

Problems of Plasma Replacement in TTP

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MANAGEMENT OF ACUTE TTP

- Recommendations of BCSH Guidelines B J Haem 2003; 120, 556-573 (Allford et al)
 - *Single-volume daily plasma exchange should be commenced at presentation (Grade A, level Ib) and ideally within 24 h of presentation (Grade C, level IV). Plasma exchange using cryosupernatant may be more efficacious than that using FFP (Grade B, level III). Daily plasma exchange should continue for a minimum of 2 d after complete remission is obtained (Grade C, level IV).*

Introduction

- The classical thrombotic lesions in TTP are
 - in the microvasculature
 - composed of platelets and von Willebrand factor
- Venous thromboembolism
 - composed mainly of fibrin

Venous thromboembolism in TTP

- The reported incidence of venous thrombosis requiring therapeutic anticoagulation in 71 consecutive TTP/HUS cases following plasma exchange therapy is 3%

(Rivizi et al, Transfusion 2000 40 896-901)

- Report of 3 cases of TTP developing DVT following plasma exchange with solvent detergent plasma (Plas+SD) associated with low levels of protein S at the time of thromboses

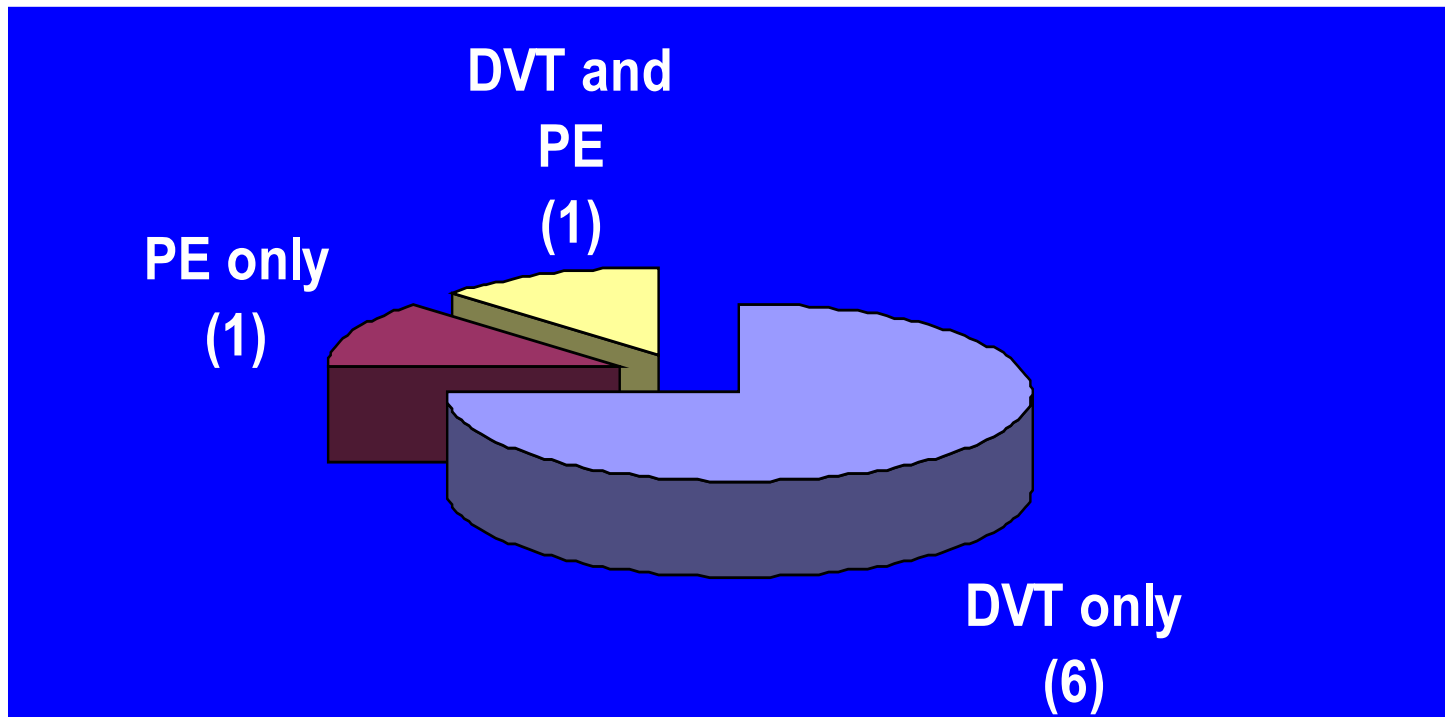
(Flamholz et al, Journal of clinical apheresis 2000 15, 169-172)

Study method

- From May 1997 - May 2002
- We retrospectively reviewed our patients with TTP with specific reference to the occurrence of VTE

Results

- 68 cases of TTP were referred for treatment or advice on management
- 8 VTE episodes were identified in 7 patients



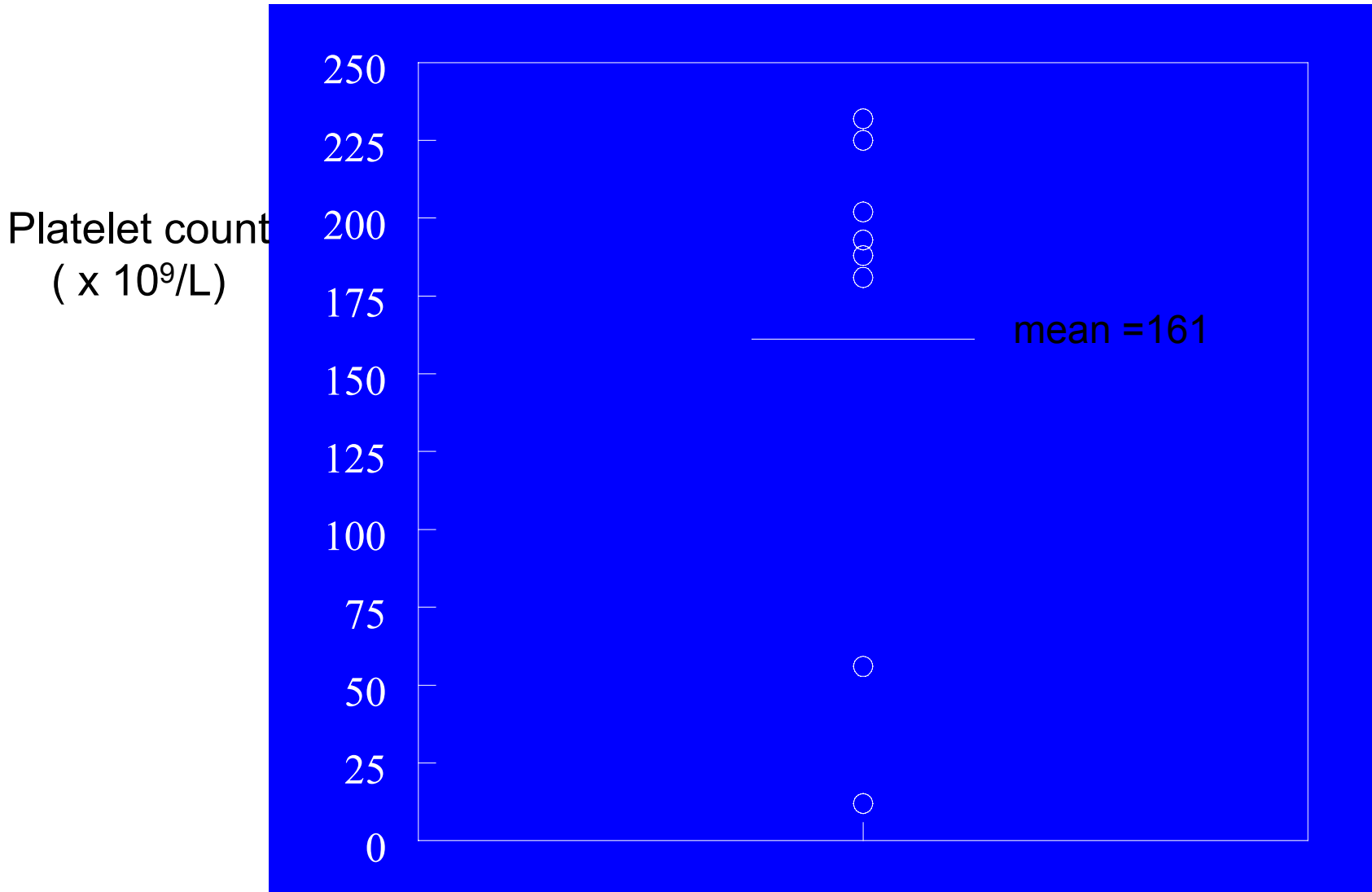
Patient characteristics

- All patients were female
- mean age 31 years (range 24-44 years)
- 5 primary presentation of TTP
- 3 relapsed TTP

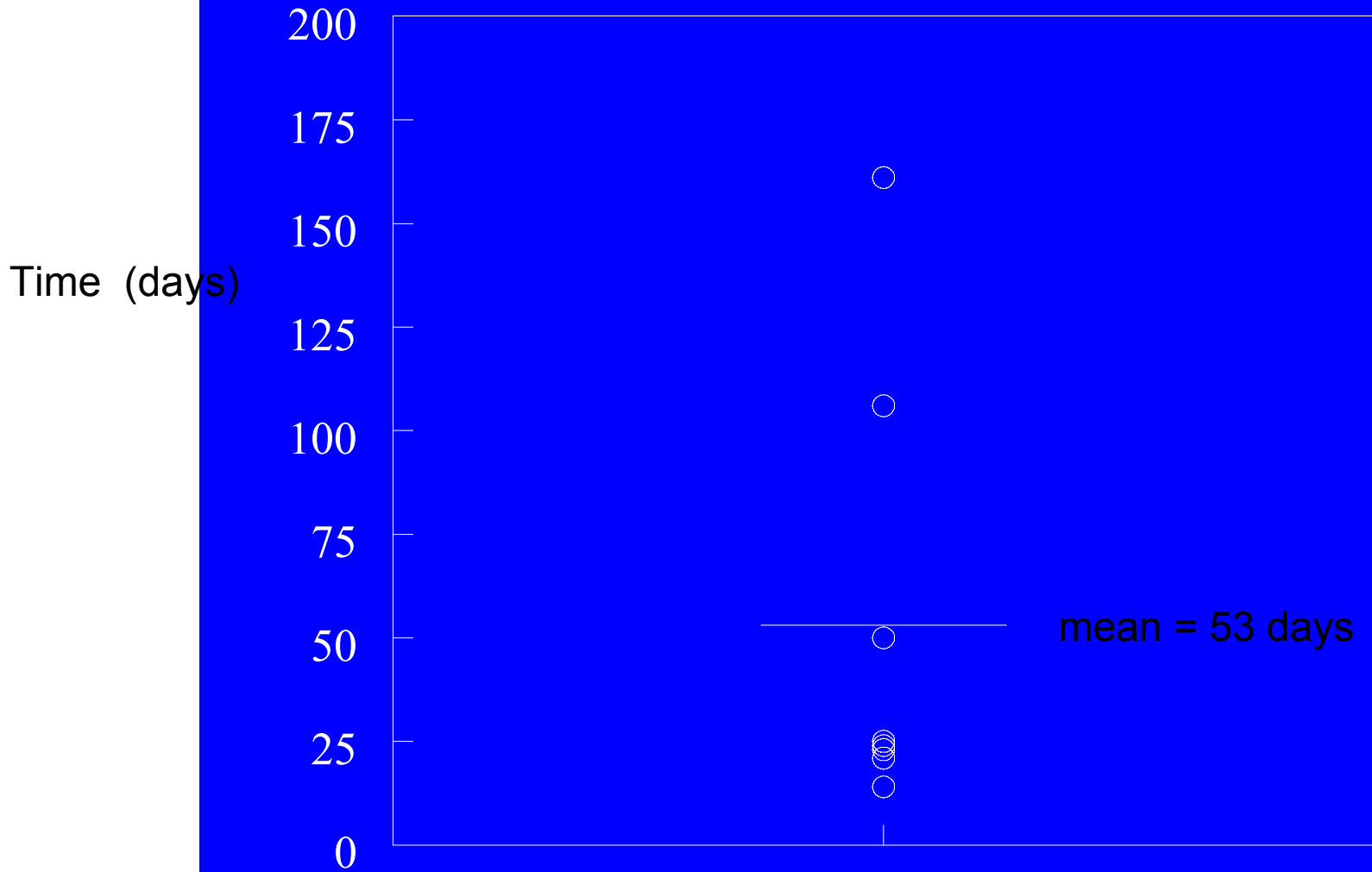
Precipitating factors for VTE

Central line	8
Pregnancy	1
Immobility	8
Obesity	3
FV Leiden heterozygosity	1

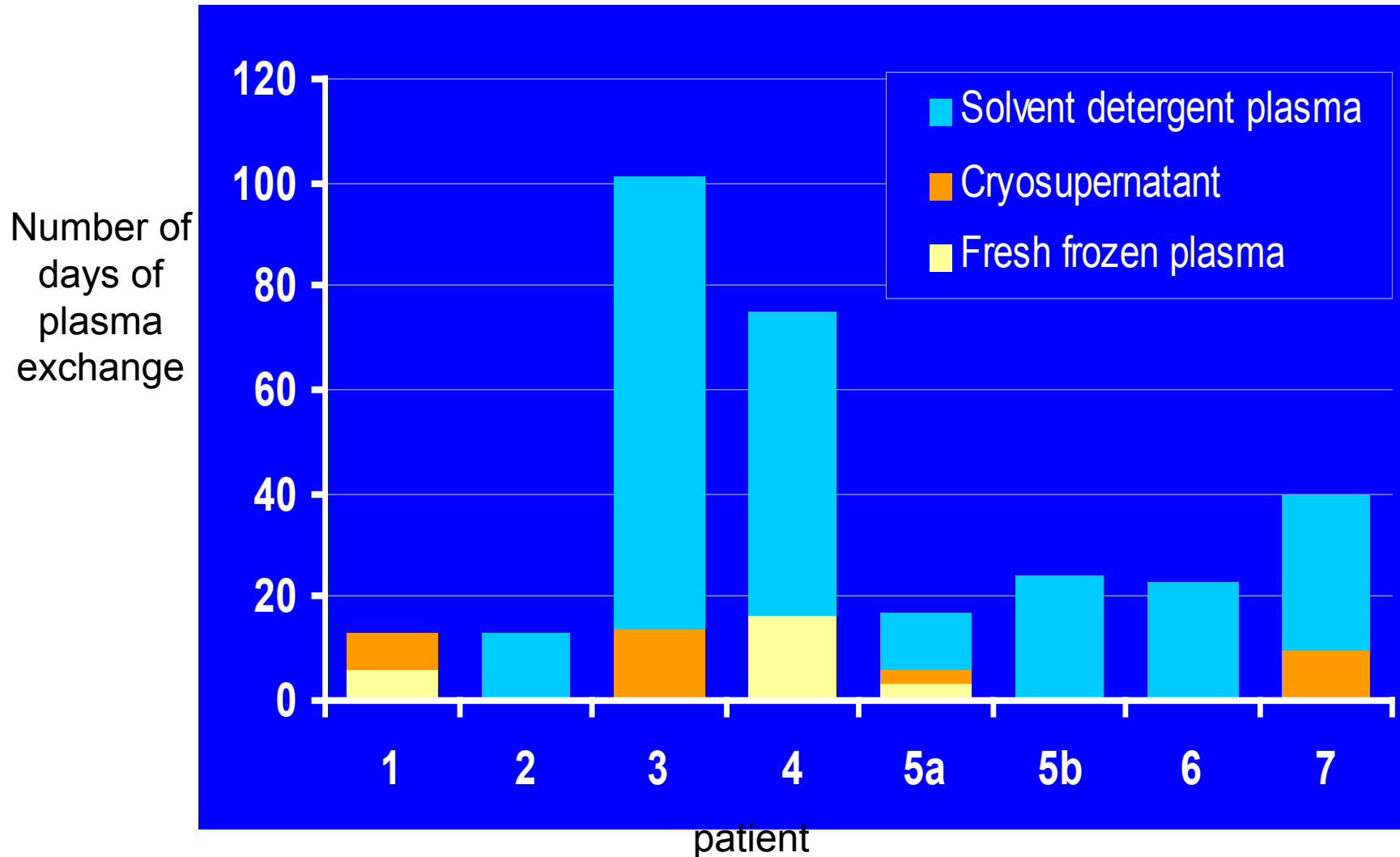
Platelet count on the day of VTE occurrence



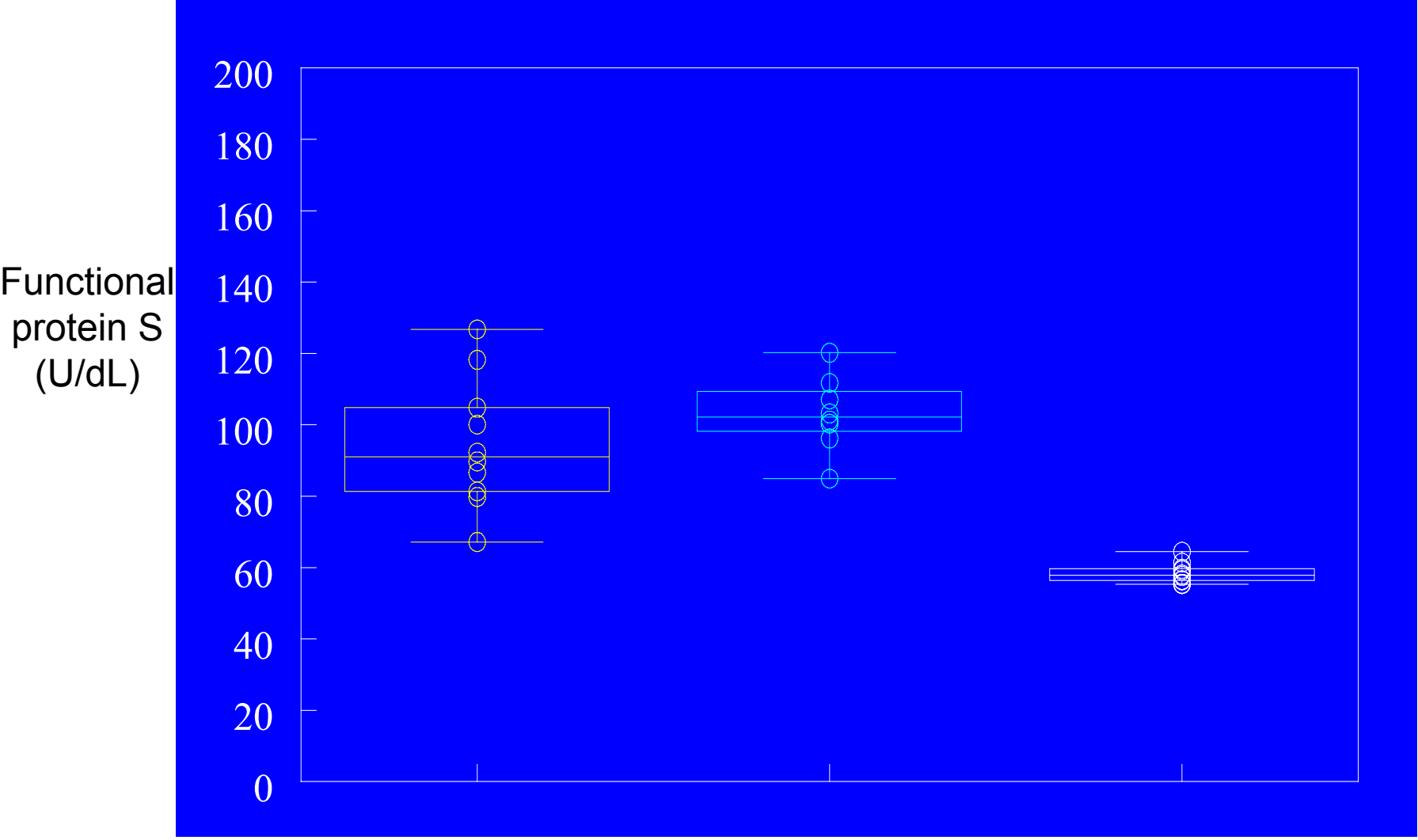
Day of occurrence of VTE from first plasma exchange



Number of days of plasma exchange and component used prior to VTE



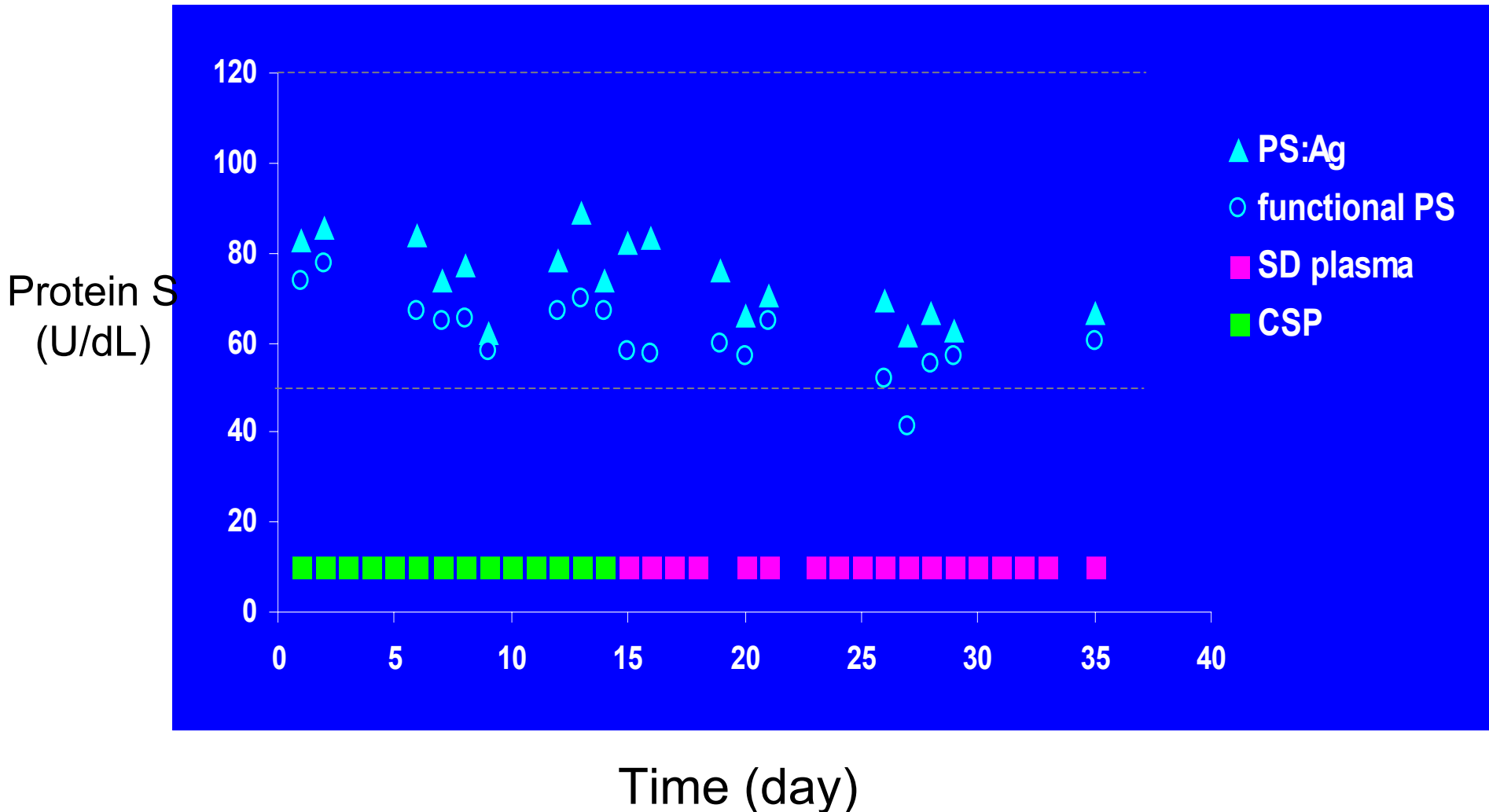
Levels of functional protein S in components



Median (U/dL) 91 102 58

Protein S levels

from presentation of acute TTP for case 3



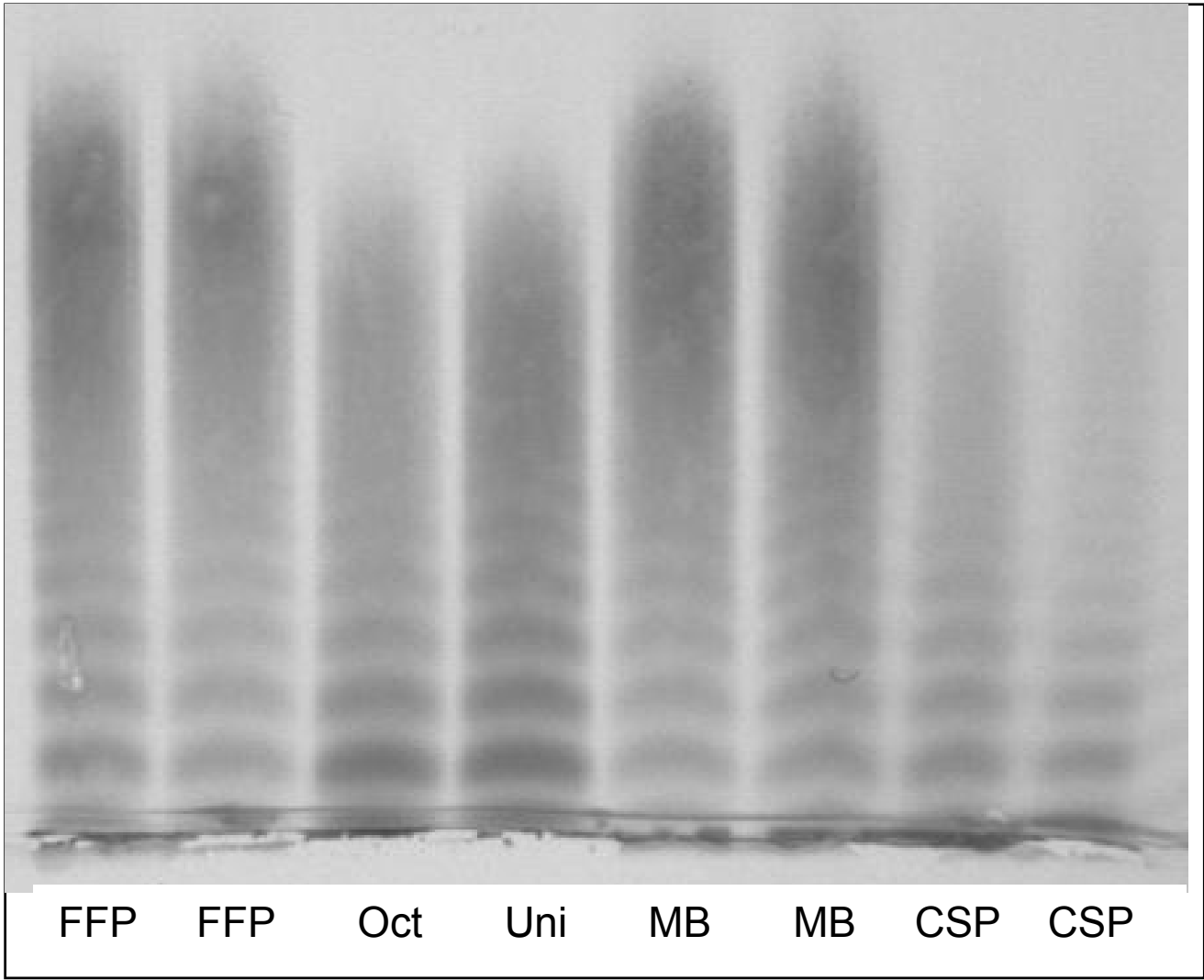
Summary

- We identified VTE in 12% of TTP cases
- 88% of these were associated with SD-plasma replacement in PEX.

WHAT TYPE OF FFP IS AVAILABLE

- Single unit, British donor standard FFP (or CSP)
- methylene blue treated/filtered single unit FFP
- solvent detergent (SD) treated pooled FFP
- psoralen S-59 and UVA light treated single unit FFP
- use of UK or non-UK plasma (male untransfused donors)
- methods in development (riboflavin)

	VWF:CP (%)	VWF:CP following overnight storage at room temperature (%)	VWF:Ag (IU/dL)	Functional PS (IU/dL)	Free PS:Ag (IU/dL)
Normal range	80-125	80-125	50-200	65-145 (M)	70-148 (M)
FFP (n=10)	113 (105-120)	110 (100-118)	82 (63-110)	91 (81-105)	81 (65-111)
CSP (n=9)	104 (96-110)	114 (107-118)	38* (20-68)	102 (98-109)	110* (98-124)
MB-plasma (n=10)	131 (108-144)	103 (96-120)	75 (62-123)	102 (100-120)	99 (89-110)
SD-plasma (Octaplas) (n=10)	99* (94-100)	119 (111-125)	83 (71-98)	58* (56-60)	65* (63- 67)
SD-plasma (Uniplas) (n=3)	102 (100-102)	115 (107-116)	109 (101-111)	57 (56-63)	64 (62-66)



PREVENTION OF VTE

- reduce immobility
- wear fitted full length grade II elasticated stockings
- when platelet count $> 50 \times 10^9/l$
 - prophylactic ASA 75mg
 - prophylactic LMW heparin high dose s/c daily

CLINICAL CHOICE OF FFP

- consider individuals risks of VTE
- initiate exchange with cryosupernatant (if available)
- median daily PEX until remission is 13 days
- remember risks of viral infection
- change to SD plasma if
 - allergic responses
 - failure to respond after 5 - 7 days

CLINICAL CHOICE OF FFP (cont'd)

- check for infected lines and remove asap
- clinical efficacy of plasma used (delayed response rate to MB treated plasma - de la Rubia et al 2001)

Conclusion

- VTE is a multifactorial disease and several known precipitating factors are present in TTP patients.
- The use of large volumes of SD-plasma in PEX may be an additional risk factor, possibly associated with protein S deficiency.
- Particularly as the median functional PS in SD-plasma is 58 U/dL compared to 91 U/dL and 102 U/dL in FFP and cryosupernatant respectively.

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