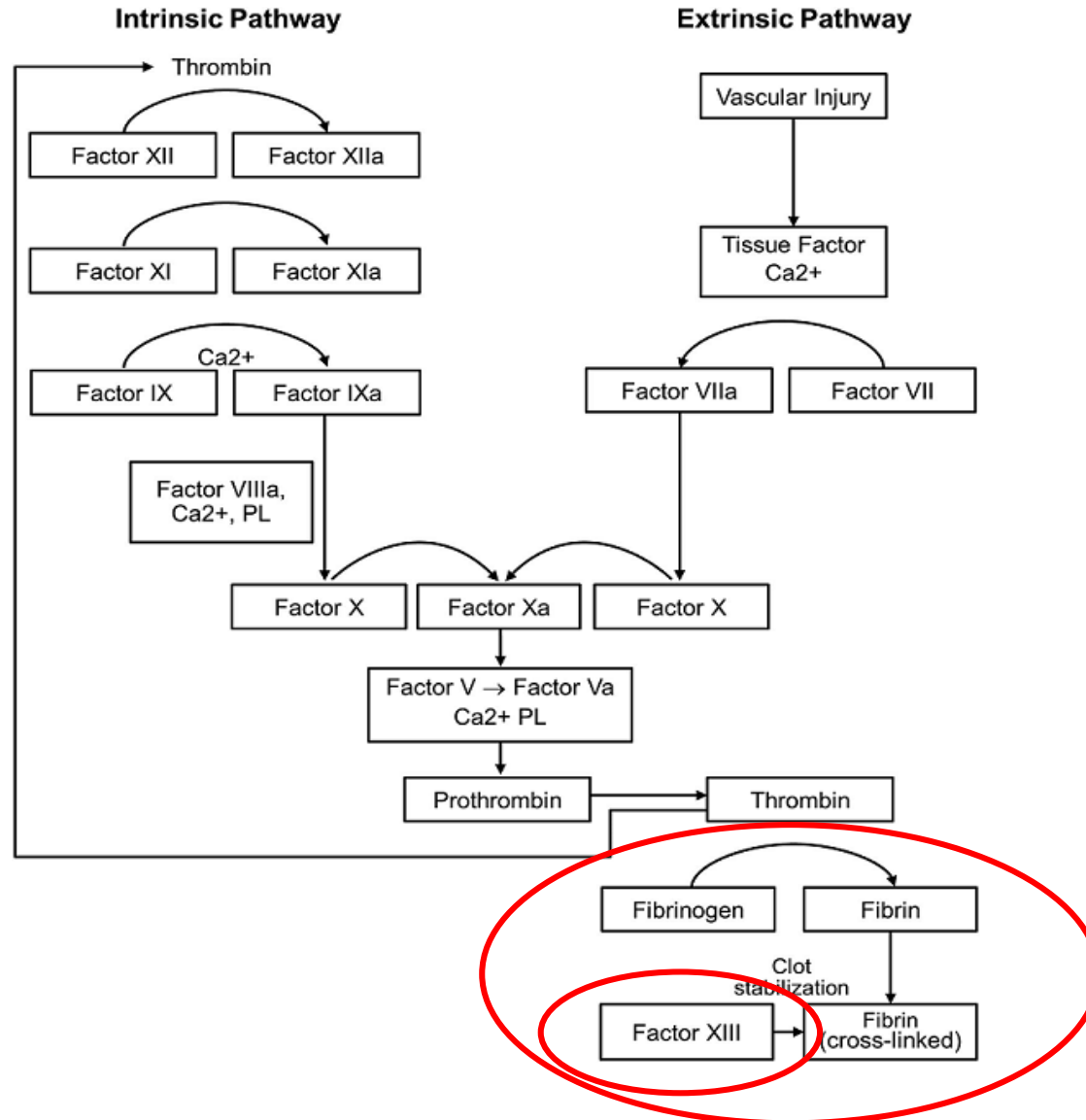
Coagulation cascade



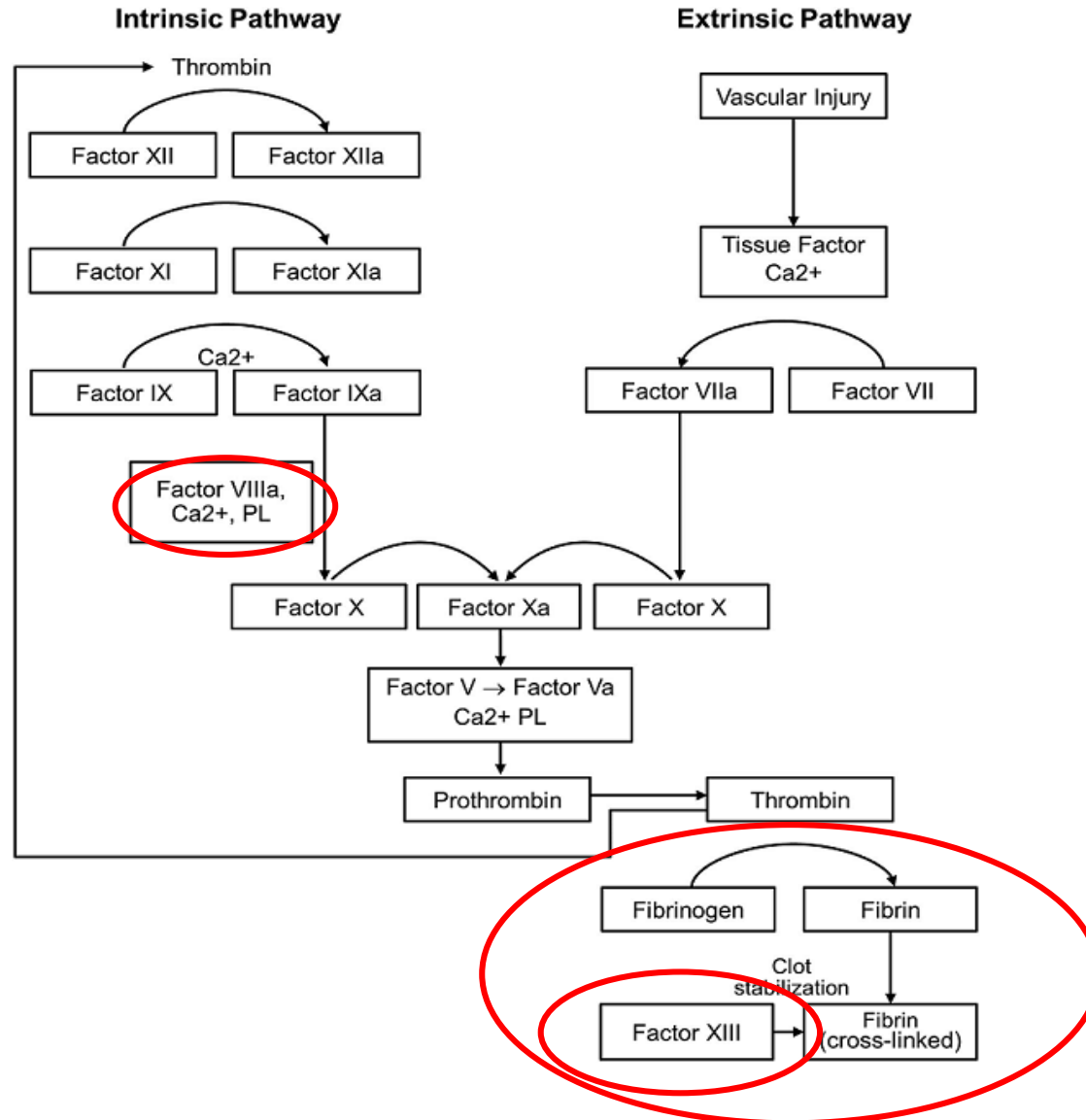
Coagulation cascade



Coagulation cascade



Coagulation cascade



Cryoprecipitate

- Frozen blood component manufactured from Fresh Frozen Plasma (FFP)
- High in fibrinogen, FVIII, FXIII, vWF and fibronectin
- Used in the UK as a source of fibrinogen



Manufacture

- Slow thaw for 16 hours at 2-6°C
- Centrifugation
- Removal of the supernatant
 - Not used in the UK
- ~50mL cryoprecipitate (Single)
- 5 units for pooled cryoprecipitate



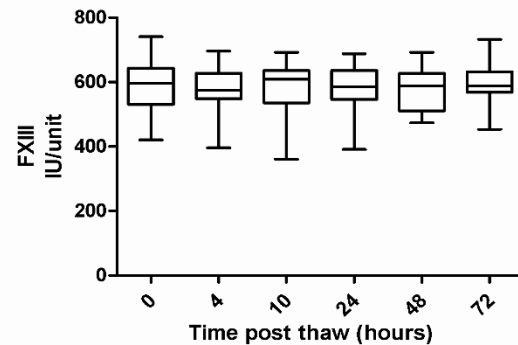
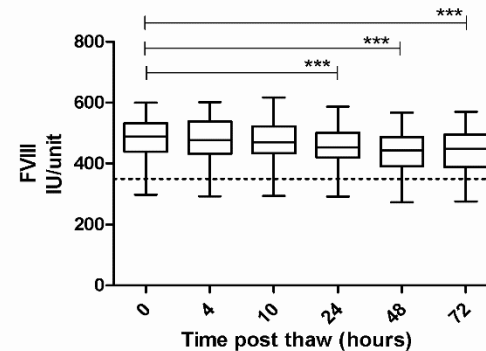
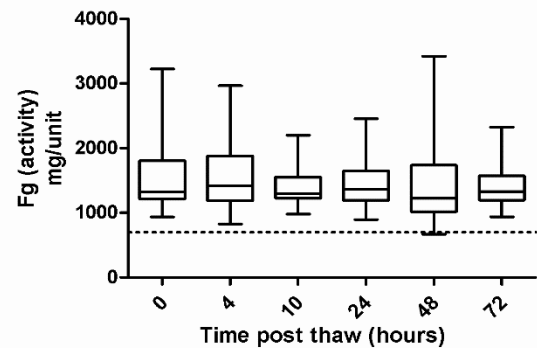
Use of cryoprecipitate

- Used in trauma / major haemorrhage for the treatment of acquired hypofibrinogenemia
 - Low fibrinogen levels and coagulopathy have been associated with inferior outcomes in major haemorrhage
- Fibrinogen supplementation has been shown to improve outcomes
- Early administration of fibrinogen may improve survival from major haemorrhage? (CRYOSTAT-II)

Current challenge

- Cryoprecipitate requires ambient storage
 - Reprecipitation of proteins
- Post thaw shelf life limited to 4 hours
 - Bacteriology risk
- Not pre thawed
- Thawing on demand may delay availability
- Short shelf life increases wastage

Post thaw ambient cryoprecipitate data

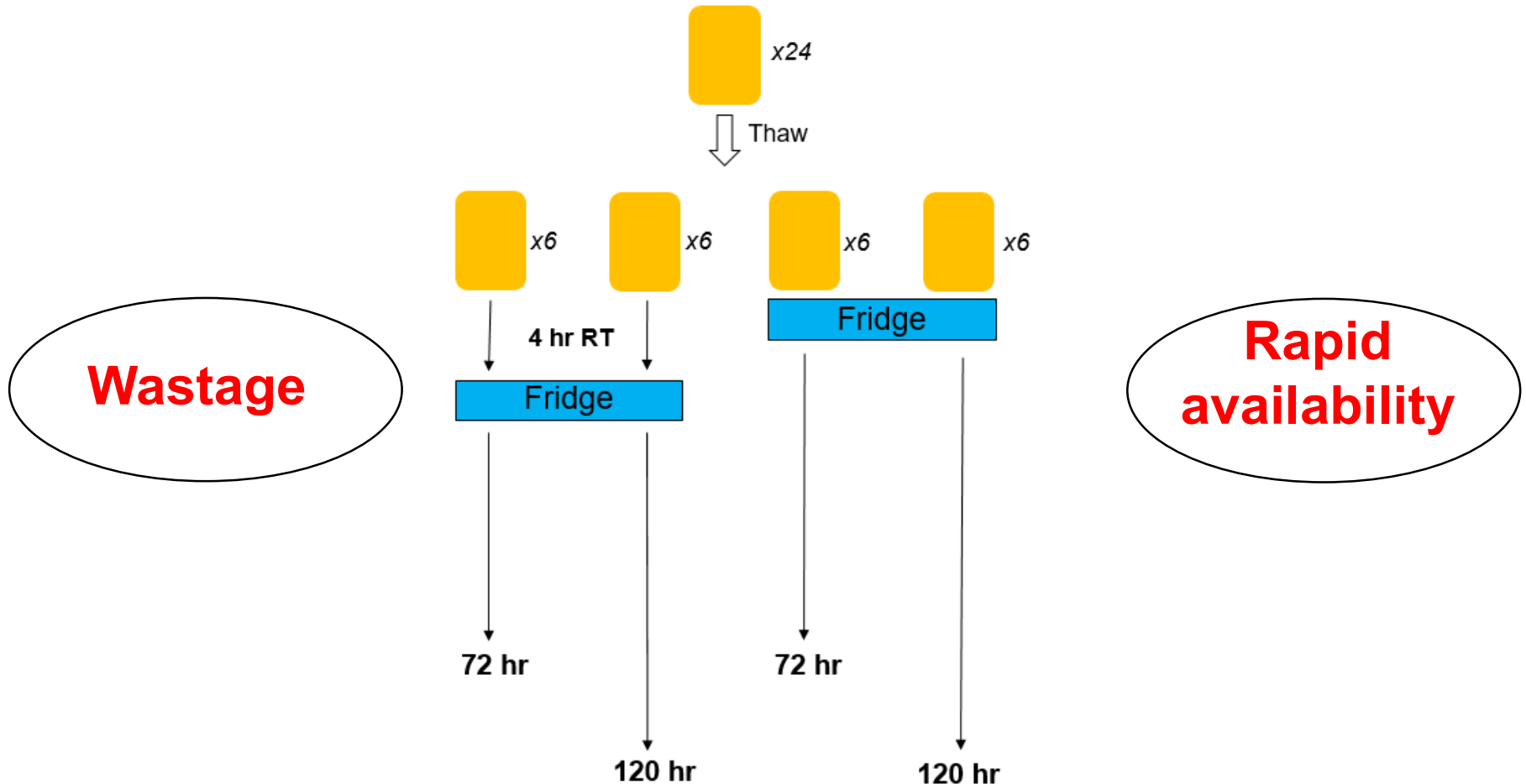


- Fg and FXIII stable for up to 72 hours
- Significant decrease in FVIII after 24 hours
- Bacteriology risk unquantified

Storage at 4°C

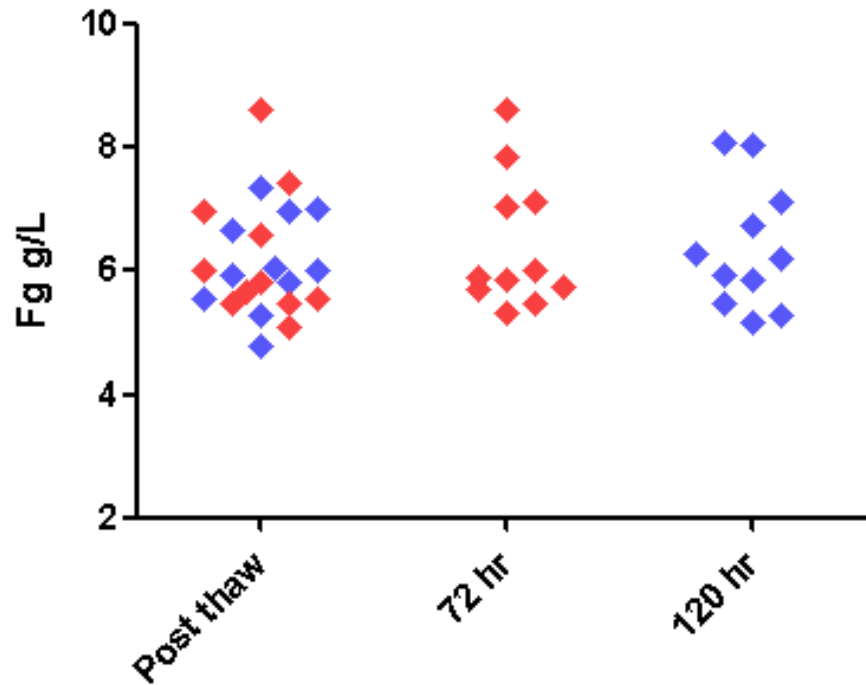
- Lower bacteriology risk
- FFP 5 day PT storage at 4°C for major haemorrhage
- Storage at 4°C causes reprecipitation of coagulation proteins
 - Reconstitute with 37°C warm

Study design



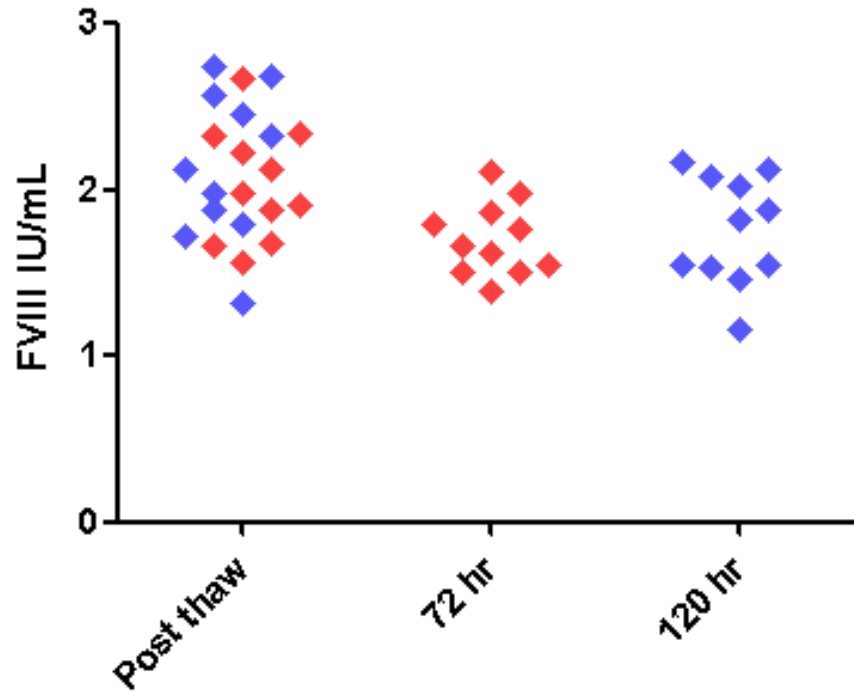
- 5 minute “warm” cycle to reconstitute precipitate
- 4 hrs at RT post warm

Fibrinogen



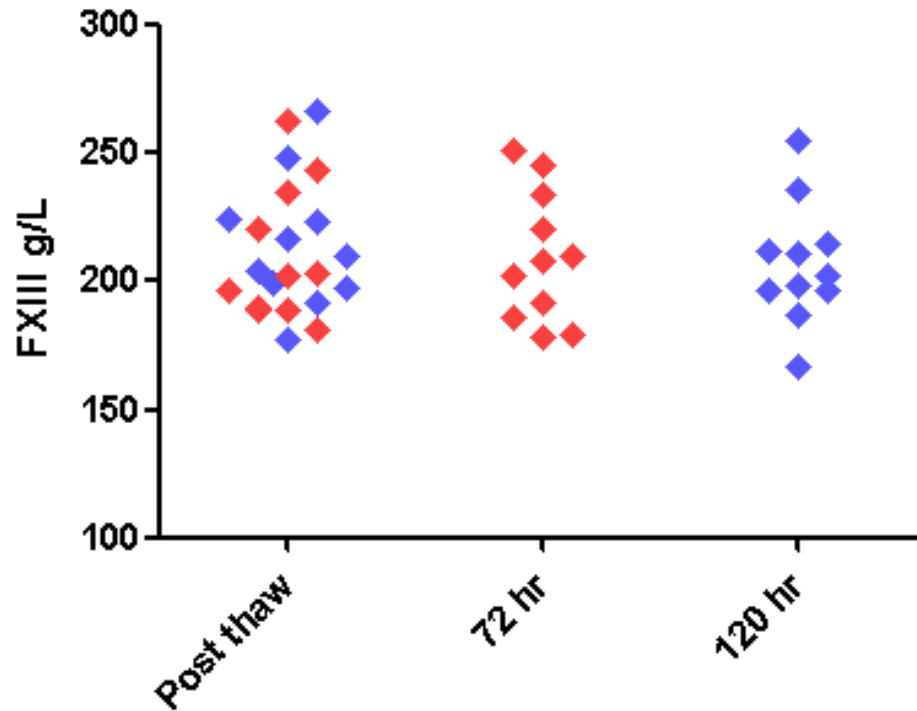
Storage	% of starting (post thaw)
72 hr	102.9
120 hr	104.1

FVIII



Storage	% of starting (post thaw)
72 hr	84.4
120 hr	82.4

FXIII



Storage	% of starting (post thaw)
72 hr	99.9
120 hr	96.6

Additional quality analysis

- vWF analysis
- Overall component efficacy
 - In vitro model of coagulopathy
- Is the fibrin network effected by reprecipitation?
 - Fibrin network analysis- Confocal microscopy

Alternatives / Clinical trials

- Fibrinogen concentrate (FC)
 - Lyophilised, viral inactivated and known concentration
 - Not licensed in UK for acquired deficiencies
- Ongoing clinical studies:
 - FC v Cryoprecipitate (FEISTY, FIBRES)
- Possible advantages with cryoprecipitate
 - Other coagulation factors may provide clinical benefit?
 - Studies may not answer this

Summary

- 4°C post thaw storage appears feasible
- Initial quality data looks acceptable
- Bacteria spiking study required
 - Very little data currently available

Acknowledgements

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