

# TRALI- the effect of male FFP

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Service



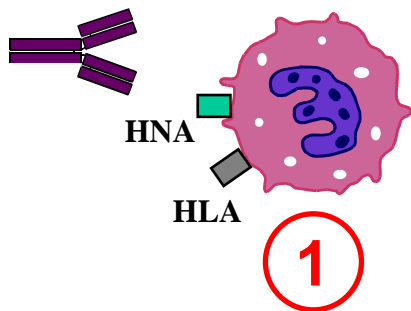
# **TRANSFUSION-RELATED ACUTE LUNG INJURY (according to SHOT)**

**ACUTE DYSPNOEA WITH HYPOXIA  
AND BILATERAL PULMONARY  
INFILTRATES OCCURRING DURING  
OR IN THE 24 HOURS AFTER  
TRANSFUSION, WITH NO OTHER  
APPARENT CAUSE  
(Imputability score since 1999)**

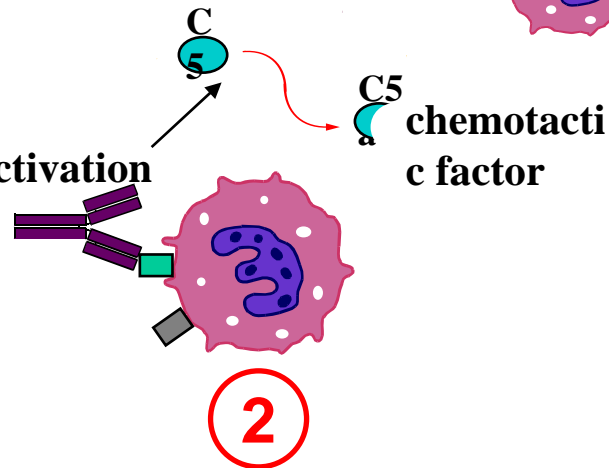


# How does TRALI occur?

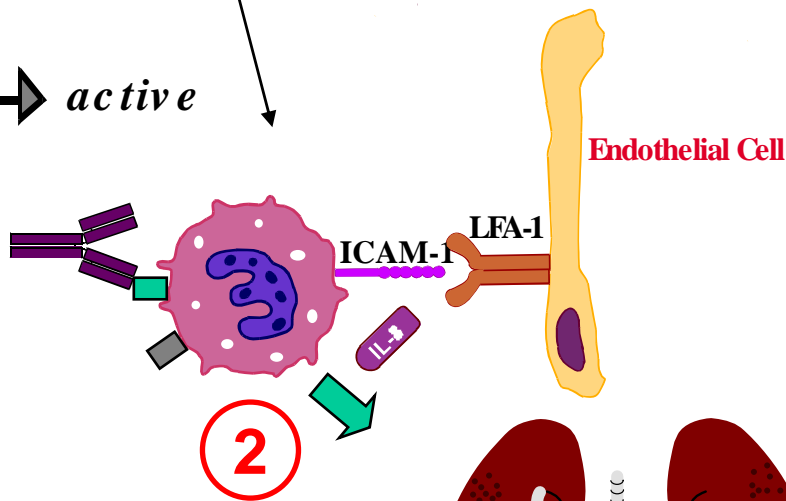
HLA/HNA antibodies in donor plasma



C' activation



Inactive → active



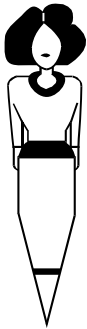
- Adherence of neutrophils to pulmonary endothelium or epithelium
- cell membrane permeabilisation
- lung oedema
- Secretion of IL-1 $\beta$ , TNF $\alpha$ , IL-8 may amplify the reaction



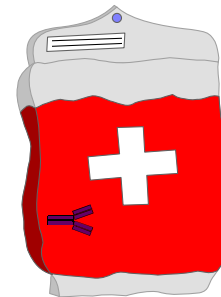
# Main source of HLA/HNA antibodies is donor plasma



A donor with a history of transfusion (excluded since April 2004)



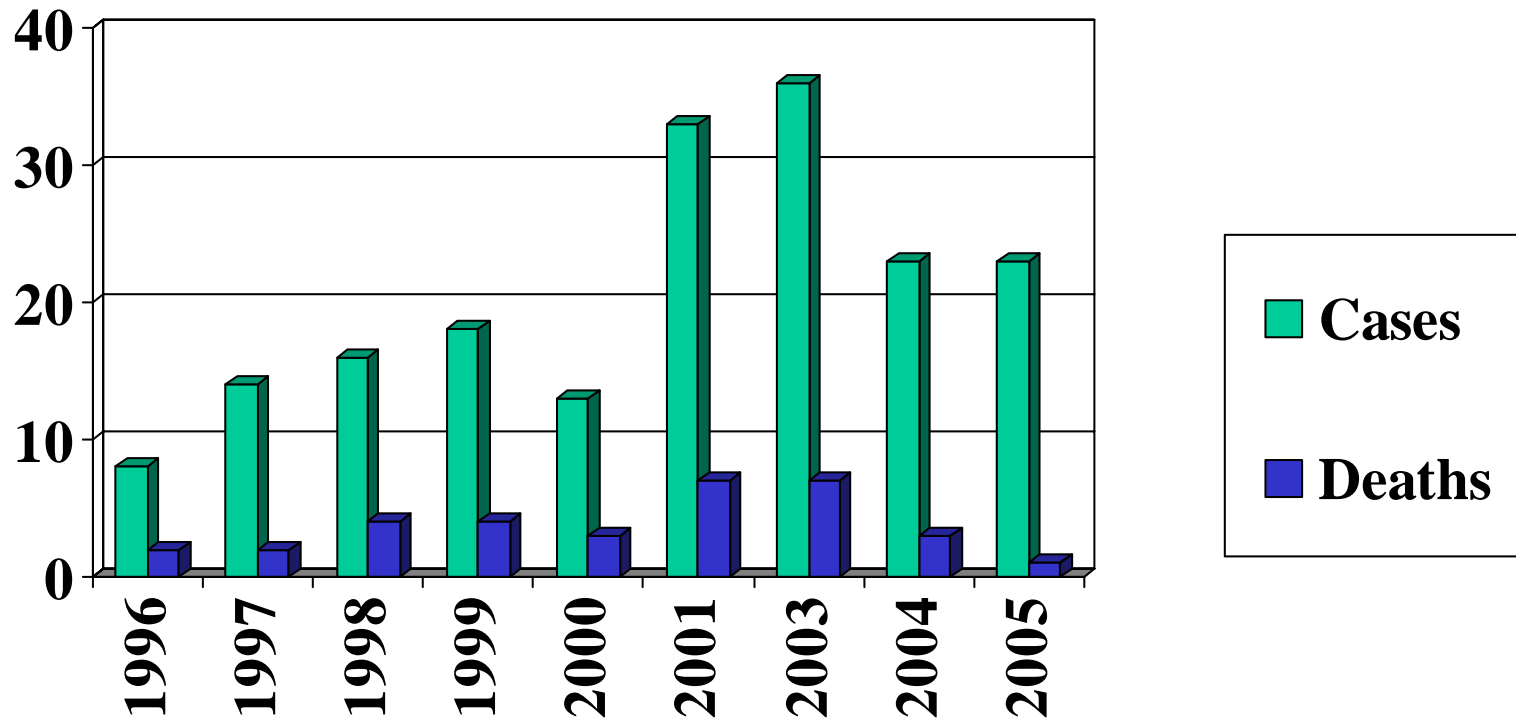
A female donor with history of pregnancy -antibodies in 10-15%



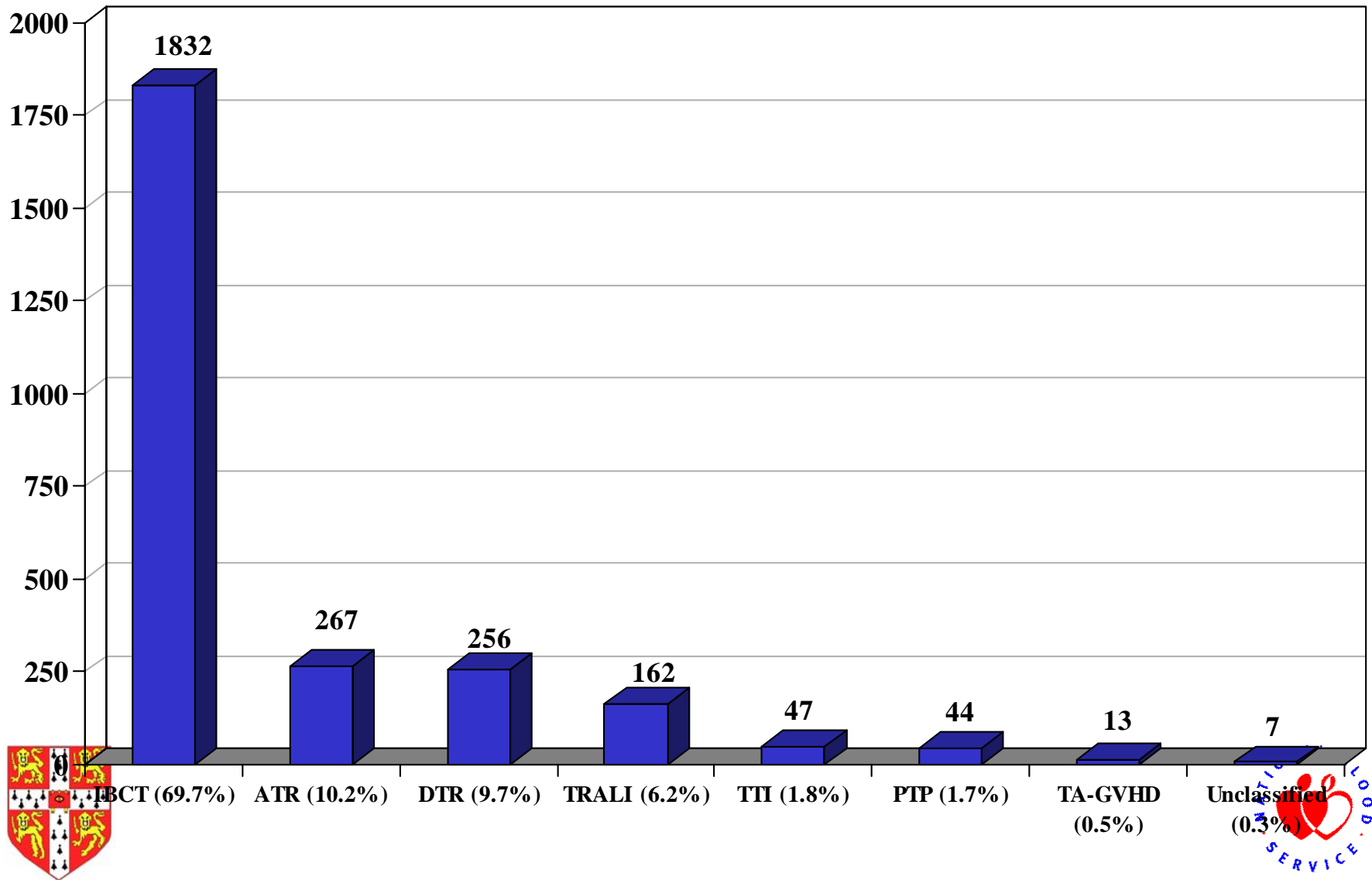
HLA/HNA antibodies



# TRALI cases analysed by SHOT 1996-2005 (n= 184)



# SHOT reports analysed 1996 - 2004 (n=2628)



# Imputability score 1999-2002 (n = 64)

## Highly likely:

- good history + incompatibility = 16

## Probable:

- good history + wk or neg serology

**OR**

- weak history + incompatibility or strong specific antibody = 16

50% in these categories!



# Imputability score 1999-2002 (n = 64)

## Possible:

- history/serology supportive but couldn't exclude other causes = 25

## Unlikely:

- negative serology + other diagnosis to explain symptoms

=

7

50% in these categories!



# Components implicated/total issues (n = 103, 1996-2002)

## HIGH PLASMA (300 MLS)

FFP /CSP 31/ 2.3 million = 1:74,000

Platelets 17/ 1.5 million = 1:88,000

## LOW PLASMA (30 MLS)

Cryoppt 1/ 0.5 million = 1:500,000

Red cells 28/15.6 million = 1:557,000

**Risk from 'high plasma' components was 5-7 times higher than from 'low plasma' components.**



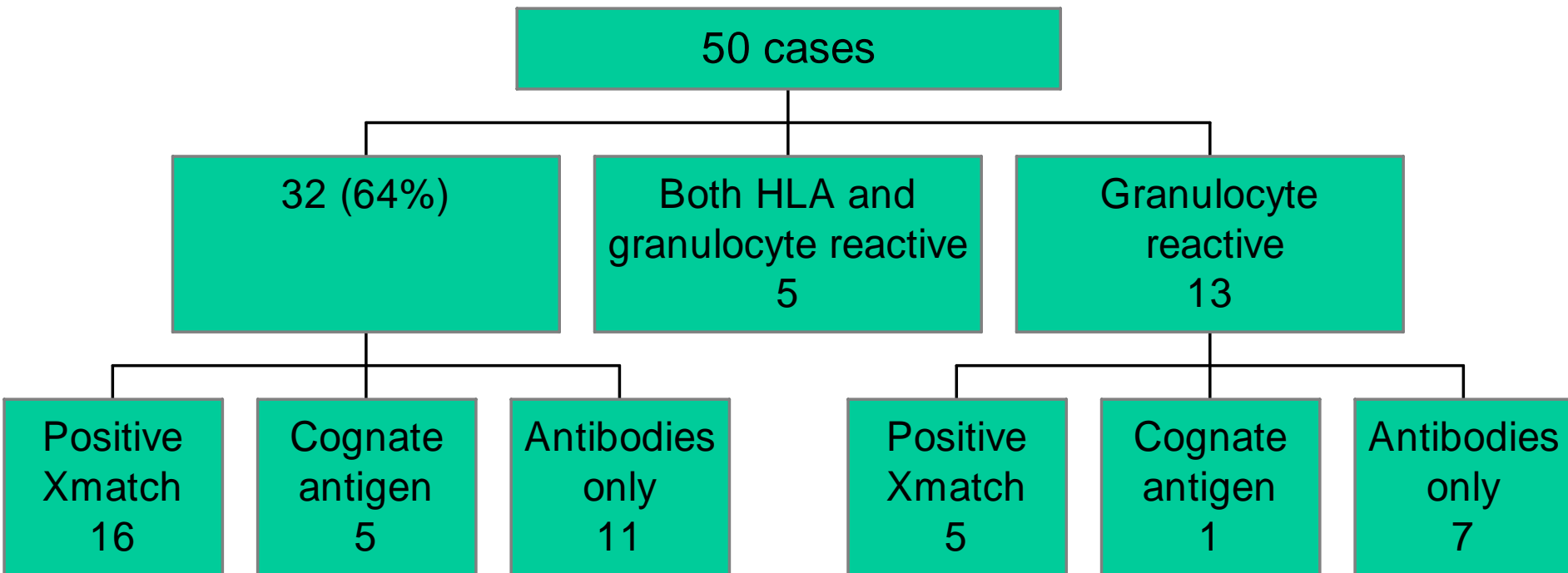
# Components implicated in highly likely/probable TRALI 1999-2002 (n=32)

	Number	Risk/ component
FFP/Plts	20	1 in 95,000
Red cells	5	1 in 1.5 million
FFP+other	7	-----

Excess risk from FFP/platelets = x15



# Positive serological investigations in donors 1998-2002 (n = 50/67)



# In what % TRALI cases would you expect to find a donor with leucocyte antibodies?

- 1 in 7 female donors have HLA antibodies (MacLennan, Navarrete, Lucas et al, Canadian Consensus Conference)
- Median donor exposure = 3 i.e. 1.5 females
- SO- 1 in 5 cases investigated would have an HLA antibody positive female donor by chance

Therefore important to show presence of corresponding antigen



# Serology by component 1998-2002

	<b>Red cells</b>	<b>FFP/plts</b>
<b>Cases</b>	13	32
<b>Ab pos donor</b>	2.6 expected 5 observed	6 expected 28 observed
<b>Gender</b>	2/2 F	18/18 F
<b>Incompatible</b>	1/1 F	13/13 F



# TRALI risk reduction project 2003- assumptions

- Donor HLA/HNA antibodies are an important cause of TRALI
- Risk highest components are FFP and platelets
- Highest risk donors are previously pregnant women
- Other possible causes of TRALI not addressed by the project



	<b>Donor selection: untransfused males/never pregnant females</b>	<b>Donor selection: make FFP from males only</b>	<b>Screening for HLA antibodies</b>	<b>Platelet additive solution</b>	<b>Pooling</b>
<b>FFP</b>	<b>Yes</b>	<b>Yes</b>	<b>No</b>	<b>No</b>	<b>Yes (SDFFP)</b>
<b>Pooled platelets (plasma component)</b>	<b>Yes</b>	<b>Yes</b>	<b>No</b>	<b>Yes</b>	<b>No</b>
<b>Apheresis platelets</b>	<b>No</b>	<b>No</b>	<b>Yes</b>	<b>Yes</b>	<b>No</b>
<b>Non-OAS blood for large transfusion in neonates</b>	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>	<b>No</b>	<b>No</b>



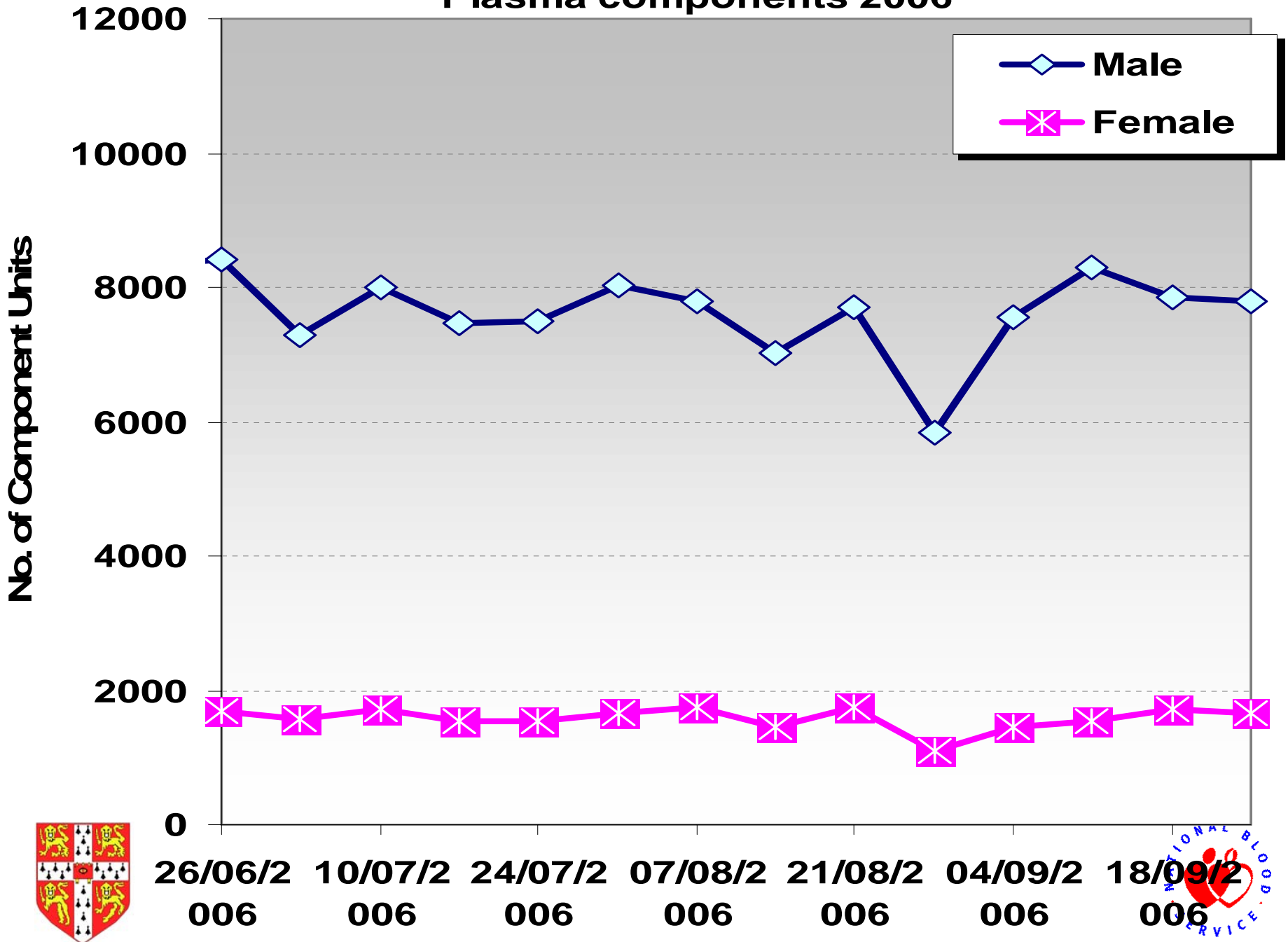
**‘Please- no more new questions for donors!!’  
Decision ‘Male FFP as far as possible’.**

**October 2003**

- **Male donations marked M - to FFP**
- **Female donations marked F- to ‘plasma discard’**
- **Did NOT swap out female FFP stocks**
- **April 2004-previously transfused donors excluded (vCJD)**



# Plasma components 2006



# FFP - UK specification

- Not manufactured from first time donors
- ALL from whole blood donations
- Leucocyte depleted by whole blood filtration
- **75% of units must contain 0.7iu/ml factor VIII**
- **To meet this spec requires same day freezing**

- NO UK PLASMA IS FRACTIONATED



2 million donations/year; 350,000 frozen products rest discarded



**DID IT WORK?**



# Change in TRALI profile since 2002

Reporting year	1999-2002	2003	2004	2005
TRALI cases analysed	64	36	23	23
Highly likely	16	20	10	3
Probable	16	2	3	3
Possible	25	6	4	3
Unlikely	7	8	6	14



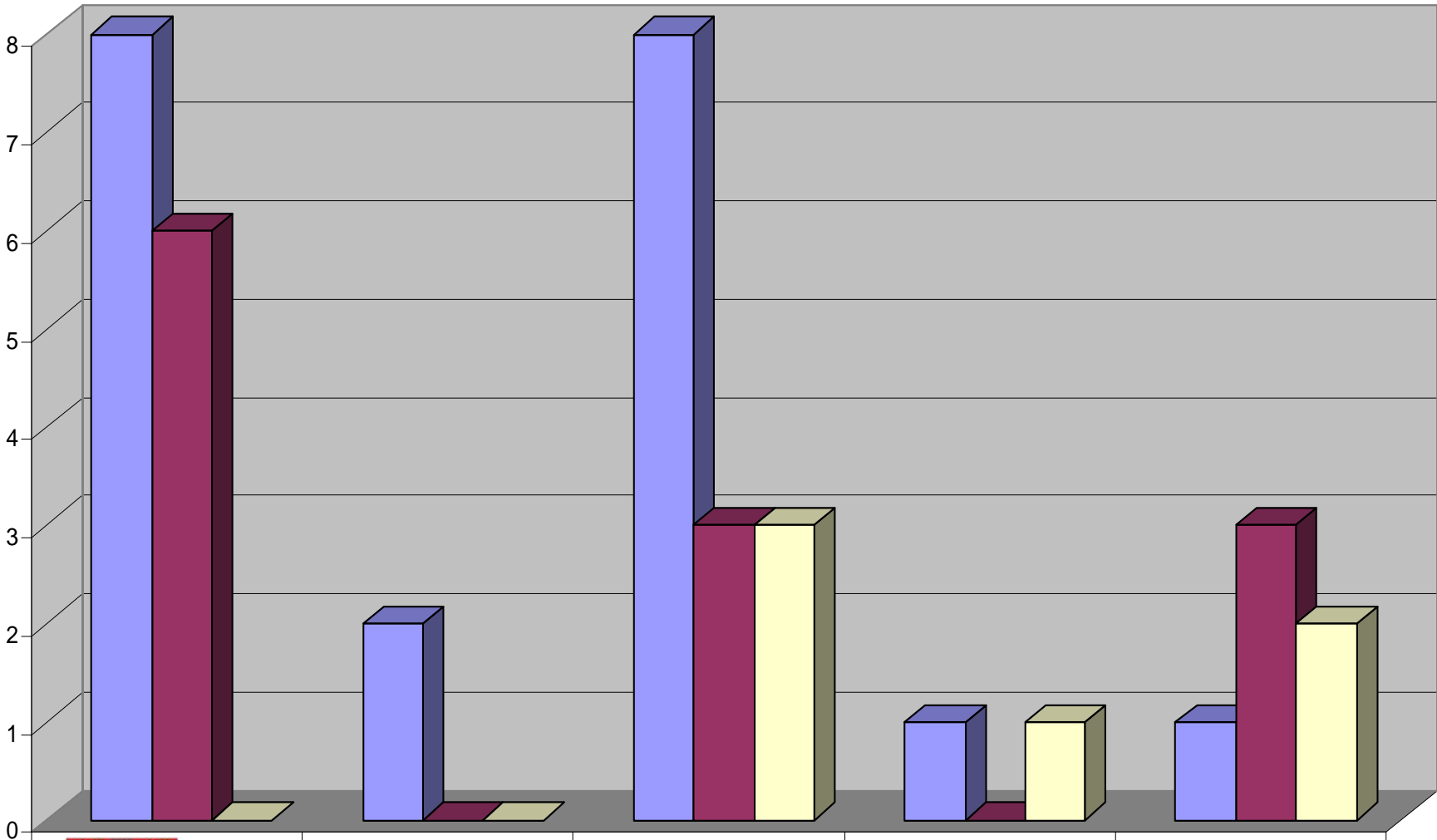
# Components implicated in highly likely/probable TRALI 1999-2005

	1999- 2002	2003	2004	2005
<b>FFP</b>	15	8	6	1
<b>Plts</b>	5	8	4	2
<b>Red cells</b>	5	1	3	2
<b>FFP +other</b>	7	3	0	0
<b>Other</b>	0	2	0	1



# CASES WITH POSITIVE X-MATCH/COGNATE ANTIGEN

2003 2004 2005



# Other important recommendations by SHOT

- Every effort must be made to avoid unnecessary transfusion of FFP and platelets
  - **Action: Clinicians administering blood transfusion**
- FFP should only be used when clinically indicated in accordance with BCSH guidelines. **Guidelines for the management of high INRs due to warfarin therapy should also be followed.**
  - **Action: Clinicians administering blood transfusion**



# No evidence to support use of FFP to improve coagulation and reduce bleeding!

- Systematic review of FFP trials- none proved benefit- (Stanworth et al, BJHaem 2004; 126:139-152)
- No correlation between any given coagulation abnormality and bleeding (Segal et al, Transfusion 2005;45:1413-425)
- FFP does not correct mildly abnormal coagulation (Omar et al, Transfusion Aug 2006:46).



# What about TRALI due to platelets?



# Sources of plasma in pooled BC plats

	<b>Plts in plasma</b>	<b>Plts in PAS</b>
PAS	-----	200 mls
Donor 1 (plasma +BC)	<b>200 mls + 25 mls</b>	25 mls
Donors 2-4 (BC only)	<b>3 x 25 mls</b>	3 x 25 mls
Total plasma	<b>300 mls</b>	100 mls



# Suspending buffy coat platelets in male plasma



# Reducing risk of TRALI from pooled platelets

- Male donor as source of plasma 'as far as possible'
- Limited by need to make BC on day of collection
- Now 80-90% of pools are in male plasma
- Would need 20°C overnight hold to reach 100%



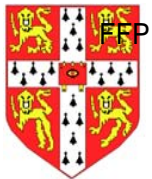
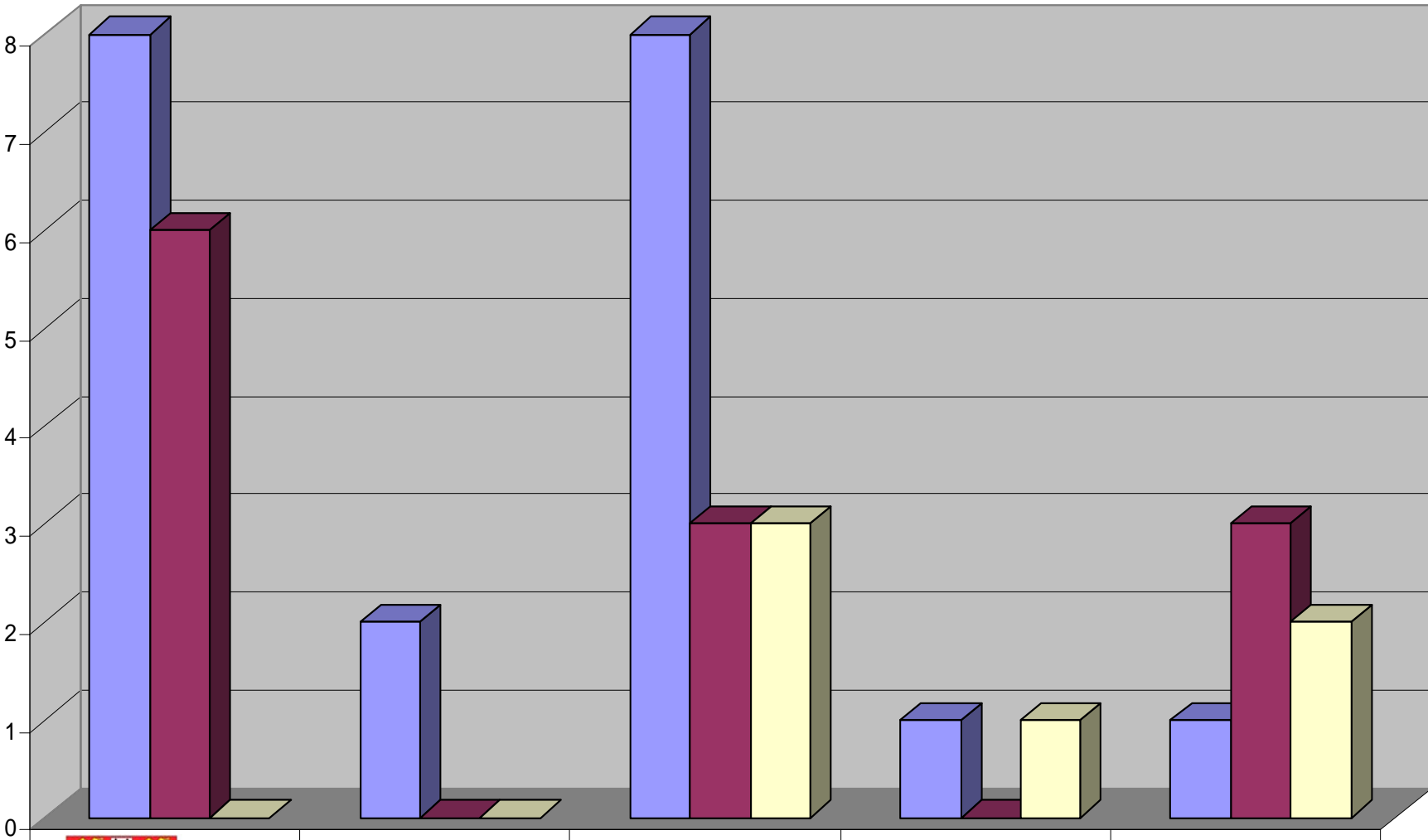
# Components implicated in highly likely/probable TRALI 1999-2005

	1999- 2002	2003	2004	2005
<b>FFP</b>	15	8	6	1
<b>Plts</b>	5	8	4	2
<b>Red cells</b>	5	1	3	2
<b>FFP +other</b>	7	3	0	0
<b>Other</b>	0	2	0	1



# CASES OF TRALI WITH POSITIVE X-MATCH OR RELEVANT ANTIBODY

2003 2004 2005



## Platelet additive solution composition (mmol/l)

	PASI	PASII*	PASIII	PASIII modified*	Plasma-Lyte	*Composol
Sodium Chloride	70	115.5	115	100	90	90
Tri-sodium citrate	30	10	10	10	-	10.9
Sodium acetate	-	30	30	30	27	27
Sodium phosphate	5	-	26	26	-	-
Sodium gluconate	-	-	-	-	23	23
Glucose	-	-	-	-	-	-
Maltose	-	-	-	-	-	-
D-mannitol	30	-	-	-	-	-
Potassium chloride	10	-	-	5	5	5
Magnesium Chloride/sulphate	-	-	-	1.5	3	1.5

# Sources of plasma in pooled BC plts

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Donors 2-4 (BC only)	3 x 25 mls	<b>3 x 25 mls</b>
Total plasma	300 mls	<b>100 mls</b>



# Apheresis platelets- could platelet additive solution reduce TRALI risk?

- Need to retain 30% plasma from 1 donor- ? extent of risk reduction
- Systems for adding to apheresis plts need evaluation
- Linkage with bacterial screening:-
  - Need to confirm that additive solutions can support 7 day storage



# Leucocyte antibody screening of apheresis donors

- Platelet donors: 75% are male
- Should we screen all the women?
- Could we afford to lose 4% of donors?
- Should we just screen potential platelet donors?
- What to do with positives?
  - Resign completely?
  - Carry on as donors of red cells in additive solution



# Acknowledgements

## **SHOT**

Liz Love, Hilary Jones,  
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## **TRALI REDUCTION PROJECT**

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## **LEUCOCYTE ANTIBODY DATA**

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Geoff Lucas

