

# **Platelet Components Issues and Opportunities**

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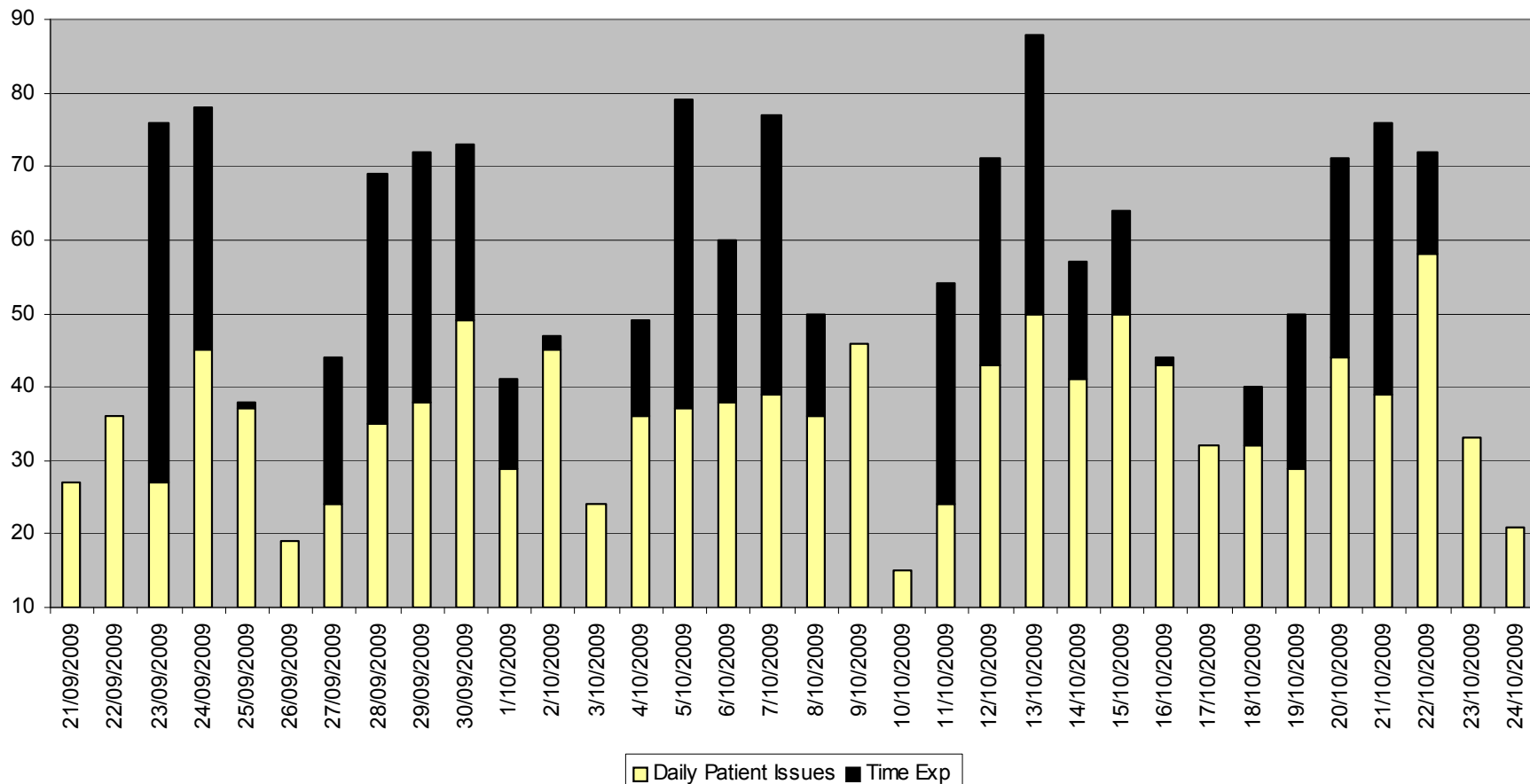
# Questions

- What constitutes an adult dose of platelets?
- What defines a 'clinically effective dose'?
- What is the optimal approach to reducing the risk of bacterial sepsis associated with platelet transfusion?
- What strategies should we use to reduce the risk of TRALI associated with platelet transfusion?
- What should we be doing to reduce the frequency of adverse reactions to platelet transfusion?

# Issues

- Significant day to day variation in demand
- Short shelf-life
  - Further reduced by impact of bacterial testing
- Together result in
  - High expiry rates
  - Intermittent supply problems

**Platelet Issues to Patients and Time Expired 21/09/2009 - 24/10/2009**



# Issues

- Multiple inventories
  - Recovered versus apheresis
  - Blood Group compatibilities
  - CMV antibody status
  - Irradiated components
  - HLA/HPA incompatibility

## What is an Adult Dose of Platelets?

Country/Organisation	Platelet Count 10 <sup>9</sup> /dose	Volume
<b>AABB</b>	≥ 300 <sup>a</sup>	Not stated
<b>Council of Europe</b>	≥ 200	> 40 ml per 60 x 10 <sup>9</sup> platelets
<b>UKBTS</b>	≥ 240	Within locally defined nominal volume range
<b>New Zealand</b>	≥ 240	200-350 ml
<b>Netherlands</b>	≥ 250	150-400 ml
<b>Australia</b>	≥ 200	> 40 ml per 60 x 10 <sup>9</sup> platelets

a. Apheresis platelets

# Platelet Efficacy Revisited

## Editorial Transfusion April 2010

A unique definition and commonly accepted level of 'adequate clinical efficacy' of platelet support are still lacking.

In the extreme scenario, we would theoretically need 192 (product variables) plus 4 (main recipient categories) or 768 randomised clinical trials to accurately test the efficacy of each product that could be used for platelet transfusion versus a 'reference' product in each recipient category.

## Barriers to Extending Platelet Shelf Life

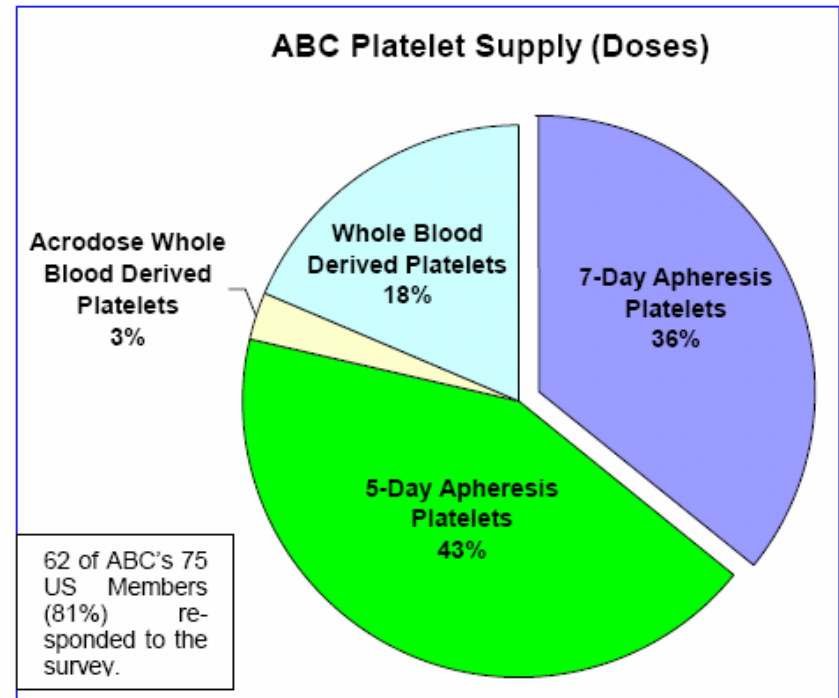
- **Bacterial safety**
  - Risk of significant bacterial growth increases with age of component.
  - Most serious adverse events associated with transfusion of older (i.e.) day 4-5 components.
  - Bacterial culture systems at Day 1 may detect only 50% of contaminated components.
- **Efficacy of platelets**
  - Data suggests that haemostatic capacity of platelets might reduce with age.

# The Passport Study

- Post approval surveillance study by Gambro and Fenwal to meet requirements of FDA for use of 7 day platelets commencing 2005.
- Involved combination of bacterial culture at 24 hours with apheresis platelets.
- Suspended January 2008 because of concerns that bacterial culture might not detect all contaminated platelet units.

# Passport Study

- Expiry rate reduced significantly.
- Regulatory expectation is that '7 day platelets will be no less safe than 5 day ones'.
- How is safety determined?
  - Clinical outcomes?
  - Positive cultures?



Survey undertaken by ABC  
in February 2008

## **Screening platelet concentrates for bacterial contamination: low numbers of bacteria and slow growth in contaminated units mandate an alternative approach to product safety**

W. G. Murphy, M. Foley, C. Doherty, G. Tierney, A. Kinsella, A. Salami, E. Cadden & P. Coakley

*Irish Blood Transfusion Service, National Blood Centre, James's Street, Dublin 8, Ireland*

- Identify low sensitivity of day 2 culture of platelets
- Propose that platelet components in stock at day 4 might be re-cultured to extend shelf life to 7 days

# Possible Solutions

- Pathogen Reduction Systems
  - Probably effective at assuring bacterial sterility
  - Concerns over impact on platelet function with extended storage
- Refrigerated platelets
  - Would reduce bacterial risk significantly
  - Good preservation of in-vitro function
  - Rapid clearance once transfused

# Platelet Additive Solution

- In vitro data suggests that platelet function might be preserved.
- Evidence suggests significant reduction in adverse reaction rate.
- Limited clinical data available on haemostatic performance.

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# Pathogen Reduction and Platelet Efficacy

- US Sprint trial suggested that clinical efficacy of Intercept platelets might be inferior and that patients would require additional platelet transfusions
- Very limited additional clinical data on platelet performance of Pathogen Reduction treated platelets has been published
- Differing regulatory decisions in Europe and US
  - Swiss Regulator recently approved Intercept treated platelet with a 7 day shelf life
  - US FDA not yet approved 5 day storage

# Clinical Evaluation of Pathogen Reduction treated platelets

- Study undertaken by Sanquin. Interim analysis reported AABB 2009
- Randomised control trial comparing clinical effectiveness of buffy coat pooled platelets suspended in plasma and PAS with and without Intercept treatment
- Designed as non-inferiority study with inferiority defined as  $\geq 20\%$  decrease in 1 hour increment
- Recruitment into PR PAS III arm suspended following interim analysis by Safety Review Board

# Clinical Evaluation of Pathogen Reduction treated platelets

	1 hour increment	24 hour increment	Bleeding episodes
Platelets suspended in plasma	17.5+/-5.4	13+/-7.9	14/64
Intercept treated platelets in PAS III	11.4+/-7.1 (34% reduction)	8+/-5.6 (34% reduction)	24/66

# Concluding Comments

- Supply of platelet components continue to present significant logistical challenges.
- Safety concerns being addressed in relation to both bacterial contamination and TRALI.
- An extension of the shelf life to 7 days would deliver significant advantages.
- Lack of good quality clinical data continues to present challenges to demonstration of clinical effectiveness and regulatory approval.