# Component procurement to improve patient safety

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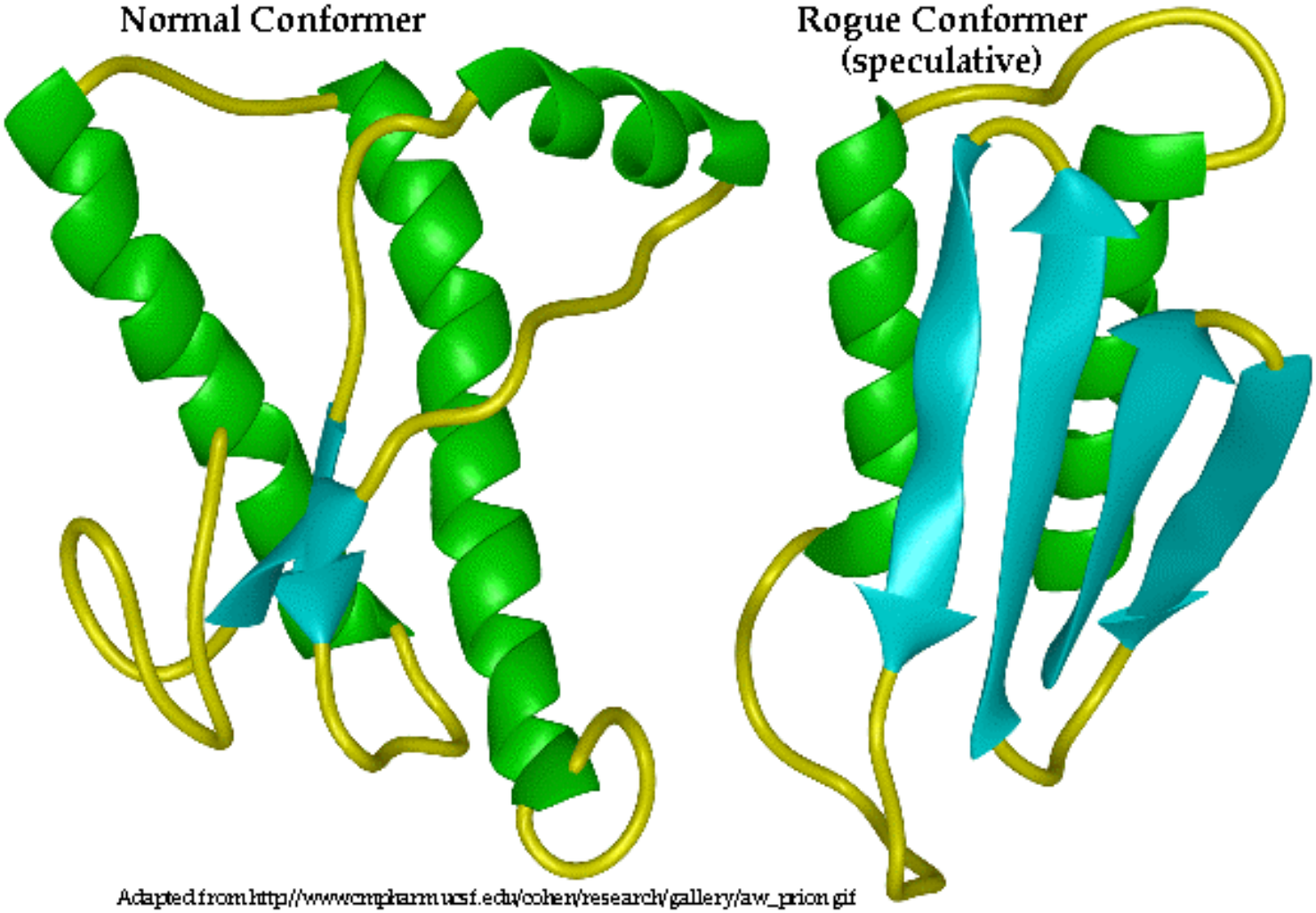
# Areas of recent concern

- Variant Creutzfeld-Jacob disease
- Transfusion-related acute lung injury
- Bacterial contamination of platelets

# Variant Creutzfeld-Jacob Disease

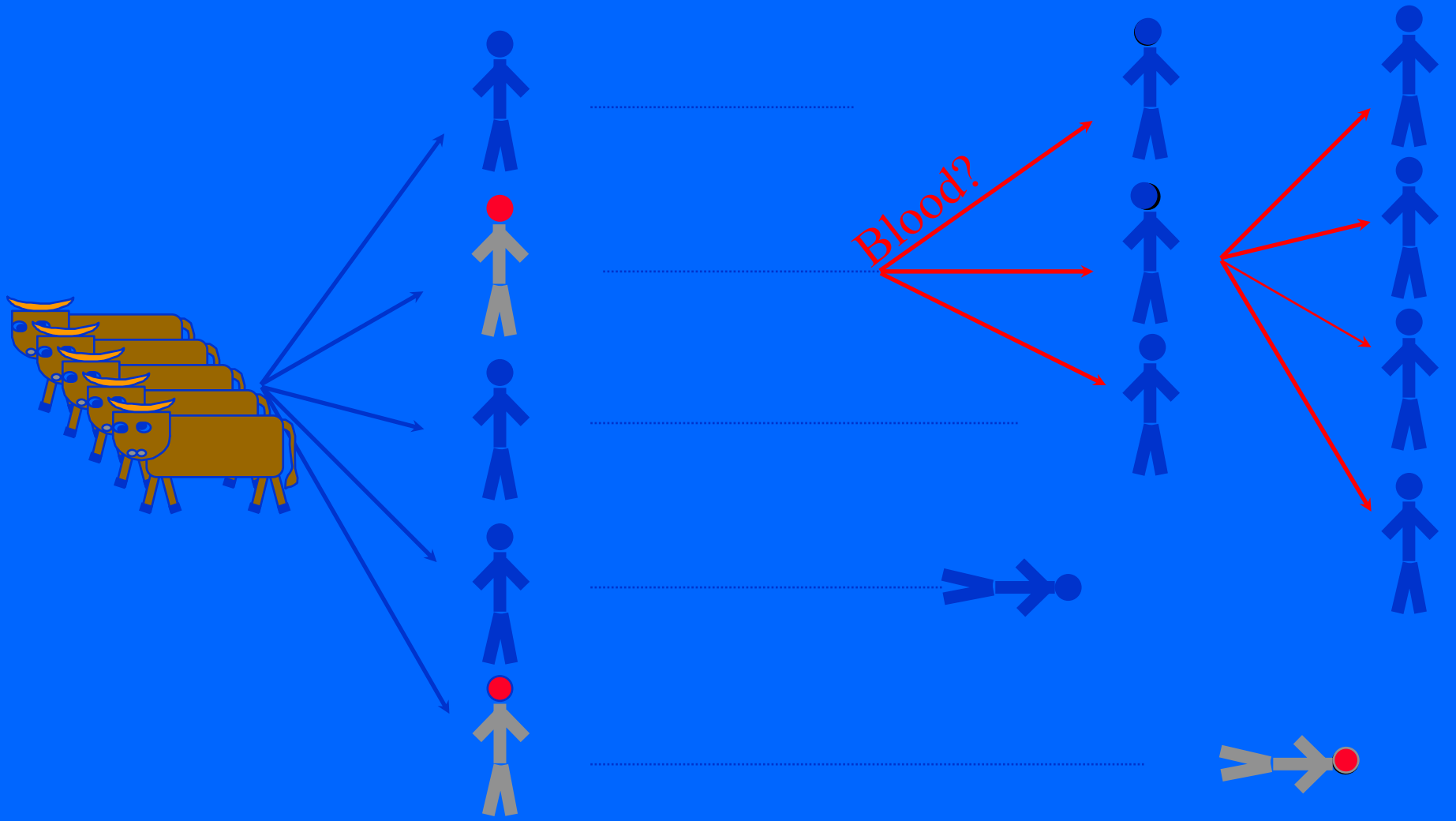
- A new transmissible prion disease
- Human form of BSE
  - first described in 1996
    - younger age of onset -20s
    - all MM genotype (37% expected)
    - 1-2 years till death
- To date 200 probable cases worldwide- 160 in UK
- Final number of cases unknown
  - ? a few hundred from BSE
  - ?secondary cases from donation of blood, organs, tissues

# vCJD- caused by prions- protein only infectious agent




Adapted from http://www.cmpharm.ucsf.edu/cohen/research/gallery/aw_prion.gif

# Potential expansion of vCJD epidemic by transfusion




(after M Busch)

# Transfusion medicine epidemiology review (TMER)

- collaboration between UK Blood Services and CJD Surveillance Unit since 1996
- aims to identify donor/recipient pairs where both have vCJD
- traces blood donations  in vCJD cases

  -donors ---> recipients and recipients ----> donors

# 4 vCJD transmissions from non-LD red cells

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| me to s | 40 months | 21 mnths* | 17 mnths* | ---- |
| ype | MM | MM | MM | MV |
| : Tx | 62 | 23 | 50s | ---- |
| ime osis | 6.5 yrs | 7.8 yrs | 8.3 yrs | PM only |

# Survey of prion protein in tonsil and appendix samples

*(Hilton et al J Pathology* 2004;203:733-9)

| | |
|---|---|
| APPENDIX/TONSILS | 3/12,674 POSITIVE |
| ESTIMATED PREVALENCE | 237/MILLION<br>95% CI (49-692) |
| This means that 1 in 4000-10,000 blood donors might be a carrier | |

# Minimising the risk of transfusion-transmitted vCJD in UK

1. Donor exclusion
2. Approach to donor screening
3. Modifications to production
   - blood components
   - fractionated plasma products
   - tissues
4. Changes in clinical practice

# Donor exclusions in UK

## (www.transfusionguidelines.org.uk)

1998: Family history of prion diseases

1990s: Received pituitary hormones, dura mater, corneal transplant

2004/5: If received blood component, I/V IgG or plasma exchange since 1980 (Does not apply to anti-D)

Other countries exclude UK residence

# Why no screening test yet for vCJD in blood donors?

- No DNA/RNA or antibodies
- Levels of prion in blood very low
- Therefore need amplification step and detection step
- Also need confirmatory test (could be a second screening test)

# Blood screening assays: donor issues to consider before implementation

- management of positives
  - to tell or not to tell….legal duty of care
  - to bleed or not to bleed... tell
- how to separate the true and false positives
- implications of true positivity - will the donor develop clinical variant CJD or not?
- psychological and social impact on donor
- impact on donor recruitment and retention
- wastage due to false positivity

# Component processing steps already implemented

1999: universal leucocyte depletion

1999: switch from UK to US plasma for all fractionated products

2004: import FFP from USA;

- for children- single unit methylene blue treated

- for plasma exchange/TTP- solvent detergent

2005 -ongoing: increase proportion of platelets by apheresis to reduce donor exposure; use apheresis plts for children

2005: reduce plasma in red cell components

STILL CONSIDERING

-platelets in additive solution to remove 70% plasma

-prion reduction filters

# Leucocyte depletion alone may remove only 40% of infectivity

Gregori et al Lancet 364;527-531, 2004

| Sample | Inoculated | Infected | Titer* (ID/ml) |
|---|---|---|---|
| Pre filtration | 106 | 45 | 11.05±3.3 |
| Post filtration | 108 | 29 | 6.25±2.5 |

*Corrected with Poisson distribution

**(post/pre)% ≃ 58%**

# Prion filtration of red cells

- Macopharma- CE marked Sept 06
- Leucocyte depletion has to be performed first
- No filters yet for whole blood, platelets or plasma
- UK Blood Services: Prion Reduction Working Group since 2004

# Assessing Macopharma prion filter

- Does it remove 3 logs of prion?
  - Independent evaluation by Health Protection Agency
- Component quality
  - loss of 40 mls red cells
- Operational considerations
  - high blockage rate-?now corrected
- Volunteer study- red cell recovery
- Patient safety studies- to start 2007

# Prion-filtered red cells in surgery and multi-transfused patients (PRISM)

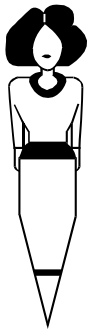
- SAFETY STUDY; Primary endpoints are adverse events and red cell alloimmunisation
- Study 0: exposure of patients to 1,2,3 units
- Study 1: cardiac surgery- 170 patients, all receiving prion-treated red cells; control cohort
- Study 2: transfusion dependent (NOT sickle/thal) randomised -prion-treated vs control- 170 in each arm, 6 transfusions each.

# Prion removal- the decisions to be made

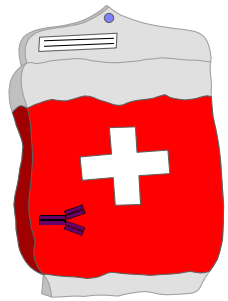
- How much would it cost (universal vs selective approach)?
- Filtration vs testing
- Final decision in UK will be by Dept(s) of Health advised by MSBTO, SEAC and UKTS.

# Transfusion-related acute lung injury

- Acute shortness of breath, low pO2, shadowing on CXR
- 10% fatal, many need ventilation and recover
- Interaction between HLA/HNA antibodies in donor plasma and corresponding antigen on patient's leucocytes

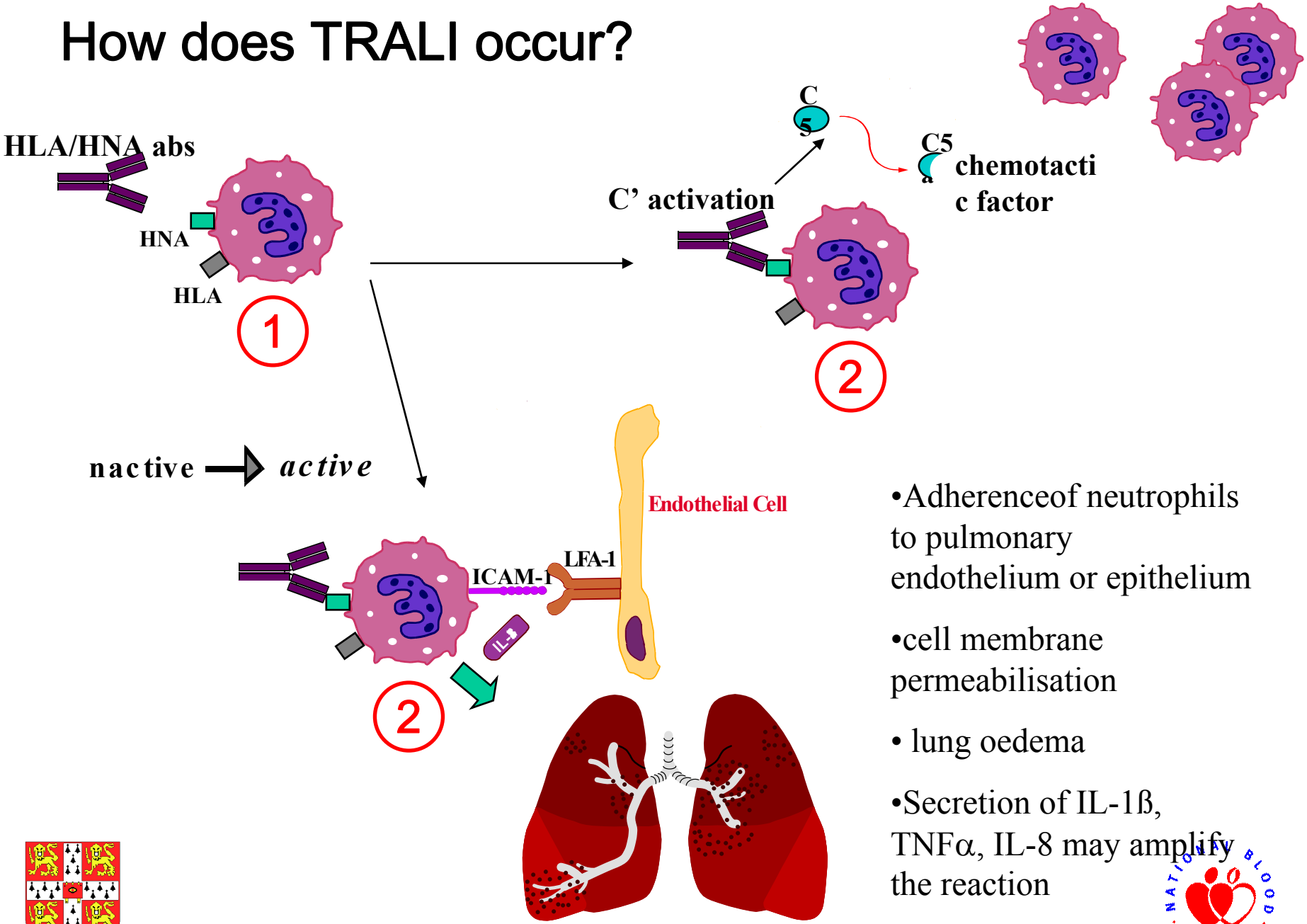


**Female donors with history of pregnancy -antibodies in 10-15%**



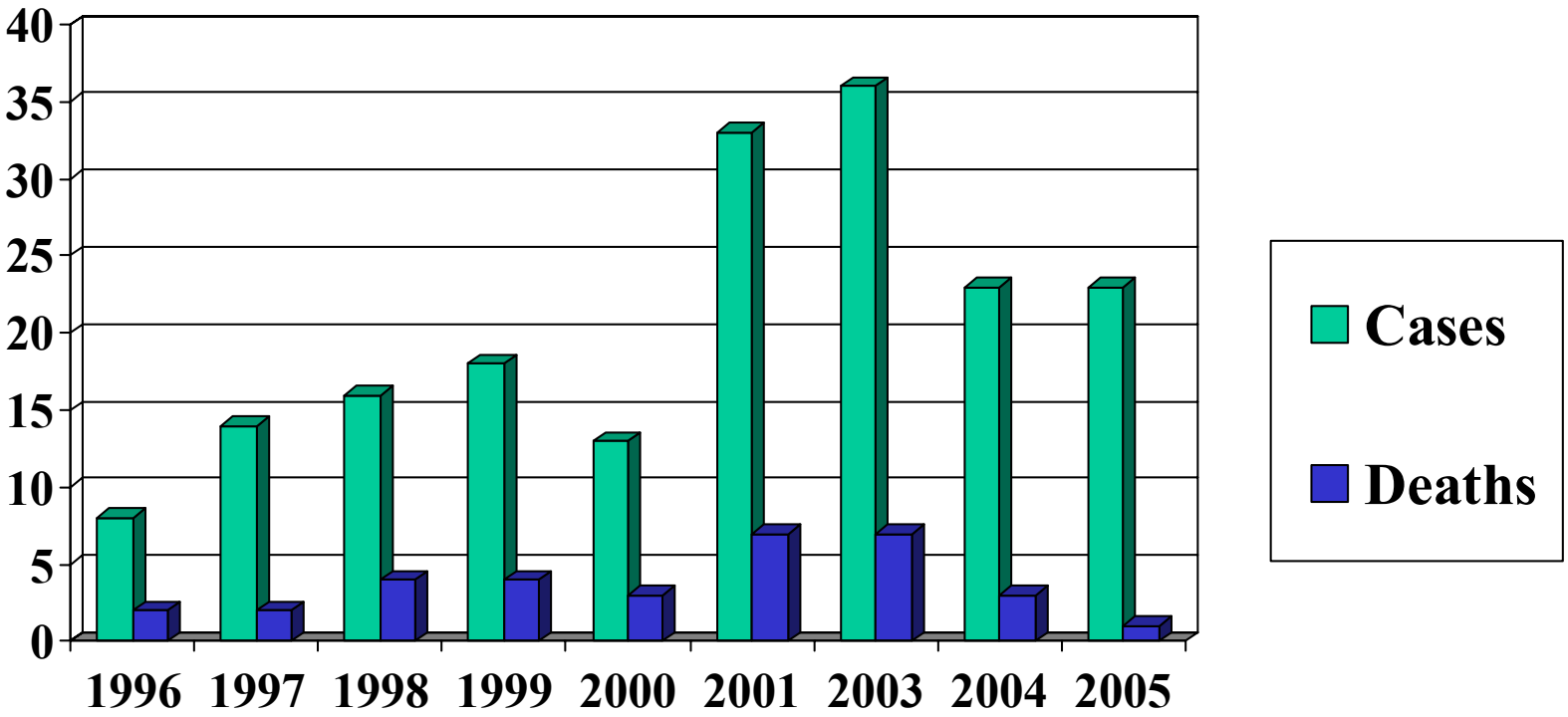
**HLA/HNA antibodies**

# How does TRALI occur?




- Adherenceof neutrophils to pulmonary endothelium or epithelium
- cell membrane permeabilisation
- lung oedema
- Secretion of IL-1ß, TNFα, IL-8 may amplify the reaction

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

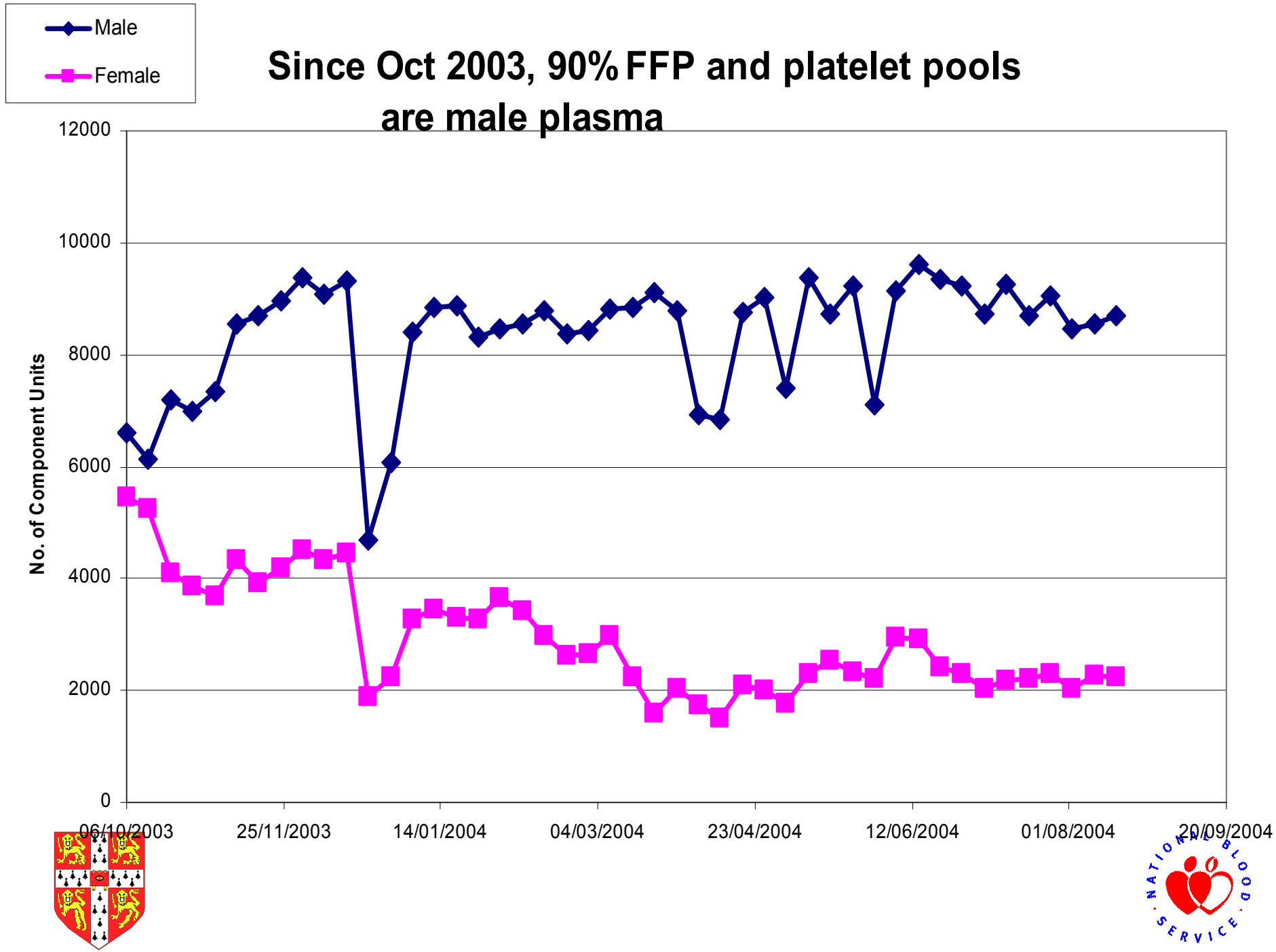


# Components implicated in highly likely/probable TRALI 1999-2002 (n=32)

| | 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
All HLA antibody pos females

# Since Oct 2003, 90% FFP and platelet pools are male plasma



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

| | 1999-2002 | 2003 | 2004 | 2005 |
|---|---|---|---|---|
| **FFP** | 15 | 8 | 6 | 1 |
| **Plts** | 5 | 8 | 4 | 2 |
| **Red cells** | 5 | 1 | 3 | 2 |
| **FFP +other** | 7 | 3 | 0 | 0 |
| **Other** | 0 | 2 | 0 | 1 |

# Transfusion-transmitted infections in UK 1995-2005

- HBV -10 + 1 HEV
- HCV -2
- HIV -2
- HAV-2
- HTLV- 2 (pre-testing)
- malaria-2
- BACTERIA- 30
  - 26 due to platelets; 4 due to red cells

# Bacterial contamination of platelets - analysis of 25 cases

- 15 pooled; 9 apheresis; 1 uncertain
- age of platelets =

  d1 (0), d2 (2), d3 (3), d 4 (6), d5 (10)

- 7 deaths -Staph aureus, Staph epidermidis, Enterobacter aerogenes, E coli, B cereus.

# Bacterial contamination of platelets - species and sources

- Donor throat/blood -group B streptococcus
- Donor skin
  - -Bacillus cereus
  - Staph aureus
  - Staph epidermidis

# Strategies to minimise bacterial risk of platelets

- Better arm cleansing-Chloroprep sponge - BEING DONE
- Diversion of first aliquot of blood - BEING DONE

THESE 2 STEPS REDUCE RISK BY 70%

NO CASES REPORTED IN 2005

- Bacterial screening- FIELD TRIALS ONGOING
- Pathogen inactivation - ?COST EFFECTIVE

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