

# Platelets – it's the special treatment needed

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## Will cover...

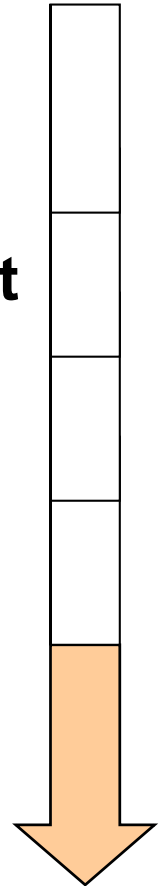
- Why 'special' platelets
- Role of HLA
- Guidelines for management of Refractory Patients
- Logistics of selected platelet provision

## Why 'Special' Platelets - Platelet Refractoriness

## Thrombocytopaenia

- Platelet count less than  $140 \times 10^9/l$
- Haemorrhage occurs  $10-30 \times 10^9/l$
- Petechiae (pinpoint haemorrhage)
- Ecchymoses (bruising)
- Easy bruising, gum and nose bleeds, haematuria and prolonged menses
- GI blood loss can lead to Iron deficiency and anaemia
- Intracranial Haemorrhage (ICH)

**Platelet  
Count**

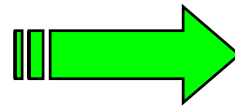


## Standard Platelets

Range of platelet products are provided by NBS:

- Pooled donor units derived from platelet rich plasma from whole blood donations ( 4 donors )
- Single donor platelet units collected by apheresis
  - Over 90,000 adult platelet doses issued in UK each year

## Pooled Platelets



## Apheresis Platelets



‘Special’ Platelets for Platelet Refractoriness

NHSBT

## Definition of Platelet Refractoriness

Corrected Count Increment (CCI) of less than between 3,000 – 5,500 per  $\mu\text{L}$  per  $\text{m}^2$  per  $10^{11}$  platelets 1 hour post transfusion.

$$\frac{\text{Platelet Count Increment } (/ \mu\text{L}) \times \text{Body Surface Area } (\text{m}^2)}{\text{Platelets Transfused } (\times 10^{11})}$$

Bishop JF, Matthews JP, Yuen K, McGrath K, Wolf MM, Szer J. The definition of refractoriness to platelet transfusions. *Transfus Med* 1992; 2: 35-41



## Practical Definition

Increase in patient's platelet count of  $<10 \times 10^9/l$  between 1 and 24 hours after the transfusion of an adult dose of ABO compatible apheresis platelets on two separate occasions.

## Causes of Platelet Refractoriness

### Non Immune (80%)

- Bleeding
- Old platelets
- Splenomegaly, hepatomegaly
- DIC
- Infection and its treatment especially amphotericin B
- Fever

### Immune (20%)

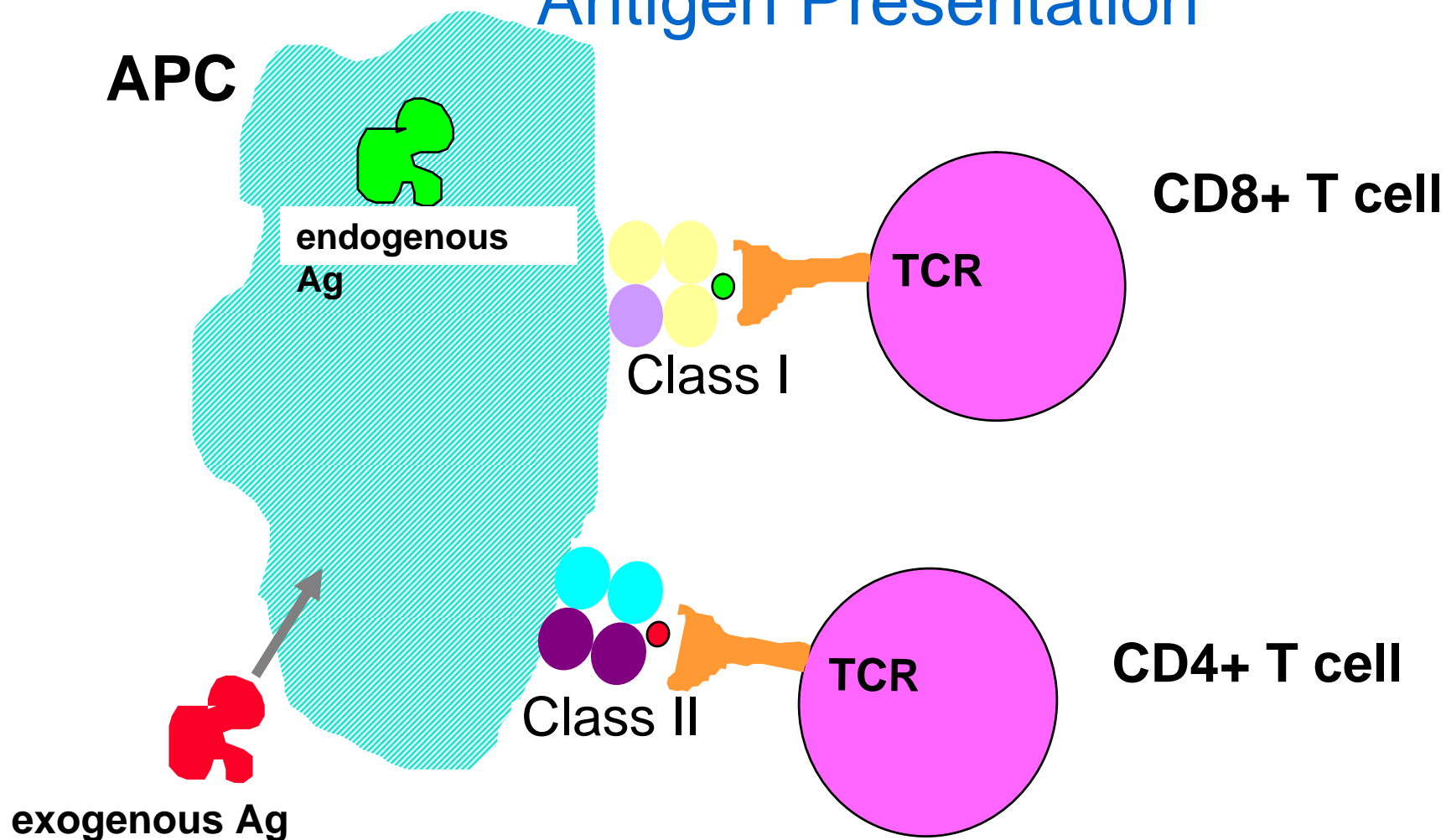
- Platelet alloantibodies
  - anti HLA (class I - >95%)
  - anti HPA (<5% HPA + HLA, HPA only <1%)
- Other antibodies
  - Autoantibodies
  - Drug-dependent antibodies
  - ABO antibodies
- Immune complexes

# Role of Human Leukocyte Antigens (HLA)

## Normal role of HLA

- Allow us to recognise “self” from “non-self”
- Provide an alert to the immune system to indicate whether we have an infection or not
- Class I molecules present endogenously derived Ag (viral infection) to CD8+ cytotoxic T cells
- Class II molecules present exogenously derived Ag (bacteria etc) to CD4+ helper T cells

# Antigen Presentation



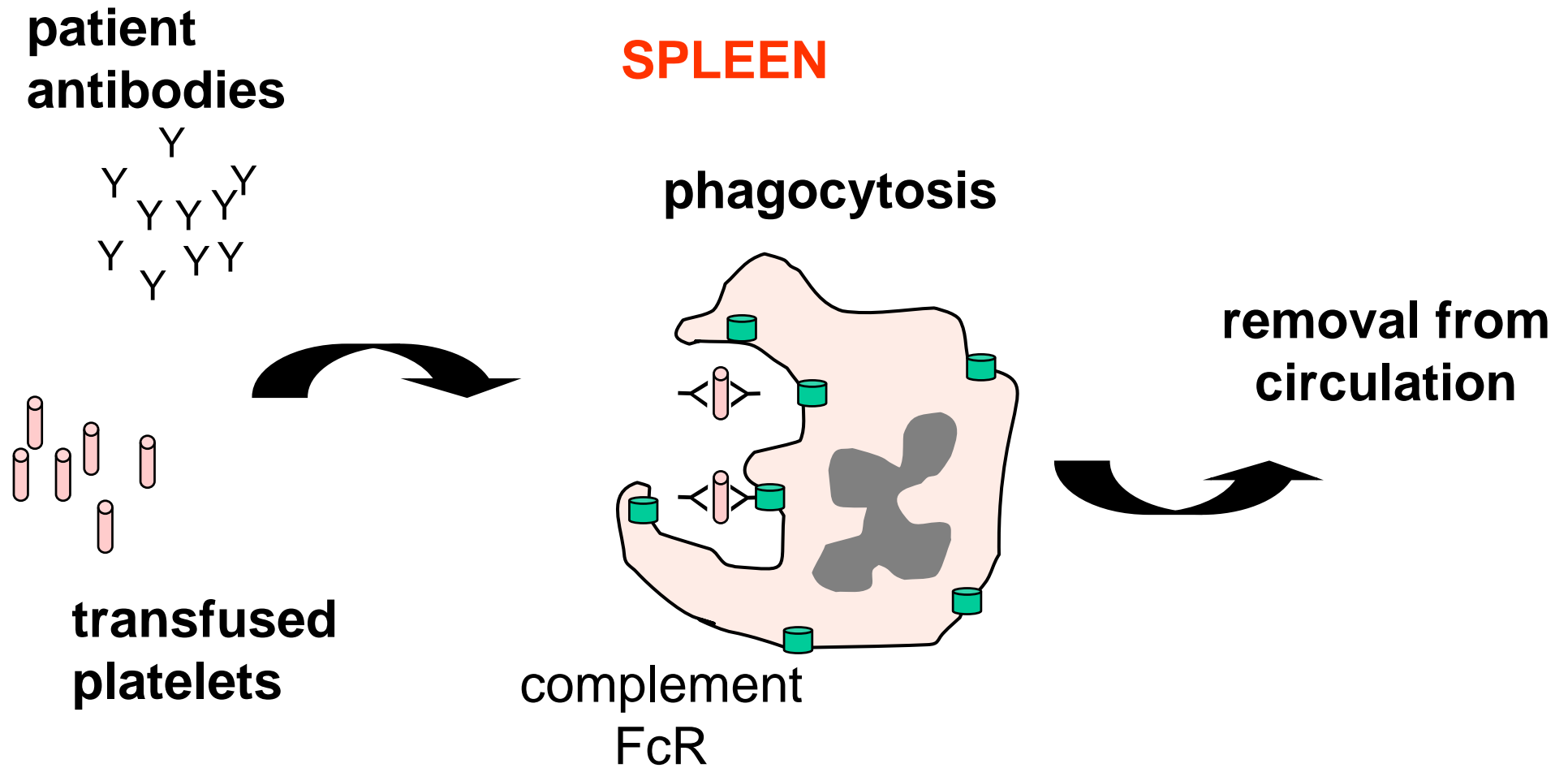
## The HLA system is highly polymorphic

	<b>2005</b>	<b>2010</b>	<b>2012</b>
• HLA-A	349	1,381	2,013
• HLA-B	626	1,927	2,605
• HLA-C	182	960	1,551
• HLA-DRA	3	3	7
• HLA-DRB	470	924	1,260
• HLA-DQA1	28	35	47
• HLA-DQB1	60	127	176
• HLA-DPA1	22	28	34
• HLA-DPB1	116	142	155

## Consequences of exposure to foreign HLA

- Exposure to foreign HLA:
  - blood transfusion
  - pregnancy
  - transplantation
- T cell activation; in transplant setting leads to graft rejection and GvHD
- Anti-HLA antibody formation in transfusion setting leading to platelet refractoriness

## HLA Antibodies and Platelet Refractoriness

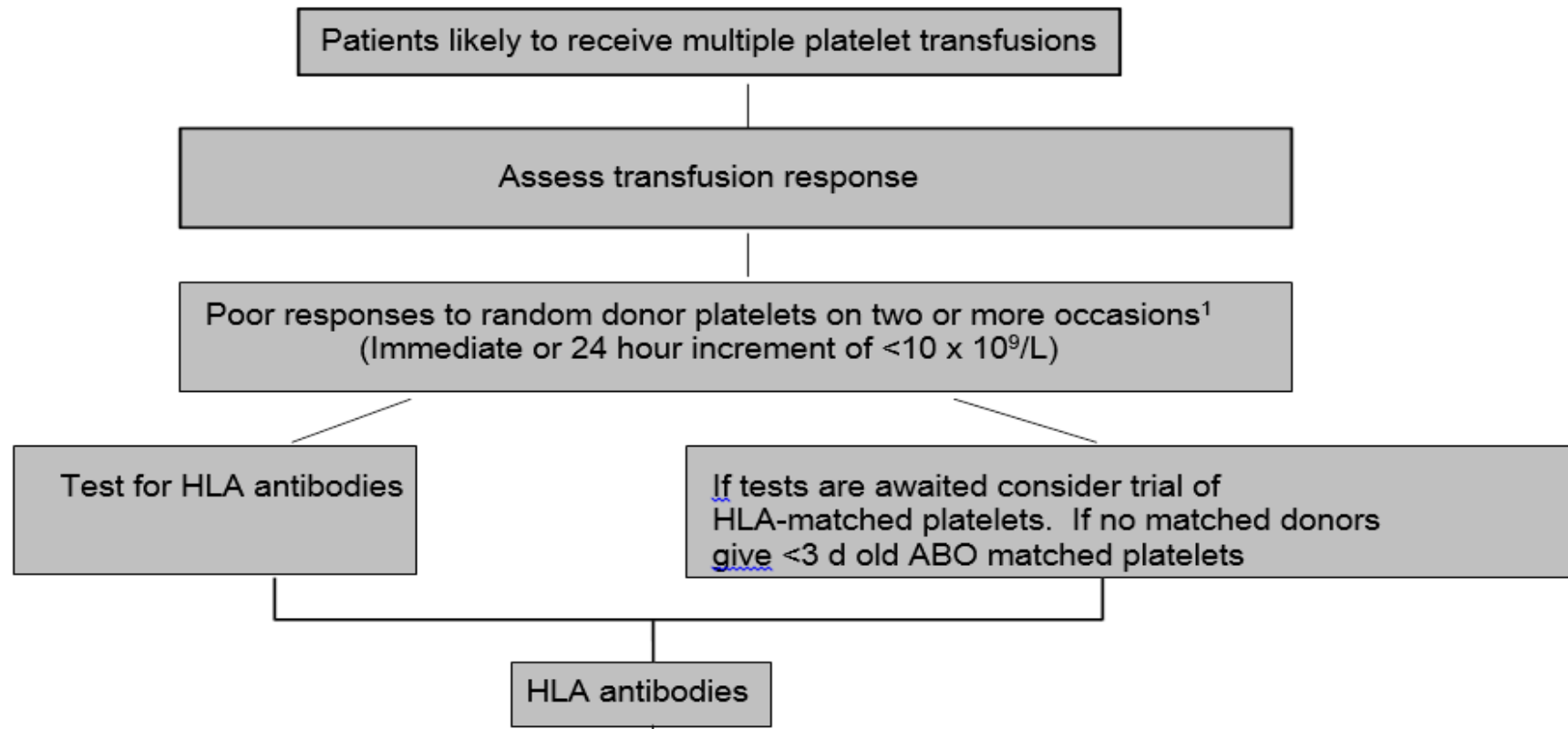




# Guidelines for management of Refractory Patients

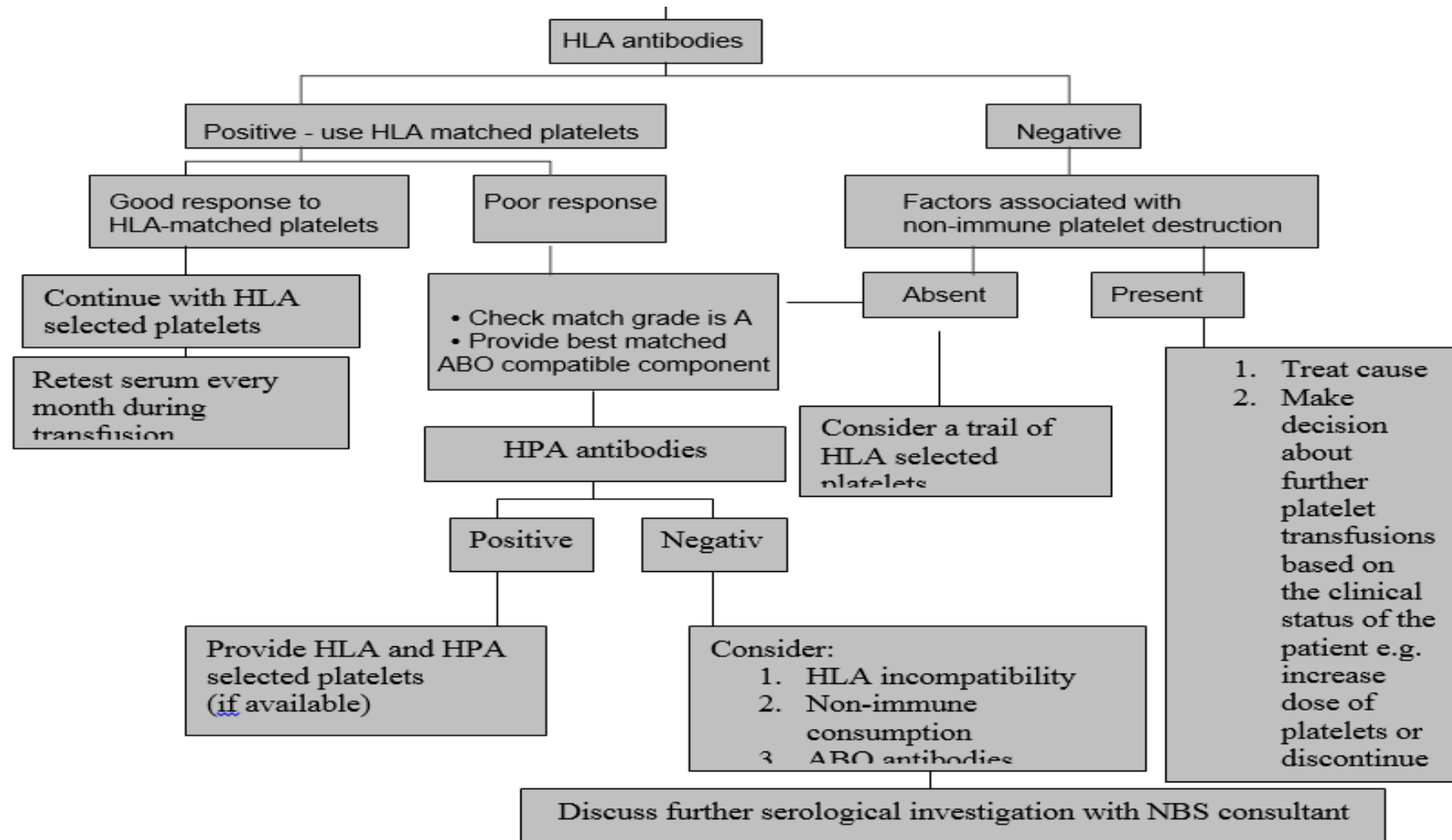
[http://hospital.blood.co.uk/library/pdf/INF139\\_1\\_1.pdf](http://hospital.blood.co.uk/library/pdf/INF139_1_1.pdf)

## Guidelines



[http://hospital.blood.co.uk/library/pdf/INF139\\_1\\_1.pdf](http://hospital.blood.co.uk/library/pdf/INF139_1_1.pdf)

## Guidelines cont.



## Reasons for Increment Data

- To aid in platelet selection (only 30% are fully matched)
  - Identify unacceptable antigens
  - Identify acceptable antigen
- To achieve better clinical response
- To identify if HPA testing is required
- To identify if PAS is required
- To identify if further samples are required for HLA antibody testing
- To not waste a precious resource
- To save money

## Case Study

- Patient PT Dob 10/08/1969 (MDS)
- HLA type A1, A3; B7, B8
- Anti HLA Antibodies (Bled 01/01/2011) – B13, B27, B38, B39, B44, B45, B64, B64
- No increment data provided but patient reported as responding well to HLA matched platelets in early 2012
- No response to regular requests for new clotted sample

## Case Study Cont.

- Oct 2012 hospital call to say patient showing poor response to HLA matched platelets
- New sample bled 13/10/2012
- Testing reveals anti HLA-A2 antibodies
- Look back reveals patient has been receiving platelets from donors with HLA-A2 antigen
- Patient now responding well to HLA matching which avoids HLA-A2 and other newly developed HLA antibodies
- Hospital now sends in regular increment data and samples for testing

## Cost 2010/11

- Platelets (1 adult dose) £230.39

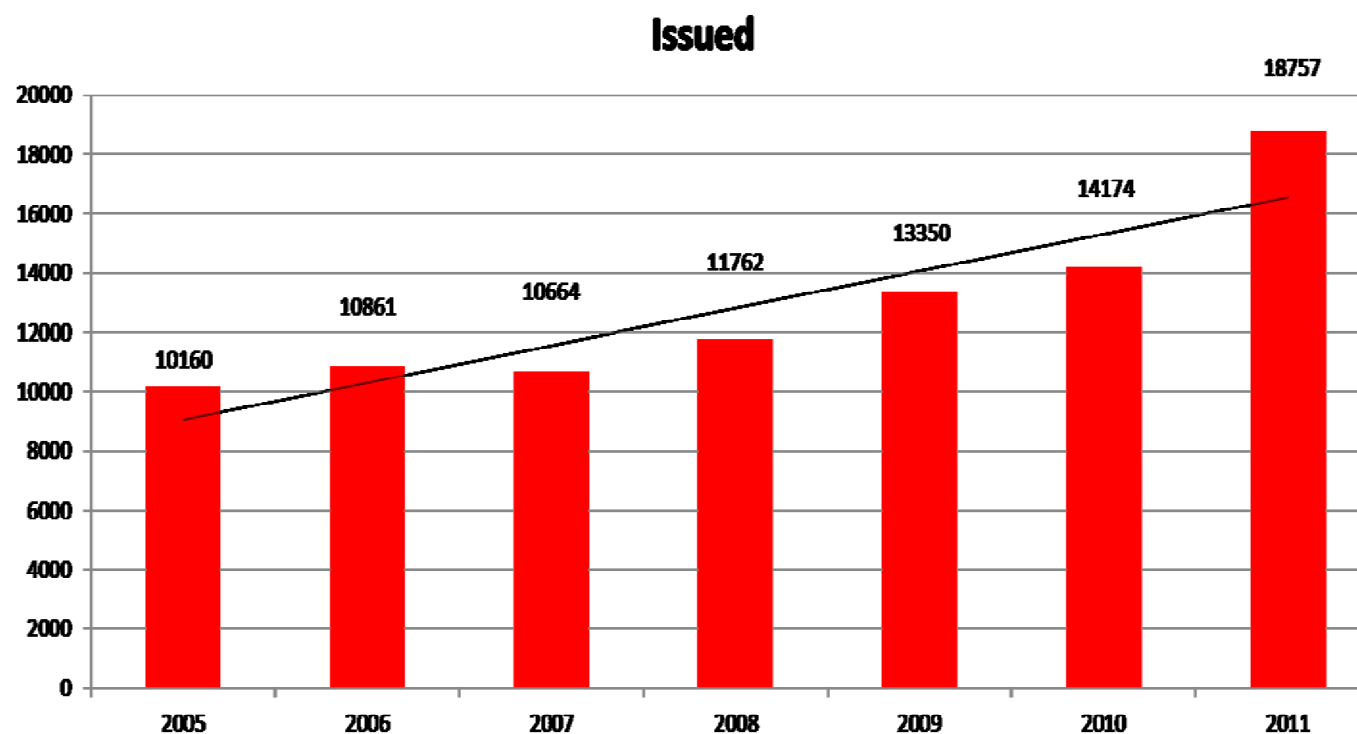
### Premium

- HLA matched £166.71
- CMV-ve £7.76
- PAS £29.43
- Irradiated £7.74
- Total £442.03

# Logistics of Platelet Provision for Refractory Patients



## Number of HLA Selected Platelets Issued



## Selected Platelets

- Receive request
- Assess request
- Tissue type and HLA antibody screen patient
- Panels searched to select donor/platelets
- Issue platelets
- Obtain increment data
- Weekly review meetings

## Match Grades

- Platelets are matched at the HLA-A and B Loci
- 'A' match = complete match (30%)
- 'B1'- 'B4' match = mismatched for between 1 and 4 HLA antigens (70%)

## Match grade 'A' examples

donor	A1, A2	;	B8, B44
Patient	A1, A2	;	B8, B44
donor*	A1, X	;	B8, X
Patient	A1, A2	;	B8, B44

\*homozygous donor

## Match grade 'B' match examples

### B1 match

donor:	A1, A2	;	B8, B27
patient:	A1, A68	;	B8, B27

### B2 match

donor:	A1, A66	;	B7, B27
patient:	A1, A68	;	B8, B27

## Not off the shelf Products

- HLA type of patient
  - A1,A2 B8,B44 – **597** in 10,000 donors compatible
  - A33,X B58,X - **0** in 10,000 donors are fully matched
- HLA Antibody profile
  - More HLA antibodies = fewer mismatched antigens can be selected
- Additional donation requirements – e.g. CMV negativity reduces donor field by approx 50%
- Repertoire of current stock

## Emergency On Call Service

- NHSBT provides an emergency out of hours service
- On Call consultant will evaluate clinical urgency with you and call staff in to select HLA matched platelets if indicated

Thank you