

# FFP - where are we now & where are we going?

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Service



# THE PERFECT FFP-----

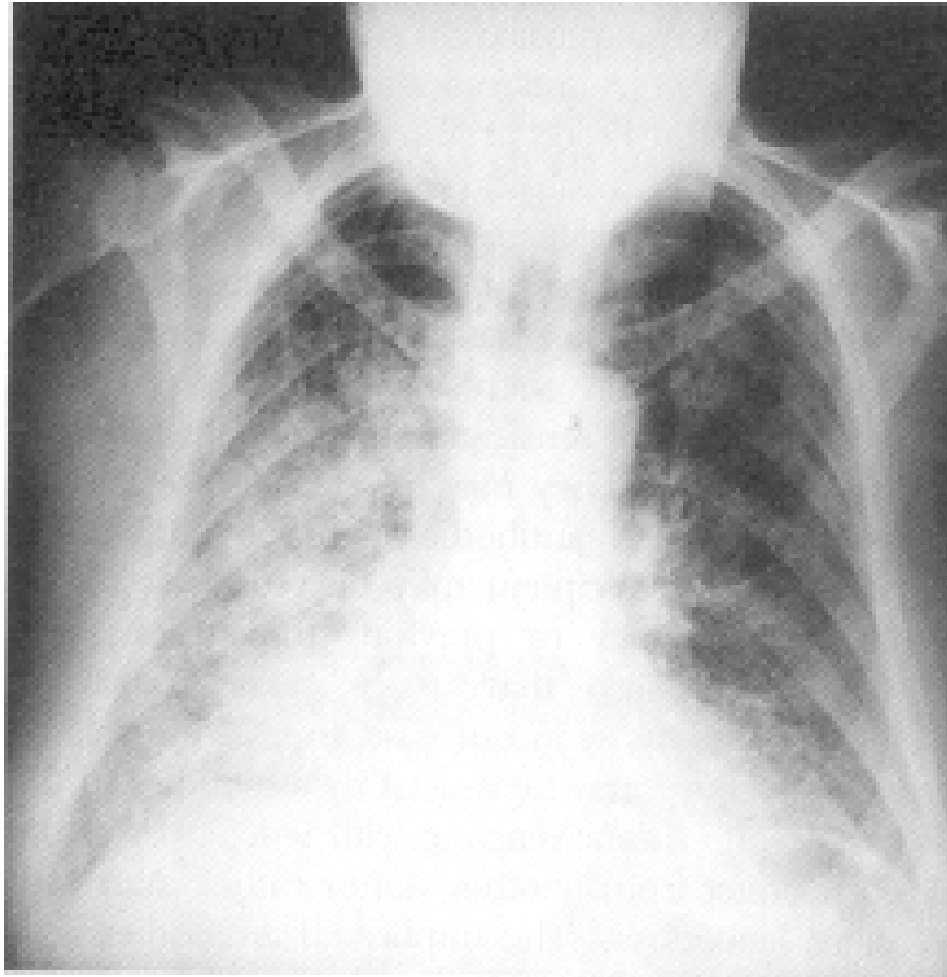
- 100% correction of coagulation defects
- No virus or vCJD transmission
- No side effects
- No additives
- No need to ABO or RhD match
- Easy to store, instantly available, long shelf life
- Cheap
- -----doesn't exist.



# Risks of FFP

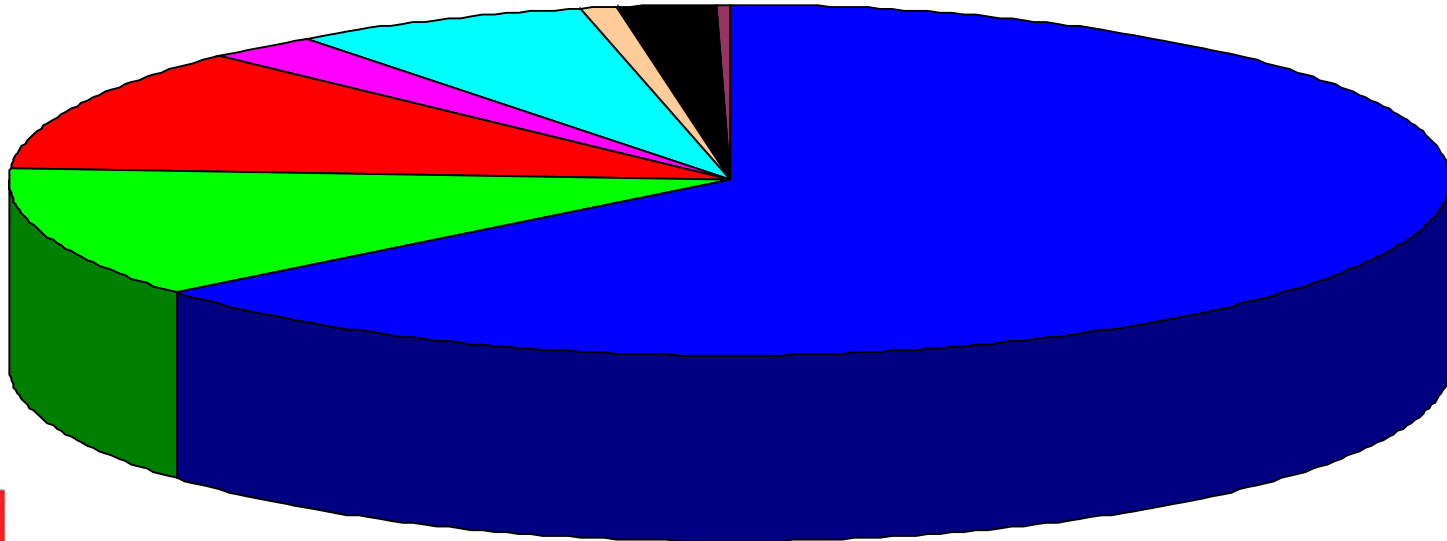
- Transfusion-related acute lung injury
- Viruses
- vCJD???
- Wrong ABO group- leading to haemolysis
- Acute reactions
- Fluid overload





# 6 years of SHOT reports 1996-2002 (n=1711)

■ IBCT (1093) 63.9%	■ ATR (209) 12.2%	■ DTR (196) 11.5%	■ PTP (43) 2.5%
■ TRALI (113) 6.6%	■ TA-GVHD(13) 0.8%	■ TTI (37) 2.2%	■ Unclassified (7) 0.4%



# Transfusion Related Acute Lung Injury

- SHOT - “Acute dyspnoea with hypoxia and bilateral pulmonary infiltrates occurring during or in the 24 hours after transfusion, with no other apparent cause”
- Frequency - ? 1 in 1,000-1 in 2,500 patients transfused.
- Would expect to see 300-750 cases/year



## 6 years of TRALI in UK

103 evaluable cases, 25 fatal (25%)

26 new cases in last 12 month reporting period

**Red cells** 23/12 million = 1: 520,000

**FFP /cryo** 31/1.8million = 1: 58,000

**Platelets** 16/1.2million = 1: 75,000

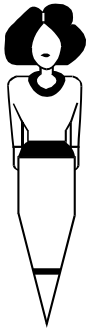
Major cause of transfusion-related morbidity and mortality



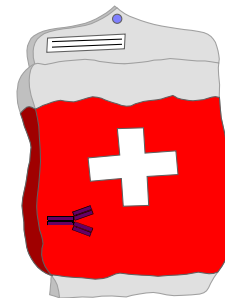
# How does TRALI occur?



**A male donor with a history of  
blood transfusion**



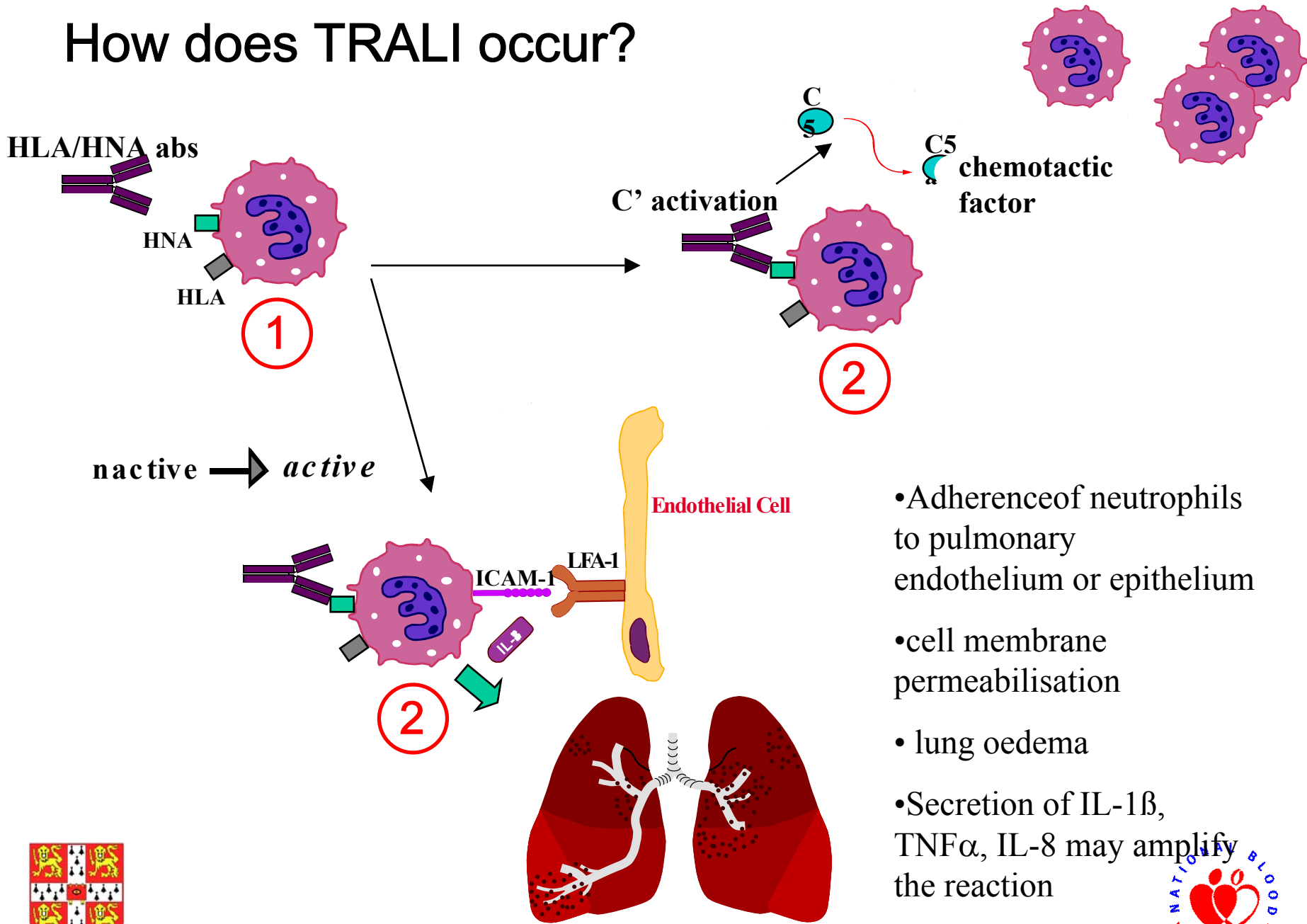
**A female donor with history of  
pregnancy -antibodies in 10-15%**



**HLA/HNA  
antibodies**



# How does TRALI occur?



- Adherence of neutrophils to pulmonary endothelium or epithelium
- cell membrane permeabilisation
- lung oedema
- Secretion of IL-1 $\beta$ , TNF $\alpha$ , IL-8 may amplify the reaction

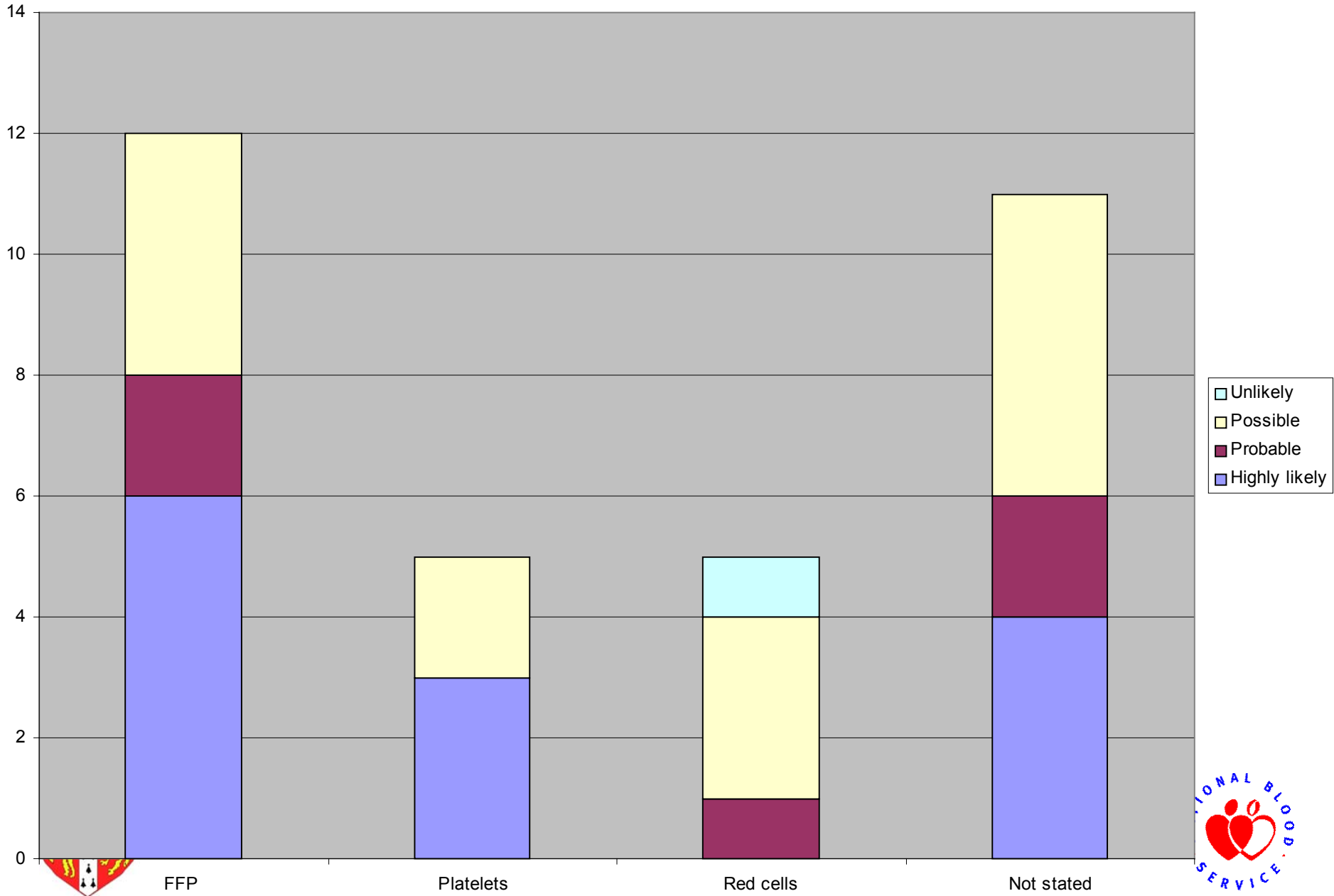


# HLA antibodies in female donors (McLennan, Lucas Navarrete et al)

- 1188 female donors tested
- 1014 (86%) negative for HLA class I and II
- 174 (14%) antibody positives
  - 77 (6%) HLA class I only
  - 49 (4%) HLA class II only
  - 48 (4%) HLA class I and II
- Specificities found in 85 samples e.g.
  - HLA-A2, A28
  - HLA-B7 B27
  - HLA-DR1, DR103



# Products implicated in TRALI including likelihood of each case being TRALI



# Diagnostic groups who developed TRALI 2002-02

- 9 cardiac surgery
- 8 haematological disease
- 5 liver disease
- 3 obstetric/gynae haemorrhage
- 3 warfarin reversal
- 1 TTP



COMMONEST USES OF FFP	No	FFP
Coronary artery/valve surgery	80	337
Malignant neoplasms of lymphoid, haematopoietic and related tissues	53	110
Aortic surgery	27	200
Diseases of liver	27	177
Renal failure	9	64



# TRALI prevention strategies under consideration

- FFP - male donors only - NBS Newcastle piloting
  - OR pooled Solvent Detergent FFP
- Platelet pools - resuspend in male plasma OR replace 70% plasma with additive solution
- Apheresis platelets- screen female donors OR platelet additive solution
- Red cells- discourage use of whole blood



# Residual viral risks of FFP in UK

- FFP IS NOT MANUFACTURED FROM NEW OR LAPSED DONORS
- HIV : 1 in 10 million
- HCV: 1 in 50 million since genome testing
- HBV: 1 in 1.2 million
- New viruses- West Nile Virus in USA
- Hepatitis A/parvovirus B19: both rare
- CMV and HTLV not transmitted by plasma (nor bacteria)



# 'Virus- safer' FFP

(1) Pathogen inactivation

- Solvent detergent
- Methylene blue

(2) Quarantining- rejected for UK as so much plasma discarded already

- Standard FFP no longer permitted in Norway, Portugal, France, Netherlands



# Solvent detergent FFP

- Needs POOLING of 500-1000 donations
- SD dissolves lipid coated viruses (4-6 log kill HIV, HBV, HCV) -SD is removed
- No effect on parvovirus B19 or hepatitis A - so genome testing required for those
- Available commercially from Octapharma- 'Octaplas' -200ml units
- No definite TRALI reported (1 possible to SHOT this year)



# Solvent-detergent FFP -coagulation data

- 20-30% loss factor VIII
- 15-20% loss factor XI
- 10-15% loss factor XIII
- All others < 5%
- Randomised trial in liver disease/transplant showed equivalent correction of coagulation



Williamson, Llewelyn et al Transfusion 1999;**39**:1227-1234.



# Increased risk of thrombosis with SDFFP -an American problem??

U/100ml	Vitex	Octaplas
Protein C	96	85
Protein S	24	64
PI	14	23

**BUT ? Risk in TTP**



# **Methylene blue FFP**

## **Currently provided for children born on or after 1st Jan 1996**

- Photodynamic process-oxygen radicals
- Single units -Blood Centres can do
- MB + white light -then MB removal
- No predicted toxicity at residual levels
- 30% loss factor VIII
- 20-30% fibrinogen loss
- >1 million units used but few trials
- Licenced as a device



# Does use of MBFFP increase demand?

- 56% increase in FFP:red cell ratio after changing to MB
- increased cryoprecipitate demand x2-3
- BUT FFP:red cell ratio was  $>1$  (0.11 in UK)
- different prescribing patterns in Spain (all CABG patients get FFP)

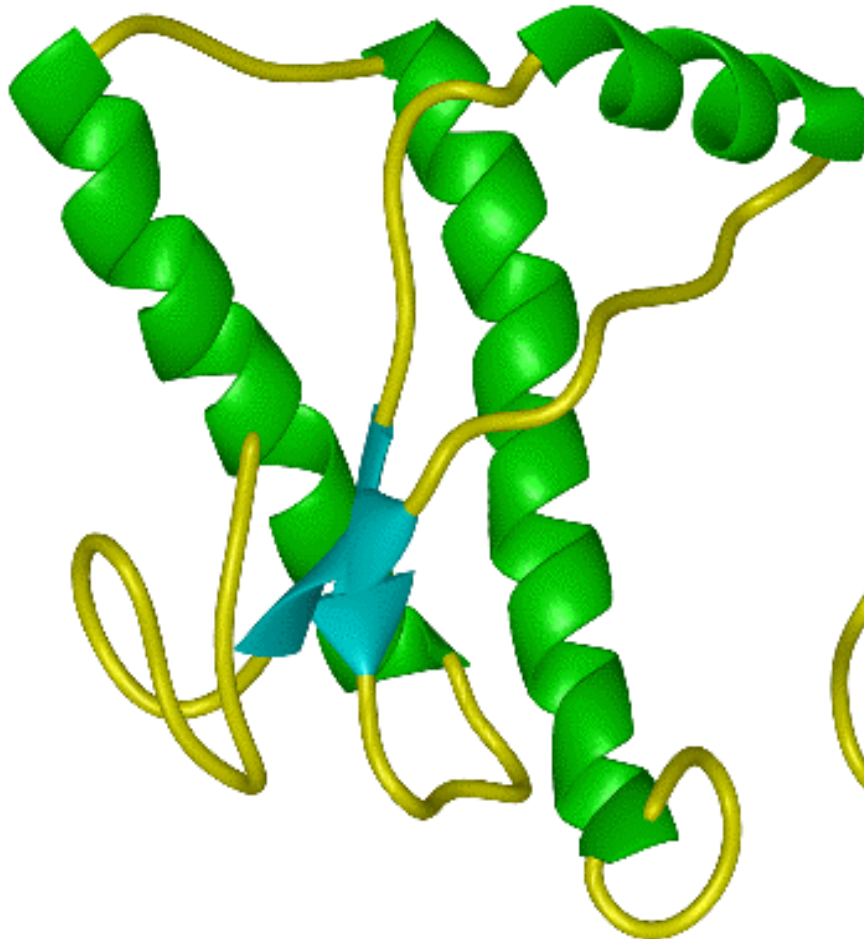


Atance et al Transfusion 2001; 41:1548-52.

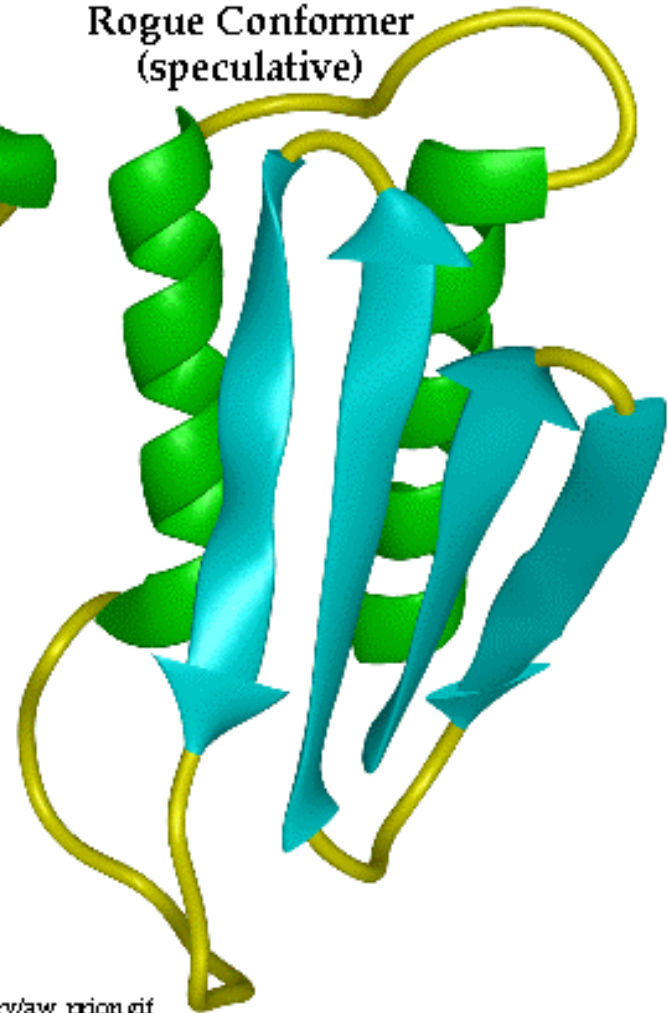


# Prion protein -change in structure

Normal Conformer



Rogue Conformer  
(speculative)



Adapted from [http://www.cmp.harvard.edu/cohen/research/gallery/aw\\_prion.gif](http://www.cmp.harvard.edu/cohen/research/gallery/aw_prion.gif)



# Importation of FFP from USA

- DoH instruction August 2002
- Import FFP for neonates and children born on or after 1st Jan 1996 (foodban)
- VOLUNTEERS from USA; males only
- Virus inactivated by NBS using MB
- Will be available in 50 and 300 ml packs
- Start date end 2003/early 2004



# West Nile Virus

- Epidemic in USA 2002
- Spread by mosquitos to humans & birds
- Asymptomatic through to encephalitis
- Transfusion- transmitted in 2002

2003- USA genome testing- 160/1.1million

- sensitive to methylene blue (and SD?)
- travellers to USA deferred for 28 days

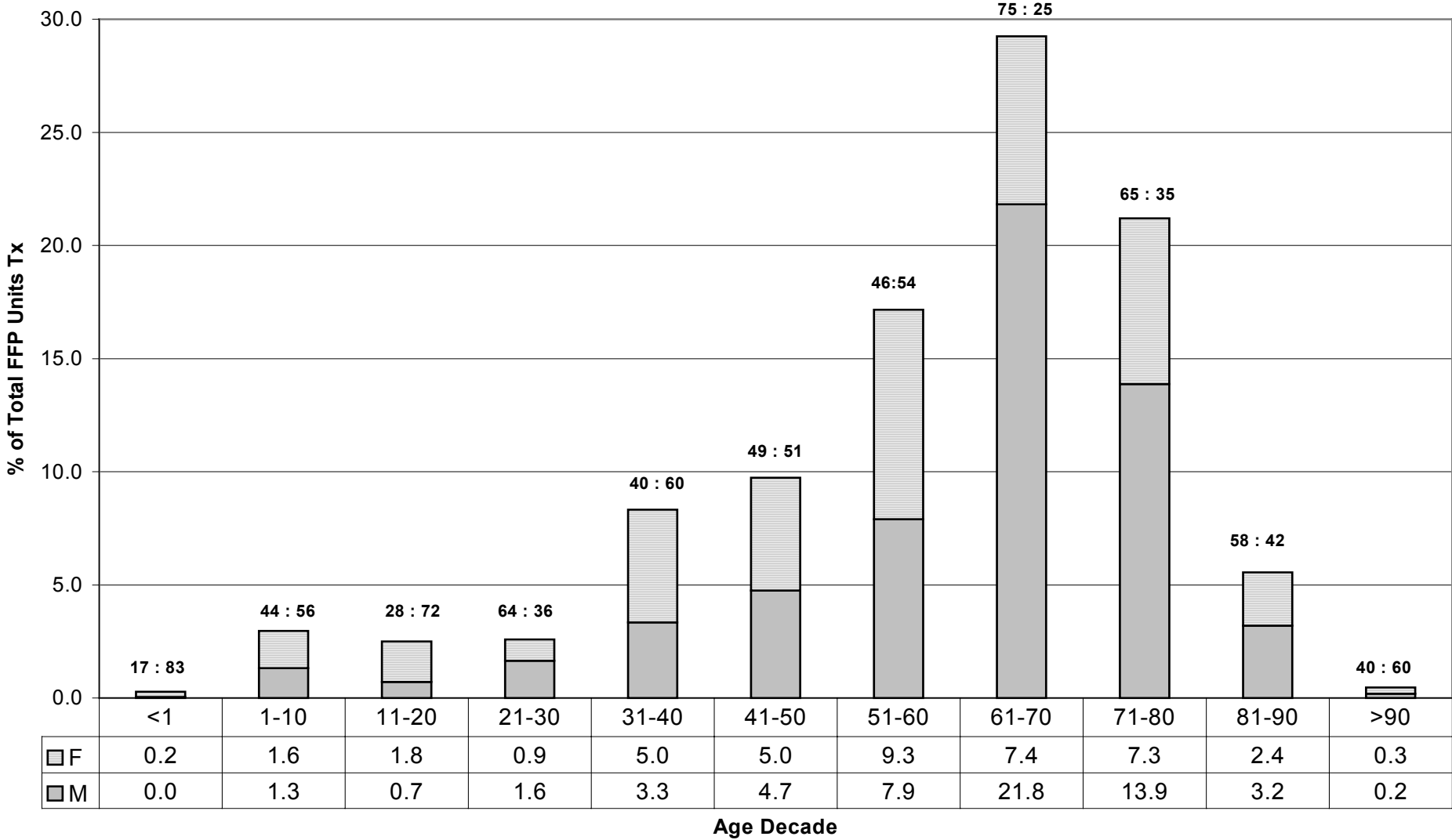


## Where are we headed?

- Virus treated FFP does not meet cost-effectiveness criteria
- More recent evaluations take TRALI into account
- No vCJD cases yet due to transfusion
- NBTC recommend VIP for all recipients
- DoH considering whether to offer to more patients



**Figure 4a Age distribution of recipients of all FFP units (n=2125)**



# Audits of FFP usage -recurrent themes

- Poor documentation of reason -? Many patients transfused inappropriately
- Poor use of coagulation tests before and after
- Underdosing
- Wastage high
- New BCSH Guidelines forthcoming



# What would we like in future?

- Better technology for assessment of causes of bleeding
- Research into ‘transfusion trigger’ for FFP on which to base guidelines
- Balance between virus safety and other hazards eg TRALI
- Balance between safety and cost

