Platelet Transfusion

P. Rebulla, MD

Center of Transfusion Medicine, Cellular Therapy & Cryobiology

Department of Regenerative Medicine

Foundation Ca' Granda Ospedale Maggiore Policlinico, Milan (Italy)

Issues

1. Preparation of platelet (PLT) concentrates
2. PLT consumption
3. PLT count vs bleeding time
4. PLT count vs bleeding
5. Effectiveness during time in onc/hem
6. Transfusion dose
7. Apheresis vs whole blood PLT concentrates
8. Bacterial detection & pathogen inactivation
9. Reactions/adverse events
10. Transfusion trigger
11. Refractoriness to random donor PLT

Some guidelines on platelet transfusion

1987 – **NIH**; *Consensus Conference. Platelet transfusion therapy.*

1989 – **Sacher**; *Current practice and guidelines for the transfusion of cellular blood components in the newborn.*

1992 – **BCSH**; *Guidelines for platelet transfusion*

1993 – **RCPE**; *Consensus Conference. Leucocyte depletion of blood and blood components.*

1994 – **CAP**; *Practice parameters for the use of fresh-frozen plasma, cryoprecipitate and platelets.*

1995 – **Blanchette**; *Platelet transfusion therapy in newborn infants.*

1996 – **ASA**; *Practice guidelines for blood component therapy.*

1996 – **BCSH**; *Guidelines on gamma irradiation of blood components for the prevention of transfusion-associated graft-versus-host-disease.*

1998 – **BCSH**; *Guidelines on the clinical use of leucocyte-depleted blood components.*

2001 – **GMA**; *Guidelines for therapy with blood components and plasma derivatives.*

2001 – **ASCO**; *Platelet transfusion for patients with cancer*

2006 – **Council of Europe**; *Guide to the preparation, use and quality assurance of blood components. R 95 (15), 13th ed.*

Platelet transfusion recipients

- Hematology/oncology
  - Chemotherapy
  - Transplantation
- Surgery

The clinical question:
Why do we give platelets to hem/onc patients?

- Bleeding treatment (therapy)
- Bleeding prevention (prophylaxis)

100 years ago

THE RELATION OF BLOOD PLATELETS TO HEMORRHAGIC DISEASE

DESCRIPTION OF A METHOD FOR DETERMINING THE BLEEDING TIME AND COAGULATION TIME AND REPORT OF THREE CASES OF HEMORRHAGIC DISEASE RELIEVED BY TRANSFUSION *

From the Hunterian Laboratory of Experimental Pathology, Johns Hopkins University

W. W. DUKE, M.D.

KANSAS CITY, MO.

JOUR. A. M. A.
OCT. 1, 1910

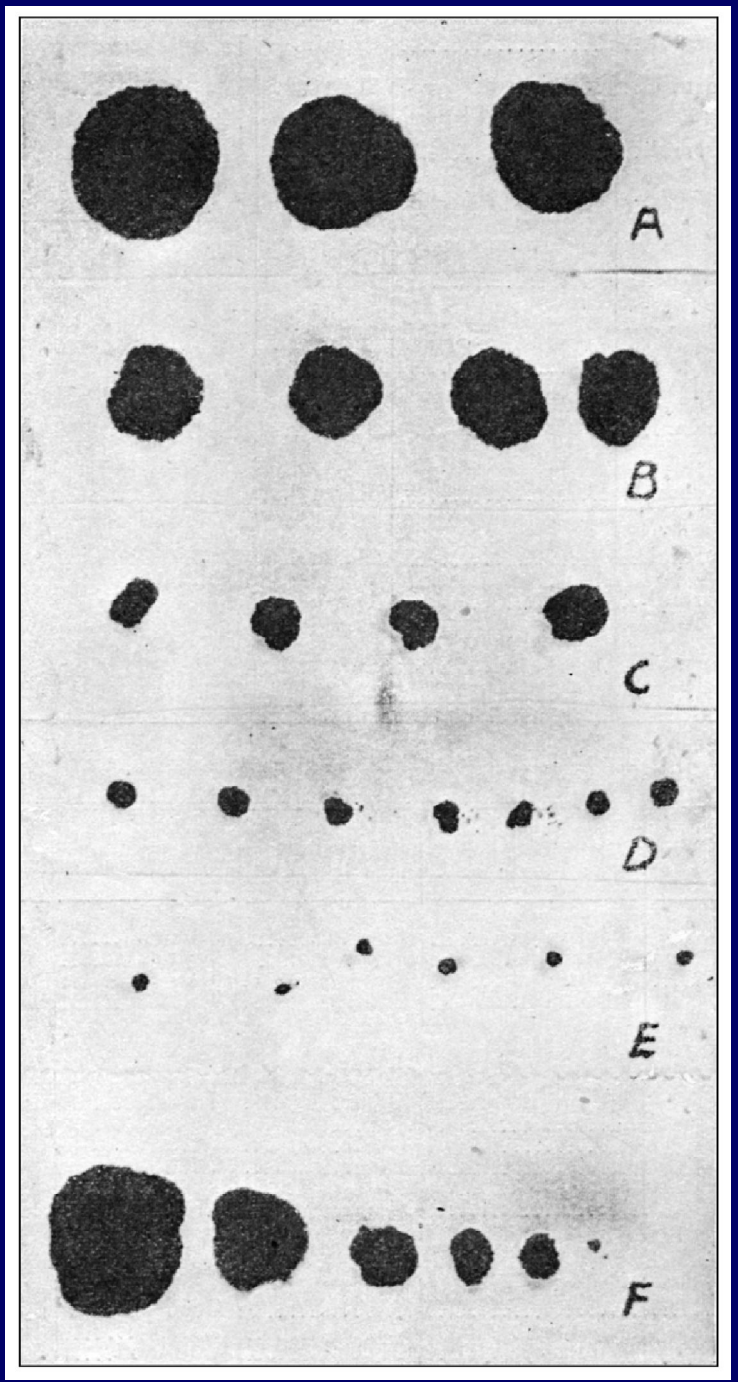


Fig 3. Great delay in bleeding time. From Case 1. Platelet count 3,000, coagulation time normal. The blots in Series A were taken immediately after the ear was pricked; Series B, 20 minutes; C, 40 minutes; D, 60 Minutes, and E, 80 minutes later. The bleeding time at this time was 90 minutes. Series F, showing a normal bleeding time, was taken after the transfusion. Platelet count was then 110,000.

WW Duke, JAMA 1910

TABLE 2.—DETAILED FINDINGS IN CASE 1

Date.	Platelet Counts.	Plates in Stained Blood Smears.	Bleeding Time. (Minutes.)	Coagulation Time.	Urine.	Stools.	Epistaxis.
May 8	6,000.	1-2 per smear.	47	5 minutes	Smoky	Tarry	Moderate.
May 9	None seen	None seen	90	5 minutes	Smoky	Tarry	Moderate.
May 10	3,000.			5 minutes	Smoky	Tarry	Moderate.
May 11		2 per smear	50 +	4½-5 minutes	Smoky	Tarry	Extreme.
(Transfusions).							
May 12	123,000.	1-3 in each field.	3	4½ minutes	Clear	Tarry	None.
May 13		1 in 3-4 fields.	3			Yellow	None.
May 14			30		Clear		None.
May 15		3 per smear.	40		Clear	Occult blood.	Slight.
May 16		1 per smear	50	5 minutes			Moderate.
May 17	1,500.	3 per smear	50		Clear	Fresh blood.	Moderate.
(Spontaneous increase in the number of platelets).							
May 18						Occult blood.	None.
May 19		1-6 per field	2				None.
May 23			2	5 minutes	Clear	No blood	None.
May 24	84,000.	3-8 per field.	4				None.

WW Duke, JAMA 1910

Transfusion.—On May 11, the patient lost over a pint of blood from the nose, and his condition became so critical that he was transfused at 2 a. m. by Dr. F. T. Murphy. An Armenian friend of about the same age was donor. That a were light yellow, but contained a small amo[illegible] of occult blood. No fresh purpuric spots appeared and the [illegible] present began to fade, disappearing completely in five days. Thirty-six hours after transfusion it could be seen from stained smears that the platelets were decreasing rapidly in number, and on the third day one could be found only after prolonged search. At this time the bleeding time was again delayed. The day following this the patient's nose began to bleed and fresh blood appeared in the stools. Since the onset of the disease the patient had had an irregular temperature, varying from 99 to 103 F. This came to normal, except for slight remissions, on May 20. Apparently the disease had run its course, for at this time plates reappeared in the blood (80,000), and hemorrhage from ear-pricks would last for only three minutes. There was no further epistaxis or melena. Convalescence was uneventful, and since then the patient has continued his vocation without symptoms.

WW Duke, JAMA 1910

Key factors for effective platelet support in oncology and hematology

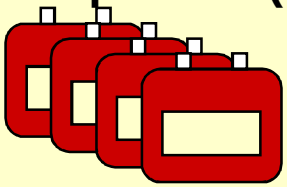
- Platelet concentrates of good quality from carefully selected blood donors
- Patient monitoring and laboratory evaluation (signs of hemorrhage and anti-HLA antibody detection)
- Prompt treatment of refractoriness

Platelet transfusion policy in “stable” hematology recipients

- Preferably match for ABO&Rh
- Transfuse 55-70 x 10^9 random-donor platelets per 10 kg recipient body weight when plt count falls below 10,000/uL
- Determine post-transfusion platelet count increment
  - At 1 hour (10-60 min)
  - At 24 hours
- Select HLA matched or compatible platelets for recipients refractory and HLA allo-immunized to random donors

Methods for the preparation of platelet concentrates

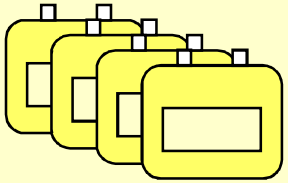
Platelet rich plasma (PRP) method



1

Four 450 mL blood units

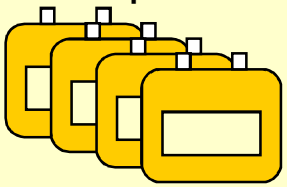
➡ **Soft** spin



2

Four 300 mL PRP

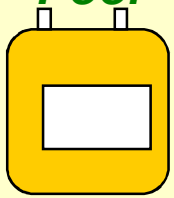
➡ **Hard** spin



3

Four 70 mL PRP-PC

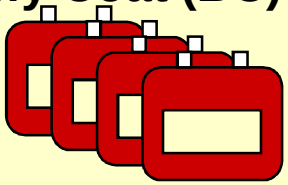
Pool



4

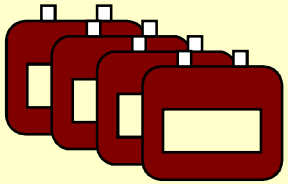
One 280 mL PRP-PC pool

Buffy Coat (BC) method



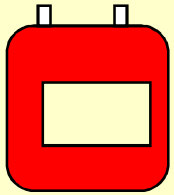
Four 450 mL blood units

➡ **Hard** spin



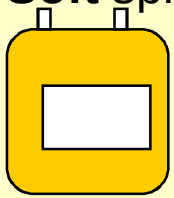
Four 50 mL BC

Pool & dilute



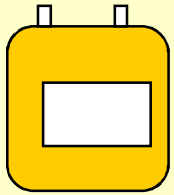
One 500 mL BC pool

➡ **Soft** spin



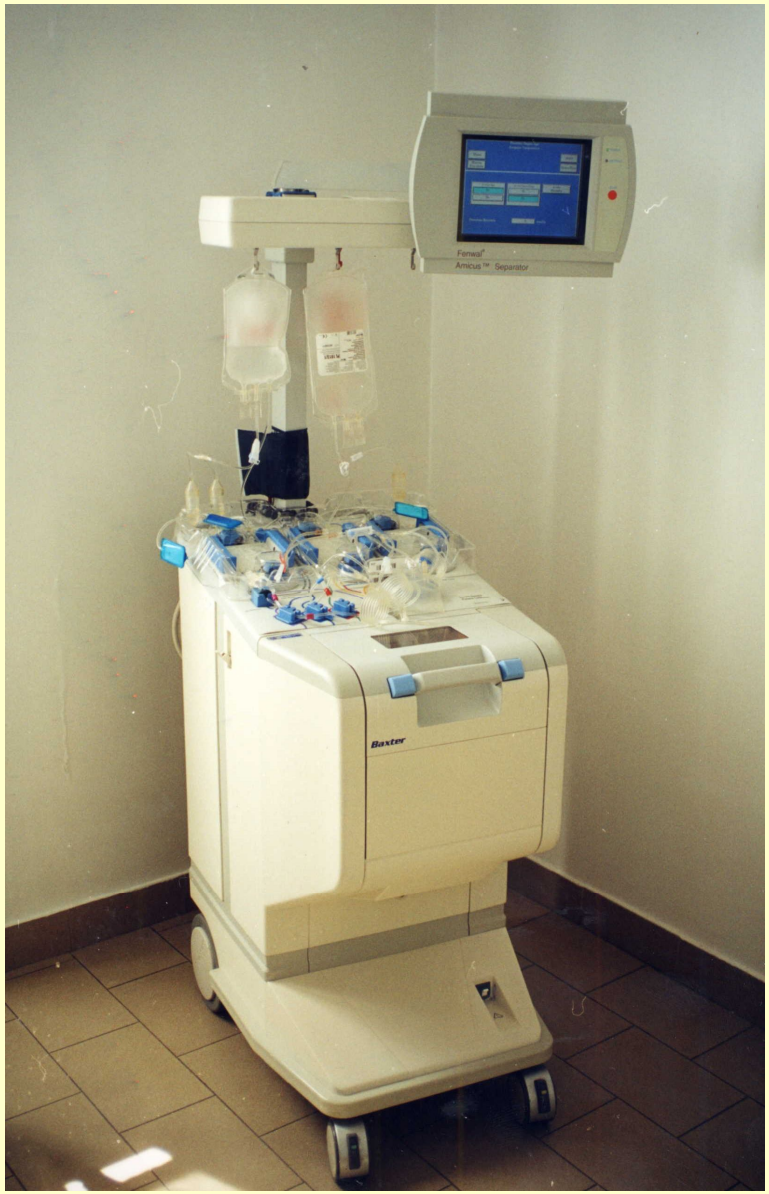
One 300 mL BC-PC pool

A P H E R E S I S

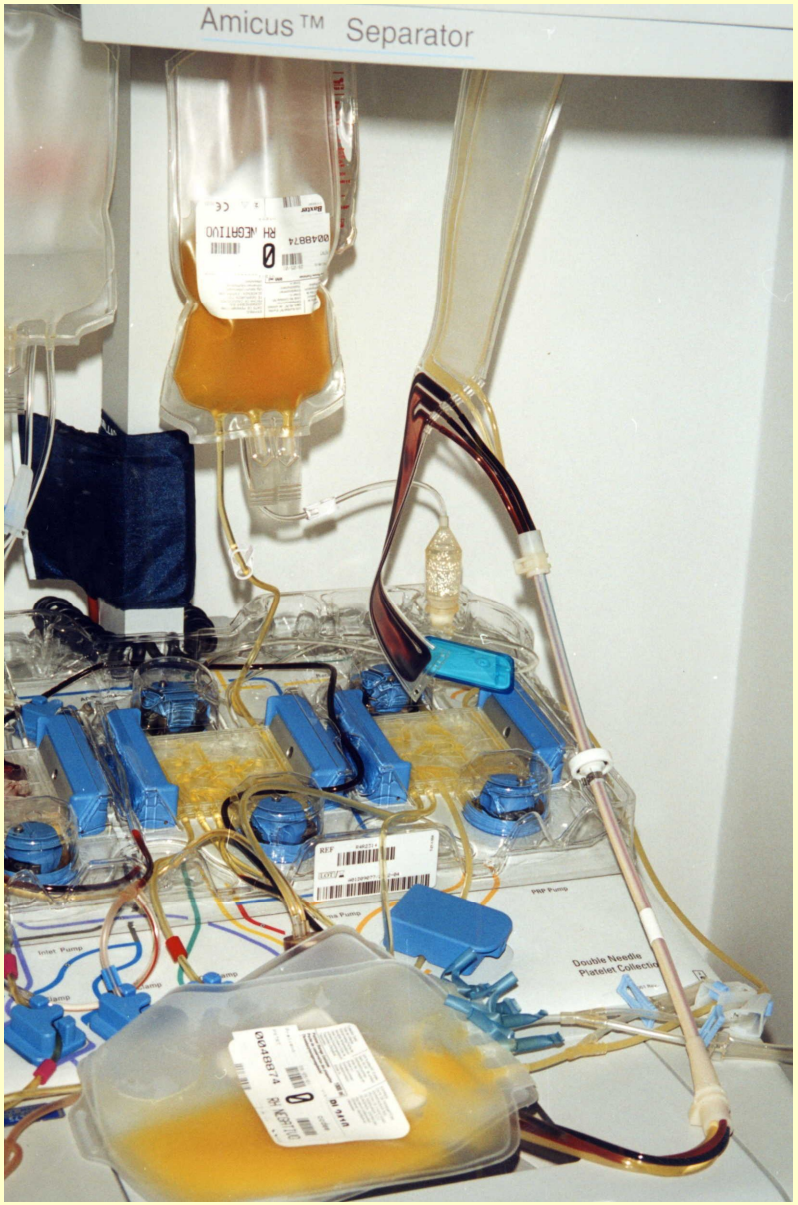


Single-donor Unit

Apheresis device

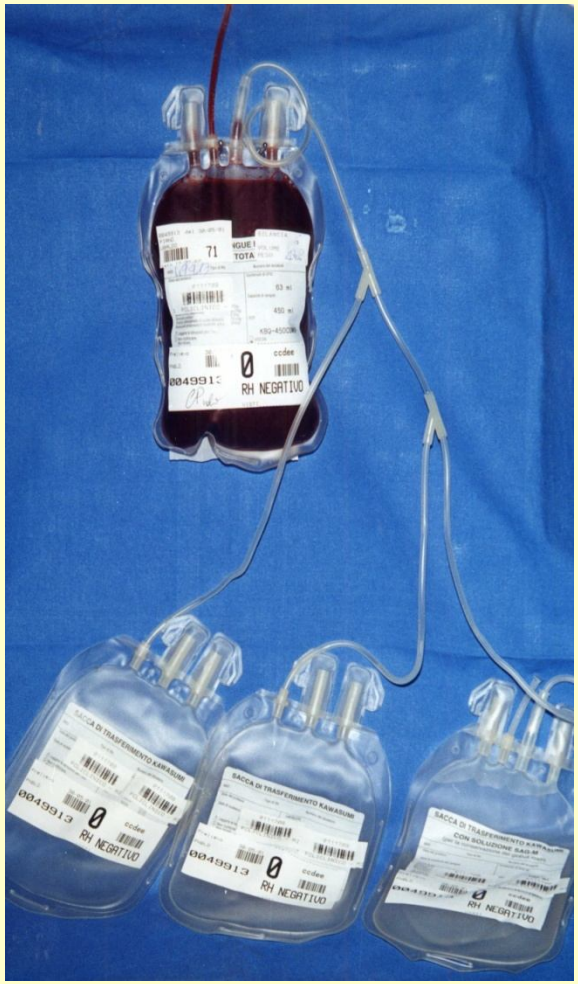


Platelet kit

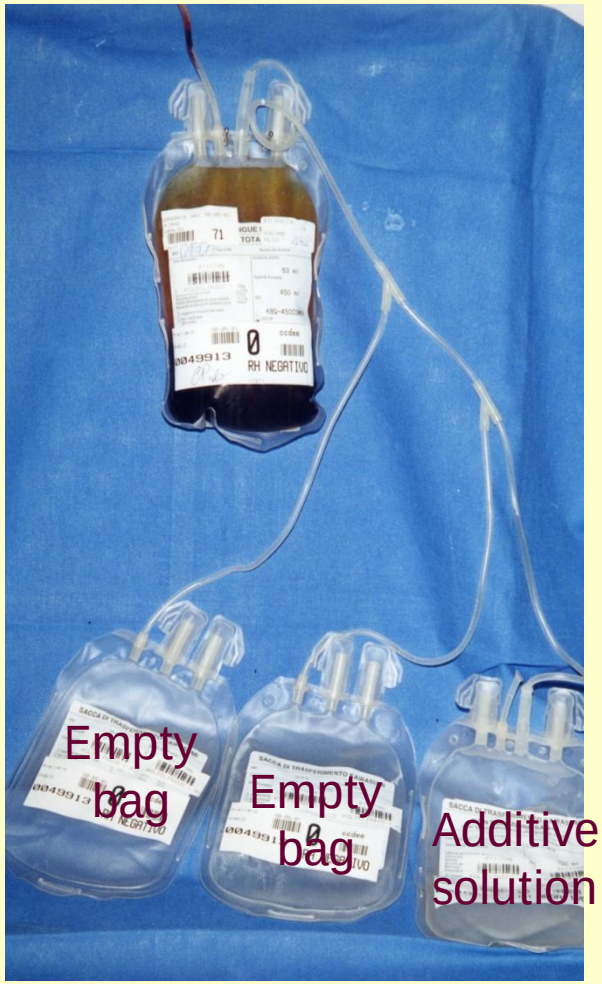


Platelet apheresis

1. Whole blood unit



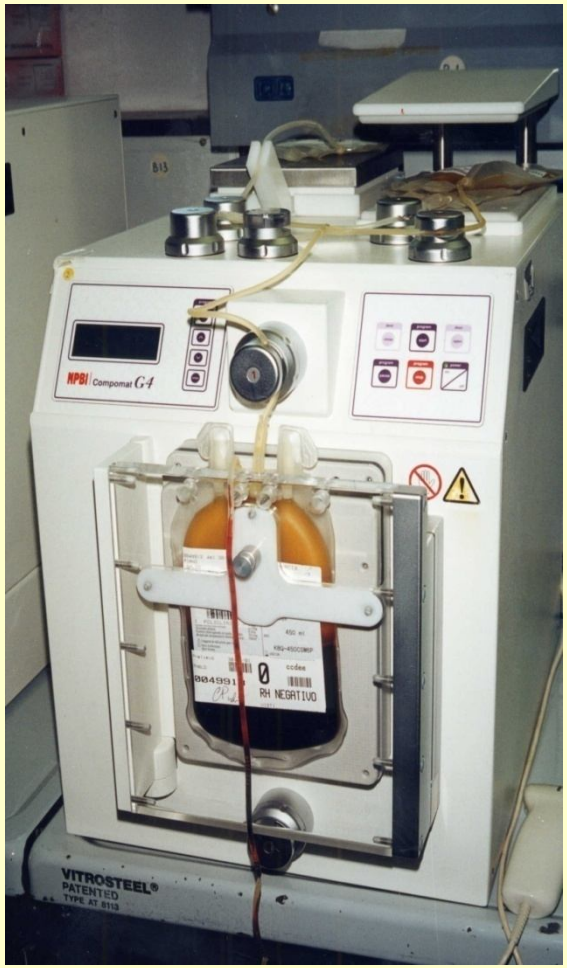
2. Centrifuged unit



3. Transfer of additive solution into red cells

Manual preparation of blood components

1. Plasma removal



2. Buffy coat removal

3. Transfer of additive solution into red cells

Automated preparation of blood components

Pools of platelets suspended in 30% plasma - 70% crystalloid solution

- Product
  - Unit standardization

Method	Source	Plt count (10^9/U)	Residual WBC after reduction (10^6/U)	pH at end of storage
PRP	AABB	>55	<0.83	>6.2
PRP	CoE	>60	<0.2	6.4-7.4
Buffy Coat	CoE	>60	<0.2	6.4-7.4
Apheresis	AABB	>300	<5	>6.2
Apheresis	CoE	>200	<1	6.4-7.4

Standards from American Association of Blood Banks and Council of Europe

Methods used to assess the effectiveness of platelet transfusions*

Method	Calculation	Criteria for an adequate response	
		10 to 60 minutes post-transfusion	18 to 24 hrs post-transfusion
Absolute Platelet Increment (API)	Post- minus pre transfusion platelet counts	NA	NA
Corrected Count Increment (CCI)	(Post- minus pre transfusion platelet counts) x (patient's body surface area)/ Number of platelets transfused	>4,500 to 5,000 platelets/m^2	>2,500 platelets/m^2
Percent Platelet Increment (PPI)	Observed/Expected Platelet count increment	>20%	>10%

* modified from Bishop et al (1992), Rebulla (1993), and Schiffer et al (2001).

Stroncek & Rebulla, 2006

Computation

$$PPI = \frac{\text{Post-Pre}}{\text{Dose/Vol}}$$

$$= \frac{\text{Post-Pre x Vol}}{\text{Dose}}$$

$$CCI = \frac{\text{Post-Pre x BSA}}{\text{Dose}}$$

PPI and CCI are conceptually similar: both take into account (1) post-transfusion increment, (2) platelet dose and (3) an index of recipient's size (blood volume or BSA)

- Product
  - Apheresis vs PRP vs BC methods

- Biochemical and clinical equivalence
- Fewer donor exposures with apheresis
- Local convenience
- Availability
- Cost analysis

- Product
  - Crystalloid storage solutions

1. Plasma-Lyte
2. Composol
3. Platelet Additive Solution (PAS)
   - -I,-II, -III, PAS-III modified
4. Intersol, SSP, SSP+

- Important component: 27-33 mmol L^{-1} sodium acetate (not in PAS-I); *plt use about 2 mM acetate/day*
- Final storage media: about 70% crystalloid solution / 30% plasma
- 'High-titer' ABO isoagglutinins which can be present in different donors are:
  1. first, diluted in the pool and then,
  2. diluted 1:3 with the crystalloid solution

Platelet swirling for quality assessment

Simple test: can be performed at time of use in the clinical ward


LAMERA SCAVI
Swirling

Transfusion Medicine, 2003, 13, 173–187

REVIEW ARTICLE

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Table 4. Platelet additive solution composition (mmol L^{-1})

	PASI	PASII	PASIII	PASIII modified	Plasma-Lyte	GAC	Composol
Sodium chloride	70	115·5	77	70	90	90	90
Tri-sodium citrate	30	10	11	11	–	11	11
Sodium acetate	–	30	33	33	27	27	27
Sodium phosphate	5	–	29	25	–		–
Sodium gluconate	–	–	–	–	23	23	23
D-Mannitol	30	–	–	–	–		–
Potassium chloride	10	–	–	5	5	5	5
Magnesium chloride/sulphate	–	–	–	1·5	3	3	1·5

Table 2. Relationship of recovery and survival of platelets after transfusion to platelet concentrate age in healthy volunteers

Platelet type	Storage medium		*n*	Percentage recovery			Survival (days)			Reference
				Day 0/1	Day 5	Day 7	Day 0/1	Day 5	Day 7	
PRP	Plasma	PL146	5	60*	38*		7·6*	5·4*		Murphy *et al.* (1982)
		PL732	7–11	53*	50*		7·0*	6·2*		
PRP	Plasma		8	87 ± 21	59 ± 17	46 ± 8†		6·4 ± 3·0	5·4 ± 1·0†	Archer *et al.* (1982)
PRP	Plasma		16			40 ± 7			6·3 ± 1·4	Rzad *et al.* (1982)
PRP	Plasma		6			49 ± 12			5·8 ± 0·2	Lovric *et al.* (1985)
PRP	85% Plasma-Lyte		6		63 (46–77)			7·7 ± 0·8		Rock *et al.* (1991)
PRP	Plasma		10	Two centres	46 ± 8‡	45 ± 8‡		7·2 ± 1	6·8 ± 1·0‡	Simon *et al.* (1987)§
			9		43 ± 9‡	45 ± 10‡		6·8 ± 1	8·0 ± 0·8‡	
PRP	Plasma		10		43 ± 10	56 ± 8		7·3 ± 1·2	6·2 ± 1·1	Heaton *et al.* (1990)
	80–90% PSM				40 ± 9	59 ± 6		6·4 ± 1·2	5·9 ± 0·7	
PRP	Plasma		5–10	55 ± 10	41 ± 11	36 ± 11	7·9 ± 1·0	6·1 ± 1·7	4·5 ± 1·6	Holme *et al.* (1990)¶
	80–90% PSM				45 ± 12	51 ± 8		6·7 ± 1·3	6·0 ± 0·7	
PRP	Plasma		9	60 ± 7	49 ± 10		8·8 ± 0·9	6·8 ± 1·2		Keegan *et al.* (1992)
PRP	Plasma		5	64 ± 12	49 ± 10		7·7 ± 1·3	6·5 ± 1·2		Holme *et al.* (1993)
Haemonetics MCS	Plasma		6–10		79 ± 20	53 ± 21		6·0 ± 1·1	5·0 ± 1·6	Slichter *et al.* (2001)
	Plasma-Lyte				79 ± 22	64 ± 14		5·9 ± 1·4	5·9 ± 0·6	
CS3000	Plasma		9	58 ± 12	58 ± 12		5·5 ± 1·5	5·6 ± 1·1		Shanwell *et al.* (1989)
CS3000	Plasma		4		78 ± 10			6·1 ± 0·9		Rock *et al.* (1989a)
CS3000	Plasma		18		53 ± 9			6·5 ± 0·8		Holme *et al.* (1994)
	PSM		18		50 ± 8			6·8 ± 0·9		
V50	Plasma		5		66 ± 7			7·3 ± 1·3		Rock *et al.* (1989b)
Spectra/Trima	Plasma		24		63 ± 11	53·9 ± 14**		6·7 ± 1·6	5·6 ± 1·9**	Dumont *et al.* (2002)
Buffy coat	Plasma		9	64 ± 6	53 ± 8		8·7 ± 1·3	6·8 ± 0·8		Keegan *et al.* (1992)
Buffy coat	PASI		9	55 ± 9	52 ± 10		7·8 ± 2·0	5·8 ± 0·5		Eriksson *et al.* (1993)
Buffy coat	Plasma		11		51 ± 16			6·5 ± 1·5		Turner *et al.* (1996)
	70% PASII		11		30 ± 14			5·1 ± 1·3		
	70% Plasma-Lyte		11		53 ± 16			5·9 ± 1·3		

PRP, platelet-rich plasma; PSM, platelet storage media.
*Data estimated from figure
†Significance of day 7 versus day 5 not stated.
‡Not significant day 7 versus day 5.
§Pack for day 7 storage different to day 5.
¶Data to day 14

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Table 3. Influence of platelet concentrate storage on platelet count increment following transfusion to thrombocytopenic patients

Platelet type	Storage medium	Patients (*n*)	Transfusions (*n*)	1–4 h CCI			12–24 h CCI			Reference
				Day 0/1	Days 2–5	Days 6–7	Day 0/1	Days 2–5	Days 6–7	
PRP	Plasma			16·6 ± 7·4 (*n* = 146)	13·3 ± 6 (*n* = 34)		12·4 ± 6·7 (*n* = 84)	8·9 ± 4 (*n* = 20)		Schiffer *et al.* (1986)
PRP	Plasma	16	32	20·1 ± 8·4	12·2 ± 8·1	10·0 ± 7·2*†	10·8 ± 4·4	7·5 ± 5·6	7·0 ± 5·5*†	Hogge *et al.* (1986)
Apheresis V50/CS-3000	Plasma	27	419	11·0 ± 5·2	D3 10·2 ± 4·8 D5 10·2 ± 4·5		6·0**	D3 5·0** D5 5·0**		Leach & AuBuchon (1993)
Apheresis Spectra	Plasma		21			14·4 ± 8·8				AuBuchon *et al.* (2002)
BC + apheresis	Plasma	26		12·3 ± 0·7 (*n* = 52)	5·7 ± 1·4 (*n* = 7)		8·6 ± 0·7 (*n* = 52)	2·9 ± 1·0 (*n* = 7)		Duguid *et al.* (1991)
BC	Plasma		31	12·2 ± 0·45			11·2 ± 0·5	D5† versus D1		Pietersz *et al.* (1988)
BC	Plasma	18	6	17·4 ± 4·8	15·5 ± 9·2		11·2 ± 9·2	7·1 ± 6·0		Eriksson *et al.* (1993)
	70% PASI‡		12	20·9 ± 10·8	15·0 ± 7·0		13·5 ± 8·3	8·0 ± 6·4		
BC	Plasma	36	41	29 (10–49)	24 (0–55)		8 (−4–23)	6 (−9–39)		Eriksson *et al.* (1996)
	70% PASI‡		57	27 (−8–79)	23 (5–41)		11 (−10–31)	6 (−7–24)		
BC	70% PASII or	9	9		22 (15–29)			11 (4–18)		Van Rhenen *et al.* (1995)
	Plasma-Lyte	9	9		24 (17–31)			14 (7–21)		
BC	Plasma	12	192	21·6 ± 10·3	19·9 ± 6·7		13·1 ± 8·8		10·0 ± 6·9	de Wildt-Eggen *et al.* (2000)
	70% PASI	9	132	17·9 ± 5·3	16·5 ± 6·7		9·9 ± 7·4		9·1 ± 6·7	
BC	65% PASII	28	28		12·6 (35–22)			8·9 (−1·7–19·7)		Van der Meer *et al.* (2001b)
BC	Plasma				13·6 ± 8·1§ (*n* = 22)	10·9 ± 5·5§¶ (*n* = 14)				Dijkstra *et al.* (2002)

CCI (corrected count increment) = (post-transfusion platelet count minus pre-transfusion platelet count) × body surface area(m^2)/dose platelets transfused (10^{11})

*Storage at day 7 in different pack to day 3.

†Not significant – day 7 versus day 3.

‡PAS units buffy coat whereas plasma units collected by apheresis.

§CCI at 15 min 4 h.

¶Significance of day 7 versus day 5 not stated.

**Value estimated from figure.

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Paired in vitro and in vivo comparison of apheresis platelet concentrates stored in platelet additive solution for 1 versus 7 days

Agneta Shanwell, Beatrice Diedrich, Cecilia Falker, Berit Jansson, Per Sandgren, Lars Sundkvist, Leif Svensson, Mervi Vesterinen, and Hans Gulliksson

Transfusion, June 2006

TABLE 1. In vitro analysis of apheresis PCs after 1 and 7 days of storage*

Variable	Day 1	Day 7	p Value
MPV (fL)	7.0 ± 0.8	7.3 ± 0.8	NS
pH	7.09 ± 0.11	7.11 ± 0.08	NS
Lactate (mmol/L)	1.3 ± 0.5	6.6 ± 1.2	<0.0001
pCO_2 (kPa at 37°C)	3.41 ± 0.52	2.91 ± 0.69	NS
pO_2 (kPa at 37°C)	18.9 ± 2.2	19.3 ± 3.4	NS
Bicarbonate (mmol/L)	7.5 ± 1.2	6.7 ± 1.6	NS
Glucose (mmol/L)	6.4 ± 0.7	3.5 ± 1.1	<0.0001
LDH (%)	4.7 ± 1.4	6.2 ± 1.9	<0.01
ATP (µmol/10^{11} PLTs)	5.64 ± 0.56	4.41 ± 0.46	<0.0001
HSR (%)	57.1 ± 7.2	64.1 ± 10.9	NS
RANTES (pg/10^8 PLTs)	110.7 ± 76.6	277.6 ± 50.8	<0.005
PF4 (IU/10^8 PLTs)	19.9 ± 9.6	59.8 ± 7.5	<0.0001

* Data are expressed as means ± SD (n = 10).
NS = nonsignificant.

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Transfusion, June 2006

TABLE 2. PLT recovery and survival time of autologous PLTs after storage for 1 and 7 days

	Recovery	Survival
Day 1	69 ± 12%	8.2 ± 1.7 days
Day 7	53 ± 13%	5.1 ± 1.7 days
p Value	<0.05	<0.005
Day 7 compared with Day 1	80 ± 32%	65 ± 26%

Kerkhoffs et al. A Multicenter Randomized Study of the Efficacy of Transfusions with Platelets stored in Platelet Additive Solution II versus Plasma. Blood 2006

Table 2 Platelet product parameters, dosage and transfusion response

		Plasma PC (n = 311)	PAS II PC (n = 373)	P-value
Numbers of platelets/product	10^9 ± sd	412 ± 93	391 ± 119	p = 0.01
Storage time	days ± sd	3.5 ± 1.3	3.5 ± 1.1	n.s.
pH	± sd	7.12 ± 0.04	7.08 ± 0.04	p < 0.0001
Product volume	ml ± sd	356 ± 19	316 ± 11	p < 0.0001
Precount	10^9/l ± sd	13.3 ± 8.7	13.7 ± 10.5	n.s.
Platelet dose/kg body weight[1]	10^9/l ± sd	5.5 ± 1.7	5.3 ± 2.0	n.s.
Transfusion response[2]				
1-hour		n = 274	n = 337	
CI		32.2 ± 17.1	24.6 ± 14.8	p = 0.001
CCI		13.9 ± 7.0	11.2 ± 6.4	p = 0.004
24-hour		n = 282	N = 334	
CI		20.6 ± 16.0	16.3 ± 14.1	p = 0.028
CCI		8.4 ± 6.9	6.8 ± 6.4	p = 0.09

n = number of transfusions. [1] Per transfusion. [2] General linear mixed model acounting for within-patient-correlation of observations (repeated measurements).

Kerkhoffs et al. A Multicenter Randomized Study of the Efficacy of Transfusions with Platelets stored in Platelet Additive Solution II versus Plasma. Blood 2006

Table 3 Platelet transfusions, red cell transfusions and transfusion interval

	Plasma PC (n = 84)	PAS II PC (n = 84)	p-value
Number of RBC transfusions	452	475	
Mean RBC /patient (± sd)	4.8 ± 4.1	5.1 ± 3.8	0.62
Number of PC transfusions	354	411	
PC transfusion interval (days ± sd)	2.0 ± 1.0	2.1 ± 1.0	0.52
Mean PC/patient (± sd)	4.2 ± 2.7	4.9 ± 2.8	0.10
Cumulative platelet dose/kg (x 10^{11}/kg ± sd)	0.22 ± 0.15	0.23 ± 0.16	0.68

Message 1

- In total (hem/onc + surg) about 45,000 platelet concentrates (or 7,700 adult platelet doses) are needed p.m.p./year
  - ➔ $45{,}000/10^6$ population

THE 2007 NATIONAL BLOOD COLLECTION AND UTILIZATION SURVEY REPORT

Table 4-2. Estimated 2006 Collection and Transfusion by US Blood Centers and Hospitals of Non-Red-Blood-Cell Components (expressed in thousands of units)

Activity	Blood Centers	Hospitals		2006 Total		2004 Total	% Change 2004-2006
		Total	±95% CI		±95% CI		
Collection/Production							
Apheresis Platelets†	10,297	642	343	10,939 (1,823)	2,467	9,161	19.4
WB-Derived Platelet Concentrates	2,215	181	108	2,396*	778	4,202	–43.0
Total Platelets	12,512	823	368	13,335*	2,795	13,362	–0.2
Plasma‡	5,286	398	139	5,684	1,129	4,651	22.2
Cryoprecipitate	1,173	24	18	1,197	393	1,164	2.8
Transfusions							
Apheresis Platelets†	411	8,681	837	9,092 (1,515)	916	8,338	9.0
WB-Derived Platelet Concentrates	223	1,073	291	1,296	495	1,537	–15.7
Total Platelets	634	9,754	934	10,388*	1,211	9,875	5.2
Plasma‡	215	3,795	271	4,010	405	4,089	–1.9
Cryoprecipitate	56	938	129	993	157	890	11.6
Outdated Non-RBC Components	424	451	80	875*	120	1,079	–18.9

*Significantly different from 2004 data.
†platelet concentrate equivalent units (apheresis packs); includes splits.
‡for transfusion, includes apheresis plasma.

Report Authors:

AABB—Barbee I. Whitaker, PhD
Westat—James Green, MA; Melissa R. King, MSPH; Linda L. Leibeg, MS; Sunitha M. Mathew, MS; Karen S. Schlumpf, MPH; George B. Schreiber, ScD

Message 2

- Approximately 7,000 platelets per microliter per day are consumed to maintain the integrity of microvascular endothelium

Blood, Vol 66, No 5 (November), 1985: pp 1105–1109

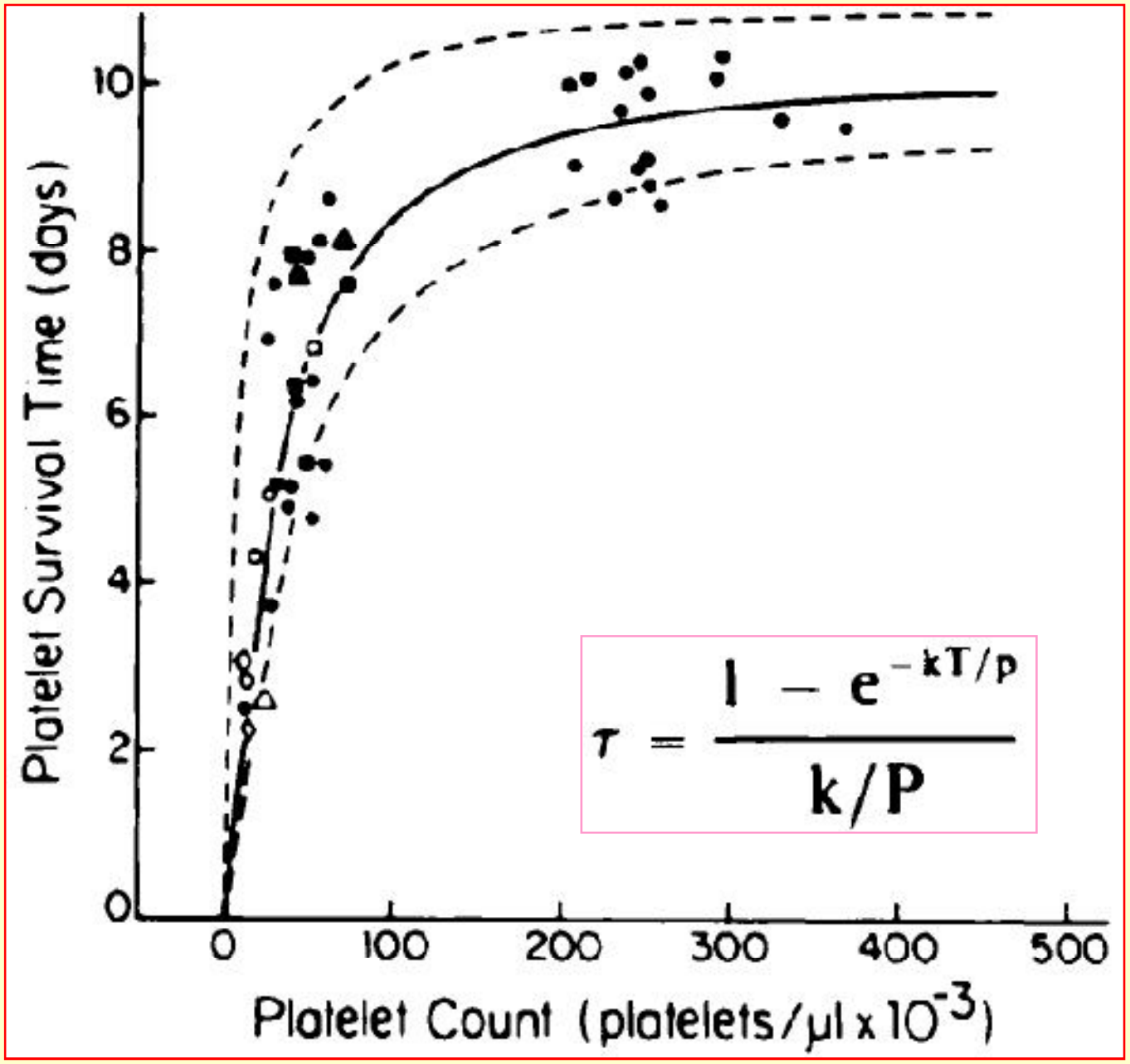
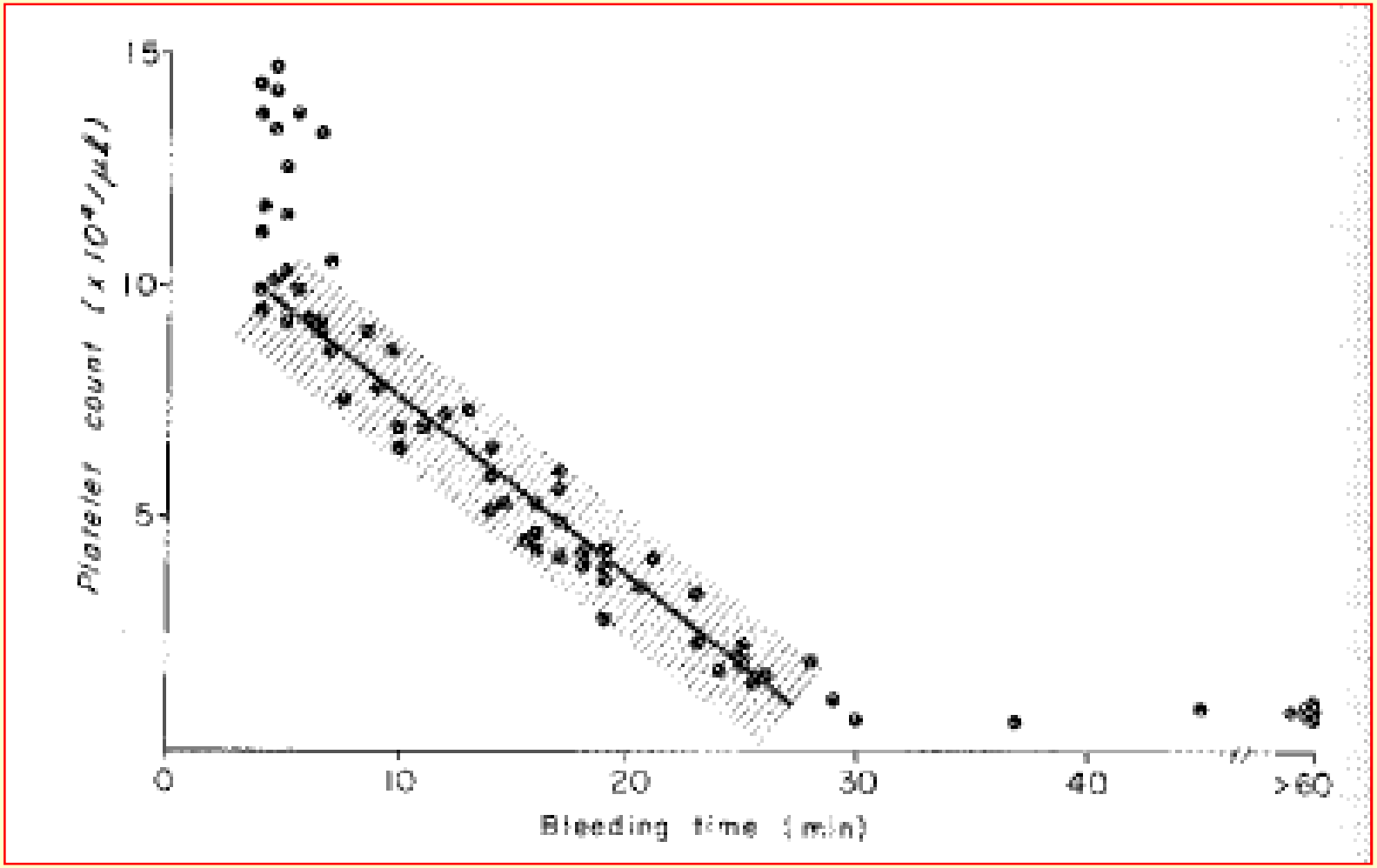


Fig 2. Relationship between platelet count and the survival of autologous (closed symbols) and donor (open symbols) ^{51}Cr-platelets in normal and thrombocytopenic subjects with no evidence of hypersplenism (circles). Complications included splenectomy (squares), splenomegaly (triangles), and prior transfusions (diamonds). The data are well correlated according to Equation 2 (solid line) under the assumption of a finite platelet life span (T) of 10½ days and a fixed rate of platelet destruction (k) averaging 4,700 platelets per microliter per day. The data are bounded by the region (between dashed lines) constituting all solutions to Equation 2 with τ in the range of from 10 to 11 days, and k in the range from 1,400 to 6,800 platelets per microliter per day.

Message 3

- Bleeding time increases as platelet count falls below 100,000 per microliter



Harker and Slichter. NEJM 1972; 287:155-159.

Message 4

- Clinically relevant bleeding occurs with no readily identifiable threshold of platelet count

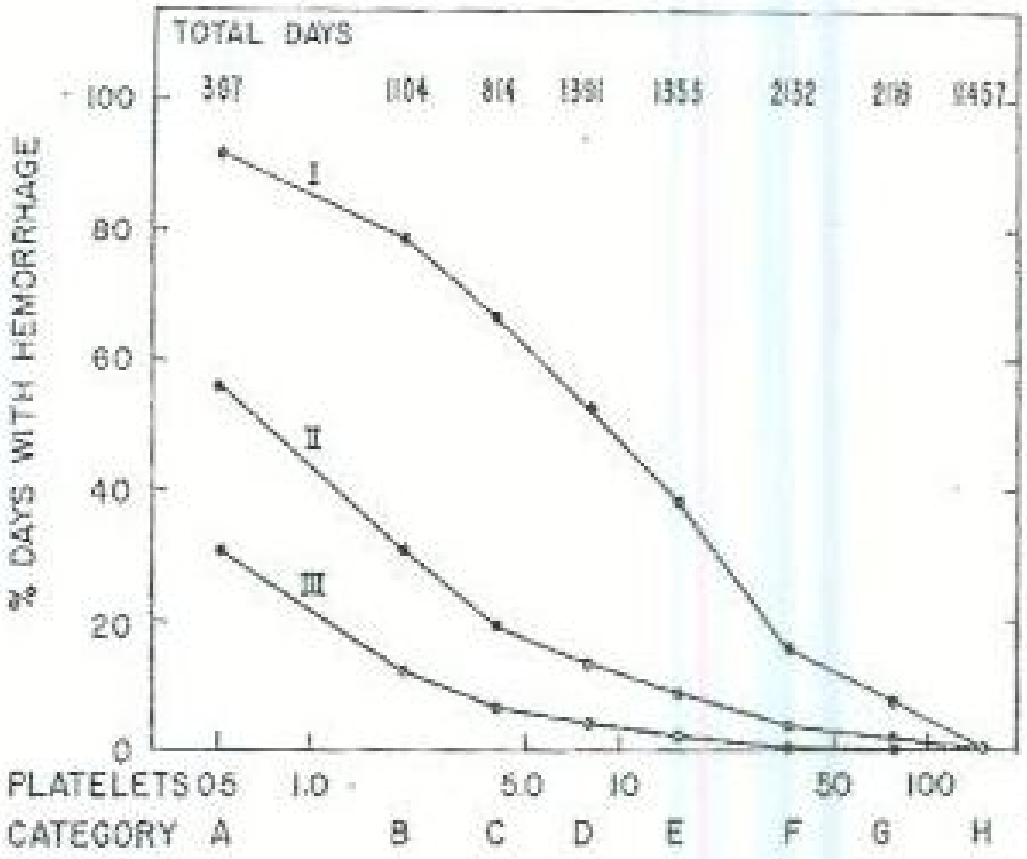


FIGURE 1. *Relation between Hemorrhage and Platelet Count.*

The percentage of days with hemorrhage for the 92 patients combined is shown for each of the 8 platelet-count categories. (Figures across the top are the total number of patient days in each of the categories.) Curve I shows data for all hemorrhagic manifestations. In Curve II skin hemorrhage and epistaxis are excluded. Curve III refers only to grossly visible hemorrhage.

GAYDOS ET AL, NEJM MAY 3, 1962

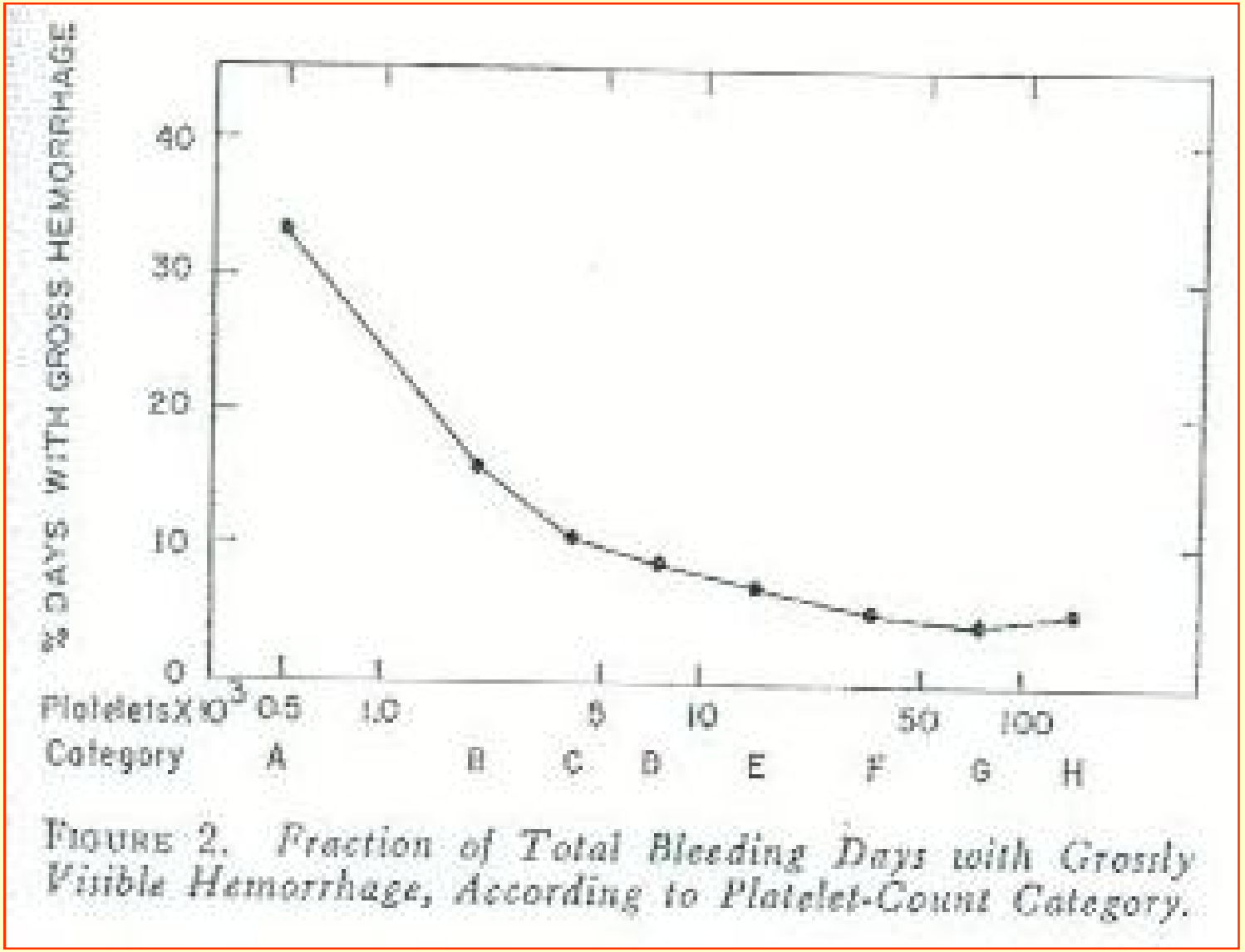


FIGURE 2. *Fraction of Total Bleeding Days with Grossly Visible Hemorrhage, According to Platelet-Count Category.*

GAYDOS ET AL, NEJM MAY 3, 1962

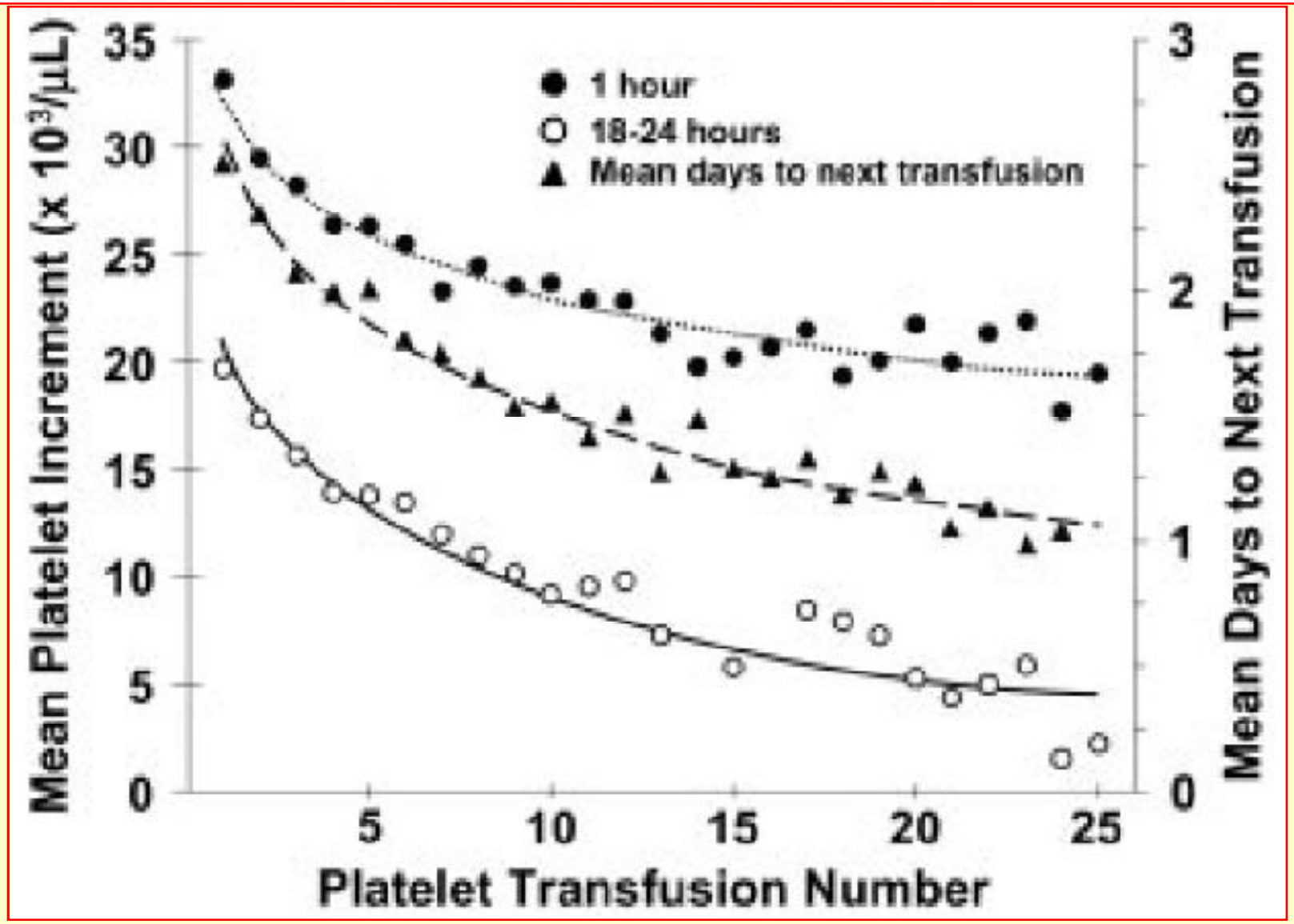
Message 5

- The efficacy of platelet support in leukemia decreases during time

Factors affecting posttransfusion platelet increments, platelet refractoriness, and platelet transfusion intervals in thrombocytopenic patients

BLOOD, 15 MAY 2005 • VOLUME 105, NUMBER 10 4106-4114

Sherrill J. Slichter, Kathryn Davis, Helen Enright, Hayden Braine, Terry Gernsheimer, Kuo-Jang Kao, Thomas Kickler, Edward Lee, Janice McFarland, Jeffrey McCullough, Glenn Rodey, Charles A. Schiffer, and Robert Woodson



Message 6

- The risk of grade ≥2 bleeding is not affected by platelet transfusion doses ranging from 110 to 440 billion platelets/transfusion

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dose of Prophylactic Platelet Transfusions and Prevention of Hemorrhage

Sherrill J. Slichter, M.D., Richard M. Kaufman, M.D., Susan F. Assmann, Ph.D., Jeffrey McCullough, M.D., Darrell J. Triulzi, M.D., Ronald G. Strauss, M.D., Terry B. Gernsheimer, M.D., Paul M. Ness, M.D., Mark E. Brecher, M.D., Cassandra D. Josephson, M.D., Barbara A. Konkle, M.D., Robert D. Woodson, M.D., Thomas L. Ortel, M.D., Ph.D., Christopher D. Hillyer, M.D., Donna L. Skerrett, M.D., Keith R. McCrae, M.D., Steven R. Sloan, M.D., Ph.D., Lynne Uhl, M.D., James N. George, M.D., Victor M. Aquino, M.D., Catherine S. Manno, M.D., Janice G. McFarland, M.D., John R. Hess, M.D., Cindy Leissinger, M.D., and Suzanne Granger, M.S.

METHODS

We randomly assigned hospitalized patients undergoing hematopoietic stem-cell transplantation or chemotherapy for hematologic cancers or solid tumors to receive prophylactic platelet transfusions at a low dose, a medium dose, or a high dose (1.1×10^{11}, 2.2×10^{11}, or 4.4×10^{11} platelets per square meter of body-surface area, respectively), when morning platelet counts were 10,000 per cubic millimeter or lower. Clinical signs of bleeding were assessed daily. The primary end point was bleeding of grade 2 or higher (as defined on the basis of World Health Organization criteria).

Slichter et al, NEJM 2010

Table 3. Primary and Key Secondary End Points, According to Treatment Group.

Characteristic	Platelet Dose*					
	Low Dose (N=417)	P Value, Low vs. Medium Dose	Medium Dose (N=423)	P Value, Medium vs. High Dose	High Dose (N=432)	P Value, High vs. Low Dose
Primary end point						
≥1 Episode of bleeding of grade 2 or higher — % of patients	71	0.60	69	0.71	70	0.94
Secondary end points						
Highest grade of bleeding during study — % of patients		0.30		0.65		0.54
No bleeding or grade 1	30		32		30	
Grade 2	58		59		60	
Grade 3	9		7		8	
Grade 4	3		2		2	
Death from hemorrhage — no. of patients	0		0	1.00	1	1.00
No. of days with bleeding of grade 2 or higher		0.90		0.91		0.99
Median	1		1		1	
Interquartile range	0–4		0–4		0–4	
Days from randomization to onset of bleeding of grade 2 or higher		0.85		0.66		0.55
Median	7		7		8	
Interquartile range	3–18		3–19		3–19	

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dose of Prophylactic Platelet Transfusions and Prevention of Hemorrhage

RESULTS

In the 1272 patients who received at least one platelet transfusion, the primary end point was observed in 71%, 69%, and 70% of the patients in the low-dose group, the medium-dose group, and the high-dose group, respectively (differences were not significant). The incidences of higher grades of bleeding, and other adverse events, were similar among the three groups. The median number of platelets transfused was significantly lower in the low-dose group (9.25×10^{11}) than in the medium-dose group (11.25×10^{11}) or the high-dose group (19.63×10^{11}) ($P=0.002$ for low vs. medium, $P<0.001$ for high vs. low and high vs. medium), but the median number of platelet transfusions given was significantly higher in the low-dose group (five, vs. three in the medium-dose and three in the high-dose group; $P<0.001$ for low vs. medium and low vs. high). Bleeding occurred on 25% of the study days on which morning platelet counts were 5000 per cubic millimeter or lower, as compared with 17% of study days on which platelet counts were 6000 to 80,000 per cubic millimeter ($P<0.001$).

… patients with bleeding vs days with bleeding…

Slichter et al, NEJM 2010

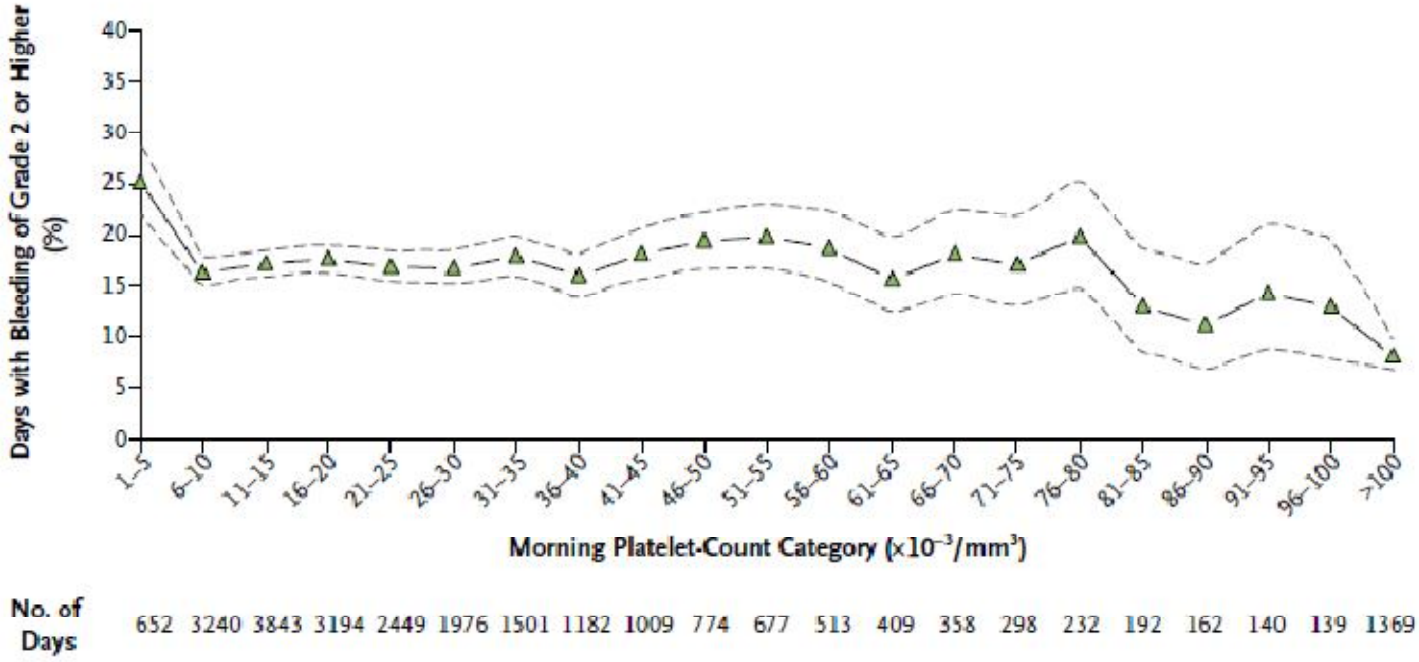


Figure 1. Days with Bleeding of Grade 2 or Higher in All Three Treatment Groups, According to Morning Platelet-Count Categories.

The percentage of days on which patients had bleeding of grade 2 or higher is shown, along with the associated 95% confidence intervals (dashed lines), according to the morning platelet-count category. Data are based on the 24,309 days during the study period on which patients had both a morning platelet count and information on bleeding of grade 2 or higher. Each patient-day was treated as a separate unit of analysis. Analyses were adjusted to take into account that for each patient, the results on various days may be correlated. The interaction between treatment group and morning platelet-count category was not significant, indicating that the effect of the morning platelet-count category did not differ significantly among the three treatment groups; therefore, the data from all three groups are combined.

Study reporting predictive value of grade 1 (minor) bleeding for future clinically relevant bleeds

The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia

Kathryn E. Webert
Richard J. Cook
Chris S. Sigouin
Paolo Rebulla
Nancy M. Heddle

Haematologica 2006; 91:1532-1539

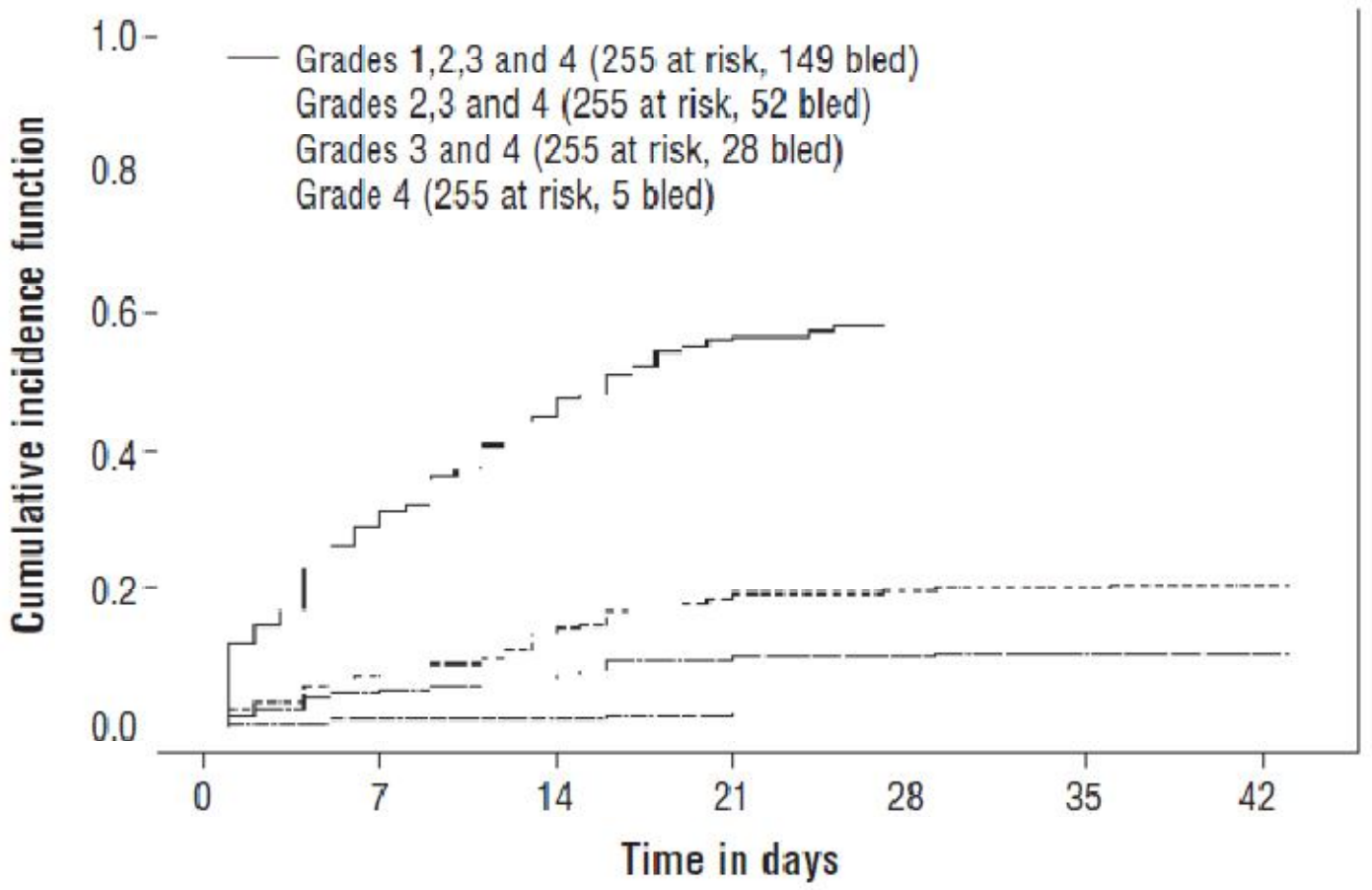


Figure 1. Cumulative incidence functions[16] for the occurrence of at least one bleed of WHO grades 1-4, 2-4, 3-4 and 4.

The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia

Kathryn E. Webert
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Haematologica 2006; 91:1532-1539

Minor bleeding predicting more severe bleeding

The majority of severe bleeds (grades 3 and 4) were preceded by bleeds of lesser severity. The presence of grade 1 bleeding on the previous day was associated with a 2.6 times increased risk of clinically significant bleeding (grades 2, 3 and 4) (RR 2.55; 95% CI (1.18, 5.49); p=0.017). When looking at the risk of severe bleeding, the presence of mild bleeding (grades 1 and 2) on the previous day was associated with a 3.1 times increased risk of severe bleeding (grades 3 and 4) bleeding (RR 3.05; 95% CI (1.17, 7.95); p=0.023). Furthermore, the presence of grade 1 bleeding, although not reaching statistical significance, was associated with a 2.8 times increased risk of severe bleeding (grades 3 or 4) on the following day (RR 2.83, 95% CI (0.95-8.40), p=0.06). Grade 2 bleeding alone was not predictive of severe bleeding (grades 3 and 4) on the next day (RR 2.86; 95% CI (0.37, 21.93); p=0.31).

Message 7

- Whole blood derived (less expensive) and apheresis (more expensive) platelets show comparable clinical effectiveness
- Choice depends on donor availability and resources

Cost analysis

- Platelet concentrates from whole blood
- Platelet concentrates from apheresis

Lopez-Plaza, Transfusion 1999; 39: 925

TABLE 1. Actual number of transfusion episodes by diagnosis and blood products and calculated total donor exposures by diagnosis (mean ± SD)*

Diagnosis or procedure	Actual blood component transfusions					Total donor exposures†	
	Red cells	Fresh-frozen plasma	SDPs	RDPs	Cryo-precipitate	Minimum	Maximum
HPCT							
BC	10±10	1±1	2±5	6±7	1±3	21 ± 24	68±79
AML	41±42	6±21	15±26	33±37	2±10	107 ± 144	396±460
CML	32±25	10±24	13±25	25±22	1±4	84 ± 72	310±273
NHL	14±13	1±2	2±5	12±19	0±0	28 ± 33	113±155
CABG							
Male	6±6	5±6	1±1	1±1	1±4	13 ± 13	22±18
Female	10±9	6±9	1±1	1±1	1±6	19 ± 25	28±32

* Rounding errors account for any discrepancies between values shown for actual transfusions and calculated total donor exposures.

† Minimum donor exposure scenario assumes exclusive use of SDPs or one donor exposure per platelet transfusion episode for all platelet transfusion episodes. Maximum donor exposure scenario assumes exclusive use of RDPs or seven donor exposures per platelet transfusion episode for all platelet transfusion episodes.

Lopez-Plaza, Transfusion 1999; 39: 925

TABLE 4. CE of SDP versus RDP transfusion therapy: baseline CE model

HPCT	
BC	$410,542/QALY
NHL	$168,700/QALY
CML	$411,506/QALY
AML	$519,822/QALY
CABG	
Male	$216,280/QALY
Female	$192,415/QALY

Lopez-Plaza, Transfusion 1999; 39: 925

Message 8

- Commercial methods are available to detect bacteria and to reduce/inactivate pathogens (and white cells) in platelets
- Cost/benefit ratio under evaluation

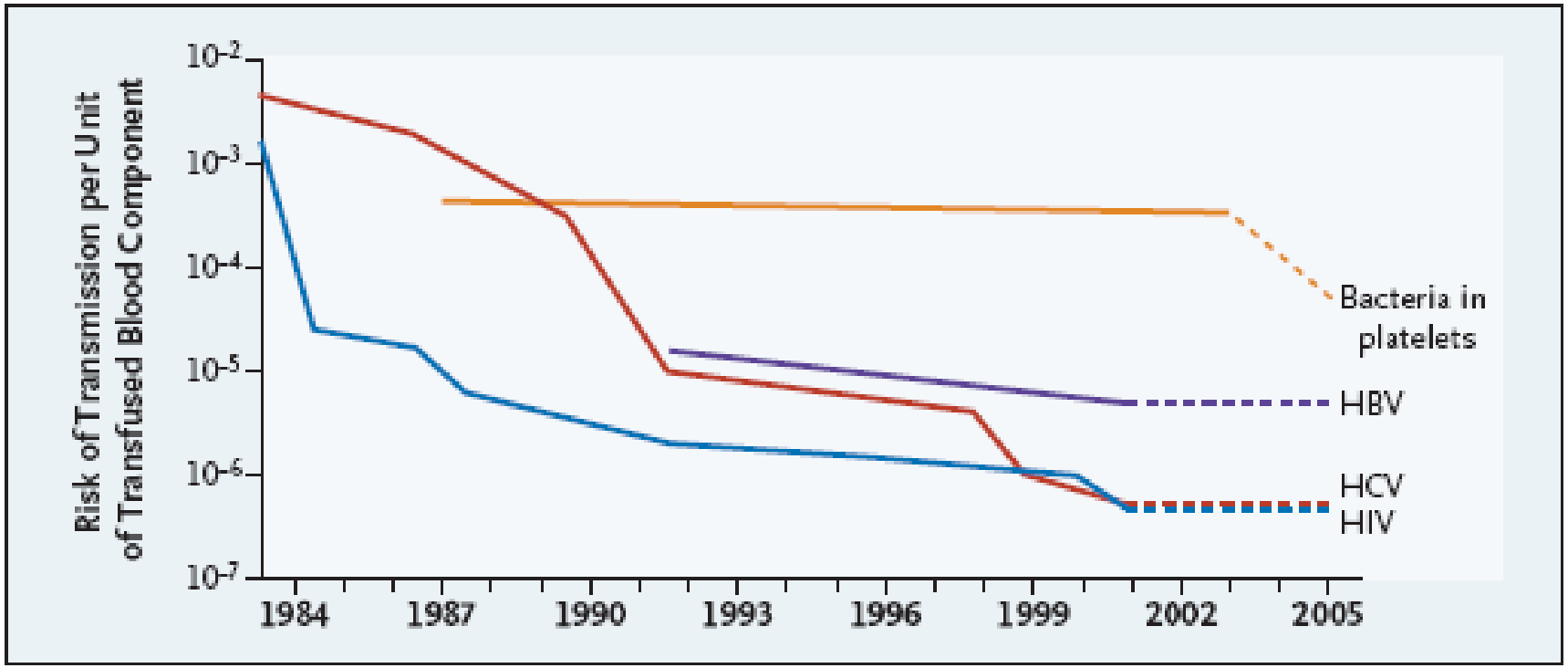
- Product
  - Bacterial detection

Moving from 5 to 7 days platelet storage is operationally beneficial. However, about **1:3,000** platelet units are contaminated with bacteria. Actual **recipient risk** depends on circumstances (strain, immune competence, co-morbidity, etc)

Critical issues:
Analytical vs clinical sensitivity
Time to detection
Inoculum sample size
Early vs late time of sampling
Testing vs inactivation
COSTS

The Continuing Risk of Transfusion-Transmitted Infections

Morris A. Blajchman, M.D., and Eleftherios C. Vamvakas, M.D., Ph.D., M.P.H.



Risks of Transfusion-Transmitted HIV, HBV, HCV, and Bacterial Infection in the United States, 1984–2005.

Changes reflect both the effects of screening tests introduced during this period and the decreasing incidence of HIV, HBV, and HCV infections in blood donors. Several measures to prevent the transmission of bacteria by platelet transfusion were implemented in or around 2004. Dashed lines represent estimates.

Bacterial Detection of Platelets: Current Problems and Possible Resolutions

Transfusion Medicine Reviews, Vol 19, No 4 (October), 2005: pp 259-272

Morris A. Blajchman, Erik A.M. Beckers, Ebbe Dickmeiss, Lilly Lin, Gillian Moore, and Ludo Muylle

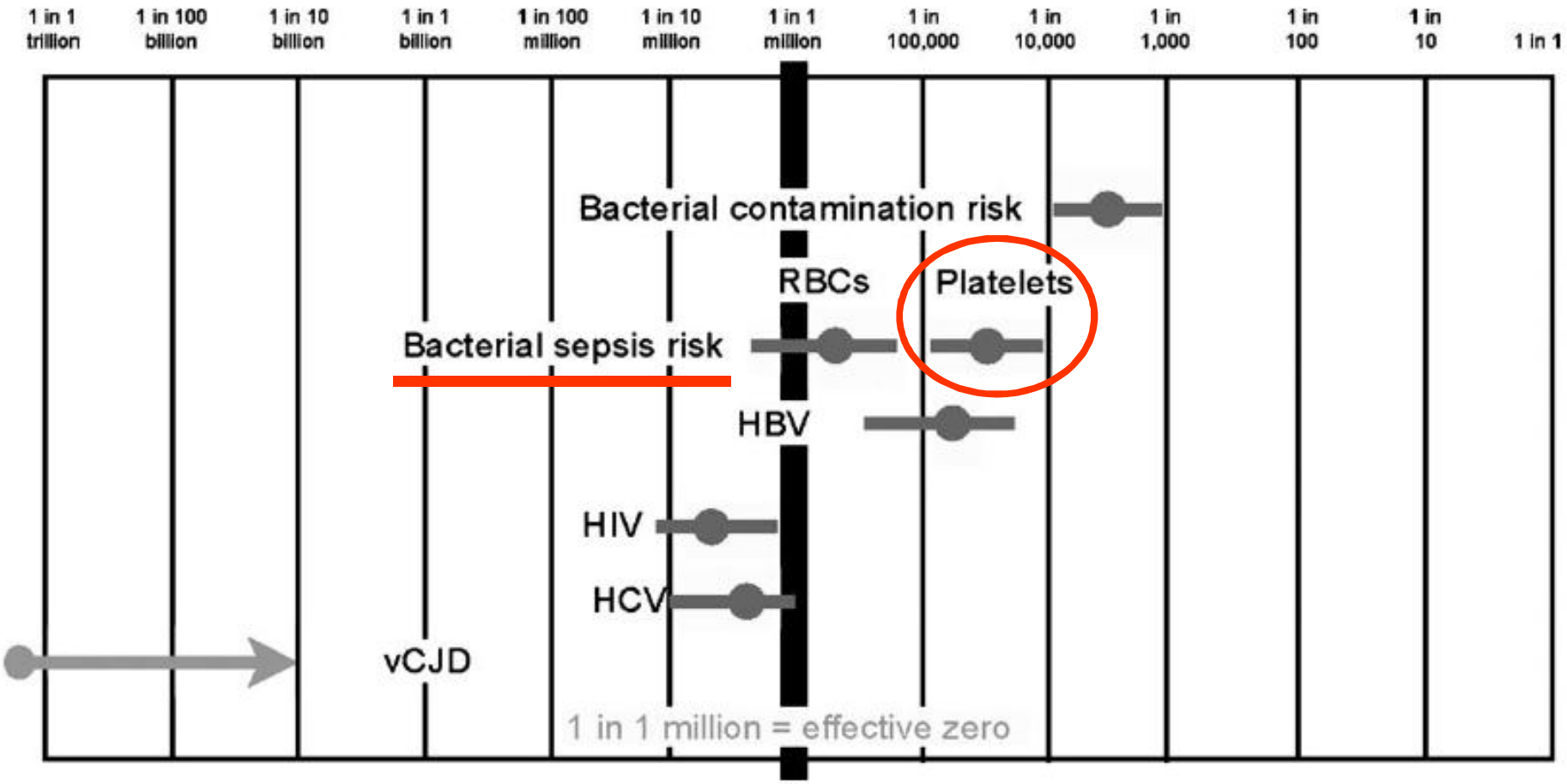


Fig 1. Transfusion risks (per unit transfused) for various transfusion-transmitted infections. HBV indicates hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; RBCs, red blood cells; vCJD, variant Creutzfeldt-Jakob disease.

Methods for detecting bacteria in platelets

Method	Threshold for detection (CFU per mL)	Reference
Fall in pH measured with a dipstick	$\geq 10^7$-10^8	Wagner 1996; Burstain 1997
Fall in glucose level measured with a dipstick	$\geq 10^7$-10^8	Wagner 1996; Burstain 1997
Loss of swirling	$\geq 10^7$-10^8	Wagner 1996
Gram Stain	$\geq 10^5$-10^6	Yomtovian 1993
Chemiluminescence detection of ribosomal RNA	$\geq 10^4$-10^5	Brecher 1994
Dielectrophoresis	$\geq 10^3$-10^5	Brecher 2005
Fall in oxygen tension	$\geq 10^2$-10^3	Brecher 2001
Solid-phase laser cytometry	≥ 10 to 10^3	Brecher 2005
Automated bacterial culture	≥ 10	Brecher 2005

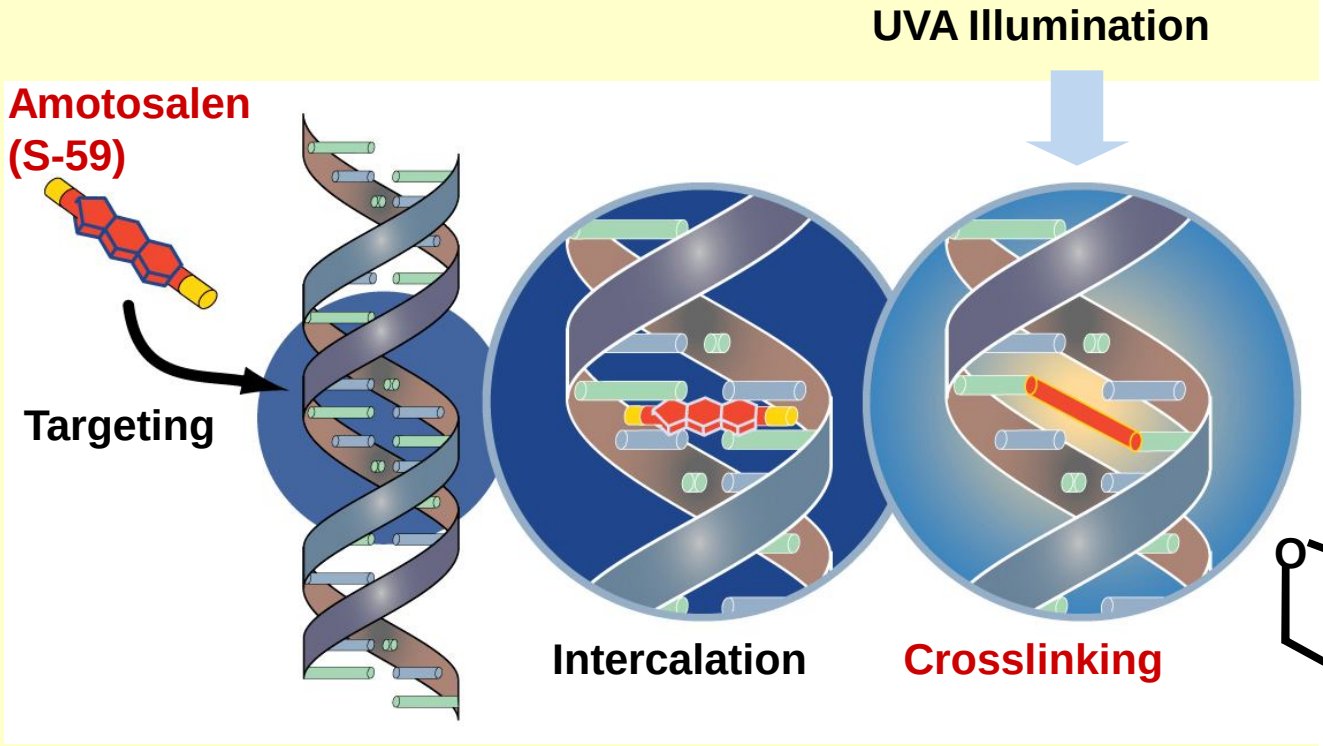
CFU = colony forming units

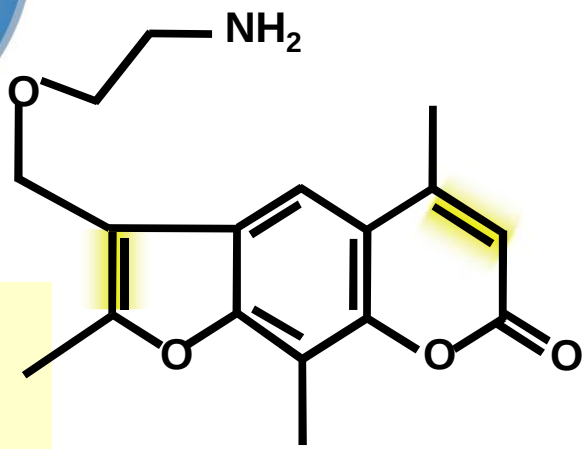
Stroncek & Rebulla, 2006

- Product
  - Pathogen inactivation

•Amotosalen (S-59)
•Riboflavin
•Others under development

INTERCEPT Blood System for Platelets and Plasma: Amotosalen + UVA (320-400 nm)





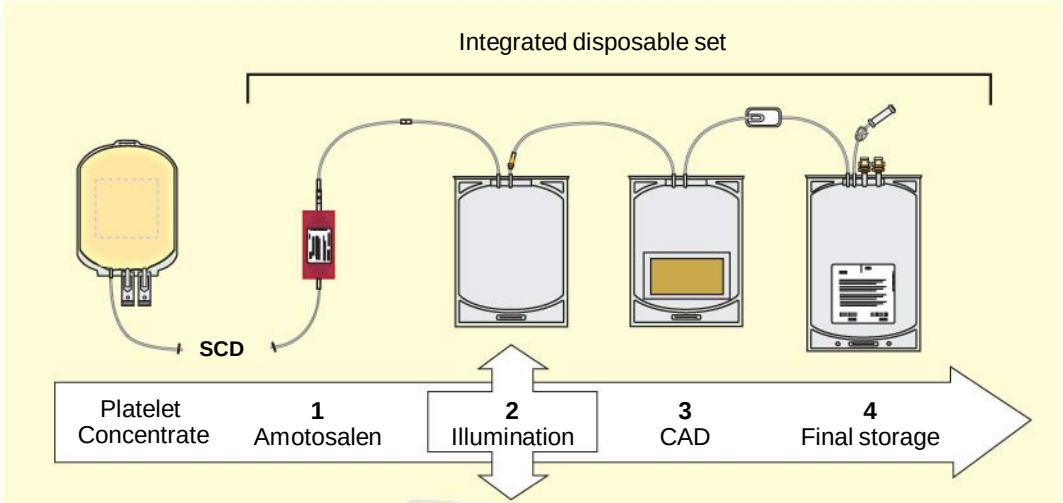
Slide from CERUS

INTERCEPT Blood System for Platelets

Platelets in 35% plasma and 65% InterSol

Compatible with apheresis and WB collection platforms

Accommodates double-doses

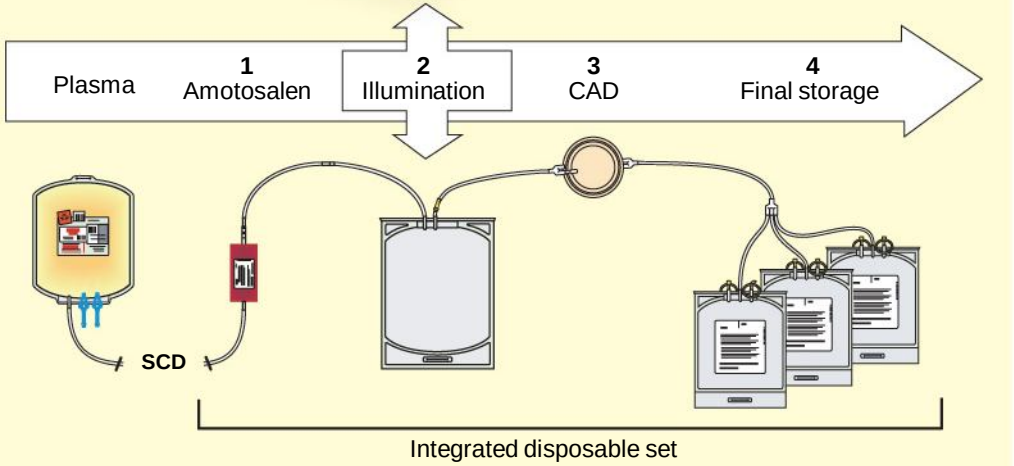


INTERCEPT UVA Illuminator

INTERCEPT Blood System for Plasma

Compatible with apheresis and WB collection platforms

One process produces up to 3 products.



Slide from CERUS

INTERCEPT: Pathogen and WBC Inactivation Claims

- **Enveloped viruses**
  HIV-1
  HIV-2
  HBV
  DHBV
  HCV
  BVDV
  HTVL-I
  HTLV-II
  CMV
  WNV
  SARS
  Vaccinia
  Chikungunya
  Dengue
  Influenza virus (H1N1) Avian flu virus (H5N1)
- **Non-enveloped viruses**
  Bluetongue virus, type 11
  Simian Adenovirus-15
  Feline calicivirus
  Parvovirus B19
  Human adenovirus 5

- **Gram-negative bacteria**
  Klebsiella pneumoniae
  Yersinia enterocolitica
- ***Escherichia coli***
  Pseudomonas aeruginosa
- ***Salmonella choleraesuis***
  Enterobacter cloacae
  Serratia marcescens

- **Gram-positive bacteria**
  Staphylococcus epidermidis
  Staphylococcus aureus Streptococcus pyogenes Listeria monocytogenes
  Corynebacterium minutissimum
  Bacillus cereus (vegetative)
  Lactobacillus sp. Bifidobacterium adolescentis Propionibacterium acnes
  Clostridium perfringens

- **Spirochetes**
  Treponema pallidum
  Borrelia burgdorferi

- **Protozoa**
  Trypanosoma cruzi
  Plasmodium falciparum
  Leishmania sp.
  Babesia microti

- **Leukocytes**

  Inactivated

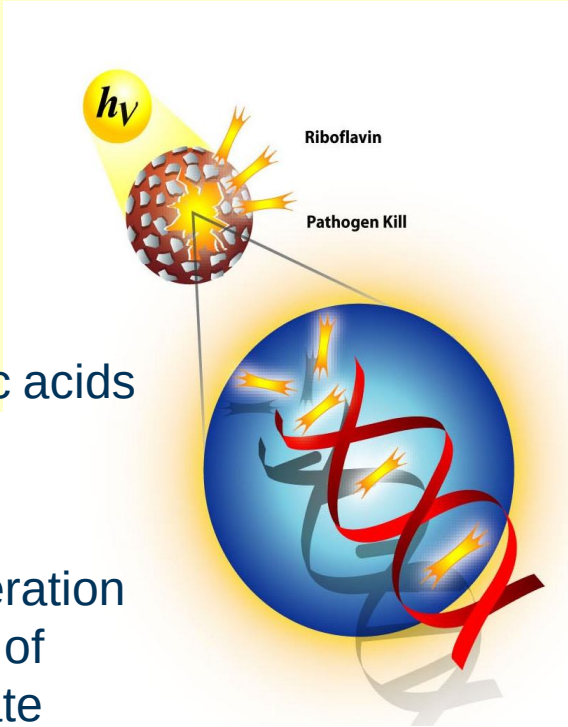
Slide from CERUS

Mirasol's Primary Mode of Action

The Mirasol PRT System inactivates disease-causing agents by altering their nucleic acids in two primary ways:

1. UV light only: reversible inactivation
   - UV light alone breaks chemical bonds in the nucleic acids of pathogens

2. UV light + riboflavin: irreversible inactivation
   - Riboflavin molecules form complexes with nucleic acids
   - UV light from the Mirasol Illuminator activates the riboflavin molecule in the complex
   - Photoactivated riboflavin induces a chemical alteration to the functional groups (such as guanine bases) of nucleic acids making pathogens unable to replicate



Slide from CARIDIAN

The Mirasol PRT Process for Platelets & FFP

1

Transfer platelet product to Mirasol Illumination bag

2

Add 35 mL riboflavin solution (500 uM)

3

Illuminate product for 6–10 min.* (6.2 J/mL)

* Illumination time depends on product volume

Slide from CARIDIAN

Mirasol Product & Process Specifications

Source product specifications

	Gen 1 Plasma-based process	Gen 2 Plasma-based process	Gen 2 PAS-compatible process
Volume	**170 – 360** ml	**90 – 360** ml	**90 – 360** ml
Concentration	**1.18 – 2.1** x 10^6/µl	**0.8 – 2.1** x 10^6/µl	**2.11 – 3.4** x 10^6/µl
Yield	**2.0 – 5.1** x 10^{11}	**Not specified**	**Not specified**

Treatment window

	Gen 1 Plasma-based process	Gen 2 Plasma-based process	Gen 2 PAS-compatible process
SDP	**2 – 22** hrs post-collect	**2 – 22** hrs post-collect	**2 – 18** hrs post-collect
BCP	**1 – 8** hrs post-pooling	**0 – 8** hrs post-pooling	**0 – 8** hrs post-pooling

Storage specifications (derived values shown between brackets)

	Gen 1 Plasma-based process	Gen 2 Plasma-based process	Gen 2 PAS-compatible process
PAS addition	**N / A**	**N / A**	**< 2 hrs post-PRT – min 135 ml**
Volume	(200 – 400 ml)	(170 – 400 ml)	**Split if >400 ml**
Concentration	(1.0 – 2.1 x 10^6/µl)	(0.7 – 2.1 x 10^6/µl)	**0.7 – 1.5** x 10^6/µl
Yield	(<5.1 x 10^{11})	**Split if >5.1 x 10^{11}**	**Split if >5.1 x 10^{11}**
Max. shelf life	**5 days**	**5 days**	**(7days)**

Slide from CARIDIAN

Reduction of Active Pathogen Load	Typical Performance	References
Viruses (enveloped, non-enveloped; intracellular, extracellular)	~3–6 log	Ruane et al. 2004 Goodrich et al. 2006 Navigant data on file
Bacteria (Gram +, Gram –)	~2–5 log	Ruane et al. 2004 Goodrich et al. 2006
Parasites	>5 log	Cardo et al. 2006 Cardo et al. 2007 Rentas et al. 2006 Tonnetti et al. 2007

Inactivation of White Blood Cells	Typical Performance	References
White blood cell inactivation	>6 log	Fast et al. 2006a (*in-vitro*)
Cytokine production and expression	Prevented	Fast et al. 2006a (*in-vitro*)
Graft-versus-host disease	Prevented	Fast et al. 2006b (animal model)
Alloimmunization & transplant rejection	Prevented	Marschner et al. 2007 (AABB abstract) Asano et al. (animal study; in press)

Slide from CARIDIAN

Platelets photochemically treated with amotosalen HCl and ultraviolet A light correct prolonged bleeding times in patients with thrombocytopenia

TRANSFUSION 2006;46:731-740.

Sherrill J. Slichter, Thomas J. Raife, Kathryn Davis, Margaret Rheinschmidt, Donald H. Buchholz, Laurence Corash, and Maureen G. Conlan

TABLE 2. Paired cutaneous template bleeding times*

Time point	Number	PCT†	Reference†	p Value‡
Before transfusion	9	29.2 ± 1.6	28.7 ± 2.5	
1-2 hr after transfusion	10	19.3 ± 9.5	14.3 ± 6.5	0.25
18-24 hr after transfusion	10	18.3 ± 9.3	18.7 ± 9.1	0.82

* Normal bleeding time, less than 8 minutes.
† Mean (±SD) in minutes. For the bleeding times of more than 30 minutes, a value of 30 minutes was used to calculate the means.
‡ Testing for treatment difference by crossover analysis.

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TABLE 3. PLT counts, PLT count increments, and PLT CCIs

Variable	PCT*	Reference*	p Value†
PLT count (mean ± SD × 10^9/L)			
Before transfusion	13.2 ± 5.3 (29)	14.5 ± 6.3 (29)	
PLT count increment (mean ± SD × 10^9/L)			
1-2 hr after transfusion	41.9 ± 20.8 (28)	52.3 ± 18.3 (29)	0.007
18-24 hr after transfusion	26.1 ± 16.5 (29)	35.2 ± 19.0 (29)	0.021
PLT CCI (mean ± SD × 10^8)			
1-2 hr after transfusion	10.4 ± 4.9 (28)	13.6 ± 4.3 (29)	<0.001
18-24 hr after transfusion	6.6 ± 3.8 (29)	9.2 ± 4.9 (29)	0.01

* The number of patients at each time point is indicated in parentheses.

† Crossover analysis t test for patients with paired data for PLT count increments at 1 to 2 hours (n = 25) and 18 to 24 hours (n = 26).

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TABLE 4. Interval to next PLT transfusion*

Transfusion sequence (number)	Interval (days) ± SD	p Value†
PCT followed by reference (17)	2.9 ± 1.0	
Reference followed by PCT (12)	3.4 ± 1.4	0.35
Any sequence		
Any PCT (25)	2.9 ± 1.2	
Any reference (22)	3.4 ± 1.3	0.18

* Interval is time from study transfusion (PCT or reference) to next PLT transfusion, which could be a study transfusion (PCT or reference) or a nonstudy transfusion. Transfusion interval could not be assessed for 6 patients (3 PCT and 3 reference) who did not receive any subsequent PLT transfusions after the first study transfusion.

† Interval between transfusions was compared by t test.

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TABLE 5. Hemostatic response to study transfusions*

Variable	PCT (n = 29)	Reference (n = 29)
Any bleeding		
Before transfusion	19 (66)	17 (59)
After transfusion	17 (59)	19 (66)
Improvement	8 (28)	7 (24)
Worsening	5 (17)	4 (14)
No change	16 (55)	18 (62)

* Data are reported as number (%).

Efficacy of apheresis platelets treated with riboflavin and ultraviolet light for pathogen reduction

TRANSFUSION 2005;45:1335-1341.

James P. AuBuchon, Louise Herschel, Jill Roger, Harry Taylor, Pamela Whitley, Junzhi Li, Rick Edrich, and Raymond P. Goodrich

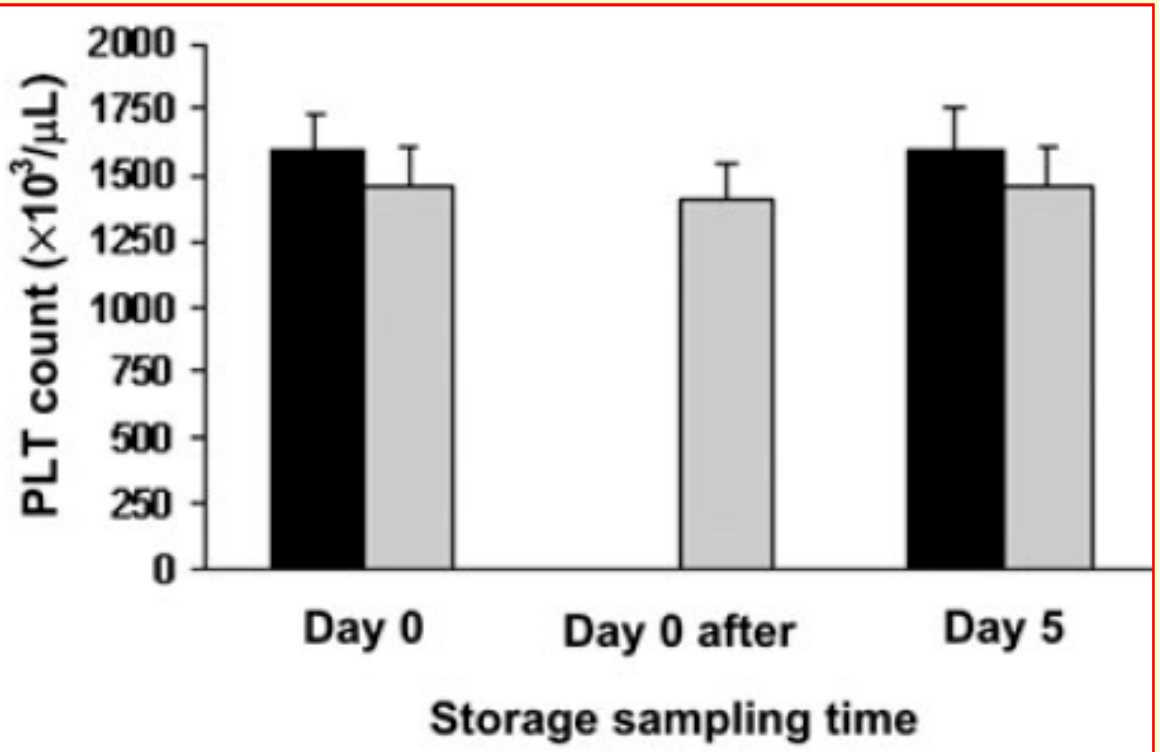

Fig. 1. PLT concentration. Results of testing before and after treatment (Day 0) and at end of storage (Day 5). (■) Mean of control units; (□) treated units. Vertical bars represent 1 SD.

Efficacy of apheresis platelets treated with riboflavin and ultraviolet light for pathogen reduction

TRANSFUSION 2005;45:1335-1341.

James P. AuBuchon, Louise Herschel, Jill Roger, Harry Taylor, Pamela Whitley, Junzhi Li, Rick Edrich, and Raymond P. Goodrich

TABLE 1. Results of radiolabeling studies*

	Control	Treated	p value
Radiolabel uptake efficiency (%)	64.2 ± 17.2	59.5 ± 21.2	>0.05
Recovery (%)	66.5 ± 13.4	50.0 ± 18.9	<0.05
Survival (multiple hit, hr)	142 ± 26	104 ± 26	<0.05

* Results of Day 5 radiolabeling with ^{111}In and autologous return. Results shown are 22 observations from the control cycle and 24 from the treated cycle.

Proceedings of a Consensus Conference: Pathogen Inactivation—Making Decisions About New Technologies

Kathryn E. Webert, Christine M. Cserti, Judy Hannon, Yulia Lin, Katerina Pavenski, Jacob M. Pendergrast, and Morris A. Blajchman

Transfusion Medicine Reviews, Vol 22, No 1 (January), 2008: pp 1-34

Table 2. Incremental Cost (US dollars) of Technologies Designed to Improve Transfusion Safety

Adverse event	Technology solution	Incremental cost/U
IBCT or ABO mistransfusion	PPI technologies (bar coding, RFID), check-type (second sample) policies	<$20
Acute or delayed alloimmune hemolytic transfusion reactions	Database unification, definitive genotyping	<$10
TRALI	HLA antibody screening	<$2
Transfusion-transmitted infection, bacterial or viral	Pathogen reduction technology	>$100

Abbreviations: IBCT, incorrect blood component transfused; PPI, positive patient identification; RFID, radiofrequency identification; TRALI, transfusion-related acute lung injury; HLA, human leukocyte antigen.

Message 9

- Platelet transfusion may be followed by reactions/adverse events
- The effectiveness of platelet transfusion can be highly variable
- Recipient clinical conditions and concurrent drug administration can heavily impact on effectiveness

Infectious adverse consequences of platelet transfusions

Consequence	Cause	Prevention
AIDS	HIV infected donor	•Donor screening and testing •Pathogen inactivation
Hepatitis	Hepatitis B and C virus infected donor	•Donor screening and testing •Pathogen inactivation
CMV disease	CMV infected donor	•Donor testing •Leucocyte-reduction •Pathogen inactivation
Sepsis or septic shock	Contamination from the platelet donors skin or from an occult or asymptomatic donor bacteriemia	•Culture product 24 or more hours after collection •Test for bacteria shortly before transfusion •Pathogen inactivation

Stroncek & Rebulla, 2007

Cumulative Risks of Early Fresh Frozen Plasma, Cryoprecipitate and Platelet Transfusion in Europe

Rut Norda, MD, Elsa Tynell, MD, and Olof Åkerblom, MD, PhD *J Trauma.* 2006;60:S41–S45.

Table 2 Of the Potential Adverse Effects, the Following Events Were Reported From the Danish, French, and Quebec Hemovigilance System, Recalculated to a Rate per 10,000 Transfusions[14,16,18]

Events per 10,000 Transfusions	Plasma	Platelet
Non-haemolytic transfusion reactions (urticaria, allergic and anaphylaxis symptom)	0,22†	0†
	0,35‡	1,04‡
	2,35§	5,42§
Congestive heart failure/volume overload	0,1‡	0,13‡
	2,06§	4,82§
Sepsis due to inadvertent bacterial contamination	0,02‡	0,28†
	0†§	0,29‡
		2,41§
Transfusion-related acute lung injury*	0,18†	0,46†
	0§	1,81§
Posttransfusion purpura	0,04†	0
Viral transmission	0	0,03‡
Severe anaphylaxis with Ig A deficiency and anti IgA	0	0
Transfusion-associated graft-versus host disease	0	0
Citrate toxicity	NR	NR
Transmission of other pathogens not tested for or recognised	NR	NR
Alloimmunisation against HLA-antigens	NR	NR

* Not differentiated in France 1997–1998.
† Reported from the Danish.
‡ Reported from the French.
§ Reported from Quebec.
NR indicates not reported.

Cumulative Risks of Early Fresh Frozen Plasma, Cryoprecipitate and Platelet Transfusion in Europe

Rut Norda, MD, Elsa Tynell, MD, and Olof Åkerblom, MD, PhD *J Trauma.* 2006;60:S41–S45.

Table 3 Other Adverse Effects Reported in the Danish, French and Quebec Hemovigilance System, Recalculated to a Rate per 10,000 Transfusions[14,16,18]

Events per 10,000 Transfusions	Plasma	Platelets
Minor allergic reactions	16,2‡	44,6‡
Febrile non-hemolytic transfusion reactions	5,3‡	24,1‡
Allergic reactions, not further specified	2,6†	19,8†
Immunological incompatibility	0,06†	3,4†
	2,9‡	1,2‡
Incorrect blood component issued	0,15*	0*
	0,84‡	2,0‡
Acute hemolytical transfusion reaction	0*	0*
Inefficient transfusion	0†	1,4†
Unknown	1,3†	12,9†
	0,88‡	0,12‡
Other reactions	0,31†	0,38†
	0,90‡	

* Reported from the Danish.
† Reported from the French.
‡ Reported from Quebec.

Immunologic adverse consequences of platelet transfusions

Consequence	Cause	Prevention
Alloimmunization	Leucocytes in platelets	•Leucocyte-reduction •UV B irradiation
Febrile reactions	HLA antibodies in transfusion recipient and IL-1β and IL-6 in platelets	•Leukocyte-reduction
TRALI	Leucocyte antibodies, bioactive lipids, or CD40L in platelets	•Exclude donors with leucocyte antibodies
Anaphylaxis	Antibodies in patients reacting with IgA, haptoglobin, antibodies or other plasma antigens	•IgA deficient platelet donors •Washed platelets
GVHD	Engraftment of donor leucocytes in an immunosupressed recipient	•Gamma irradiation of platelets (25 Gy)
Rh D alloimmunization	Transfusion of platelets from RhD-positive donors to RhD-negative recipients	•Administer Rh immune globulin within 48 hours of transfusion
Hemolysis	Anti-A and Anti-B in donor's plasma	•Exclude donors with high titers of anti-A or anti-B
Hypotension	Generation of bradykinin by the bedside filtration of platelets in a patient taking angiotensin-converting-enzyme (ACE) inhibitors	•Prestorage or in laboratory leucocyte reduction

Stroncek & Rebulla, 2006

Factors associated with decreased platelet transfusion effectiveness

Non-immune Factors

Clinical factors

Splenomegaly
Infection
Fever
Bleeding
Disseminated Intravascular Coagulation

Drugs

Amphotericin
Vancomycin
Ciprofloxacin
Heparin

Patient Factors

Male gender
Increased weight & height
Previous pregnancies
Prior transfusions

Immune Factors

Antibodies

HLA
Platelet-specific
Erythrocyte

Other

Platelet Product

Age

Stroncek & Rebulla, 2006

Measuring the concerns of cancer patients with low platelet counts: the Functional Assessment of Cancer Therapy–Thrombocytopenia (FACT-Th) questionnaire

David Cella
Jennifer L. Beaumont
Kimberly A. Webster
Jin-Shei Lai
Linda Elting

Support Care Cancer
DOI 10.1007/s00520-006-0102-1

Received: 1 December 2005
Accepted: 6 June 2006

Appendix

FACT-Th© additional concerns

Below is a list of statements that other people with your illness have said are important. By circling one (1) number per line, please indicate how true each statement has been for you *during the past 7 days.*

		Not at all	A little bit	Some-what	Quite a bit	Very much
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
Th1	I bleed easily	0	1	2	3	4
Th2	I bruise easily	0	1	2	3	4
Th3	I worry about problems with bruising or bleeding	0	1	2	3	4
Th5	I am bothered by nosebleeds	0	1	2	3	4
Th7	I am bothered by pinpoint bruising beneath my skin	0	1	2	3	4
Th8	I am bothered by blood in my urine or stool	0	1	2	3	4
Th10	I avoid or limit *physical activity* (because of concem with bleeding or bruising)	0	1	2	3	4
Th12	I am *frustrated* by not being able to do my usual activities	0	1	2	3	4
Th13	I worry that my treatment will be delayed (because of low blood counts)	0	1	2	3	4
The items below are excluded from the 11-item ThS						
H7	I feel fatigued	0	1	2	3	4
Th4	I worry about the possibility of serious bleeding	0	1	2	3	4
Th6	I am bothered by bleeding in my gums or mouth	0	1	2	3	4
Th9	I am inconvenienced by platelet transfusions	0	1	2	3	4
Th11	I avoid or limit *social activity* (because of concern with bleeding or bruising)	0	1	2	3	4
Th14	I worry that my treatment dose will be reduced (because of low blood counts)	0	1	2	3	4
Th15	For women only: I am bothered by vaginal bleeding	0	1	2	3	4

Measuring the concerns of cancer patients with low platelet counts: the Functional Assessment of Cancer Therapy–Thrombocytopenia (FACT-Th) questionnaire

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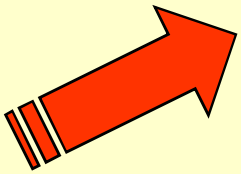
Conclusion: The FACT-Th is a reliable and valid measure for assessing the impact of thrombocytopenia on patients' lives. It can distinguish cancer patients with and without thrombocytopenia and is responsive to increase in platelet count over time. The FACT-Th may therefore prove useful as a measure of self-reported symptoms and concerns related to thrombocytopenia in clinical trials evaluating new pharmacologic agents and/or platelet transfusion practice.



Vox Sanguinis (2006) **91**, 63–69

DOI: 10.1111/j.1423-0410.2006.00785.x

ORIGINAL PAPER

Feasibility and usefulness of self–assessment of bleeding in patients with haematological malignancies, and the association between platelet count and bleeding

S. J. Stanworth,[1] C. Dyer,[1] A. Casbard[2] & M. F. Murphy[2]

Appendix I Self-assessment bleeding form. Please refer to your information sheet. Since completing your assessment form yesterday have you experienced:

		YES	NO
• Bleeding gums or lips		☐	☐
more than 1 h of continuous bleeding ☐ or *less than 1 h of continuous bleeding* ☐			
• Nose bleeding		☐	☐
more than 1 h of continuous bleeding ☐ or *less than 1 h of continuous bleeding* ☐			
• Blood shot eyes		☐	☐
• Any new vision impairment		☐	☐
• Red spots or bruising on any part of your body that you can see		☐	☐
If yes, are there more spots than the day before?	*yes* ☐ *no* ☐		
Mild/moderate ☐	Extensive ☐		(see definitions)
• Any bruised, swollen and painful joints or muscles		☐	☐
• Bleeding from invasive sites (e.g. Hickman line)		☐	☐
• Bright red blood in vomit		☐	☐
• Coughing up blood		☐	☐
• Visible blood in urine		☐	☐
• Abnormal vaginal bleeding	not applicable ☐	☐	☐
If yes, are you having to use more than two pads per day?	*yes* ☐ *no* ☐		
• Bright red blood in stool		☐	☐
• Black, tarry stool		☐	☐
• Bleeding episode other than described above		☐	☐
Please describe			

Vox Sanguinis (2006) **91**, 63–69

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ORIGINAL PAPER

Feasibility and usefulness of self–assessment of bleeding in patients with haematological malignancies, and the association between platelet count and bleeding

S. J. Stanworth,[1] C. Dyer,[1] A. Casbard[2] & M. F. Murphy[2]

Results Nineteen patients were included in the study. Four-hundred and ten days of thrombocytopenia were eligible for assessment of bleeds. Self-assessment was feasible, as defined by the total proportion of days on which self-assessment was completed (70%, 288 thrombocytopenic days). There was 86% agreement between bleeding data collected by self-assessment and by medical examination using a structured assessment form. Examples of discrepancies included the duration of petechiae/bruises and the reporting of minor bleeding. There was no evidence for an association between patients' morning platelet count and daily WHO bleeding grade. The incidences of WHO grade 1 and grade 2 bleeding on days with platelet counts $\leq 10 \times 10^9$/l, 11–20 $\times 10^9$/l, and $> 20 \times 10^9$/l were similar and did not reveal higher rates of bleeding at lower counts.

Message 10

- Stable hem/onc patients can be safely transfused for bleeding prophylaxis with a pre-transfusion platelet count trigger of 10,000 platelets per microliter

TABLE 1. FEATURES OF THE TRIAL.*

VARIABLE	THRESHOLD, 10,000 PLATELETS/mm³	THRESHOLD, 20,000 PLATELETS/mm³
Total no. randomized	144	132
No. whose study records were not received	9†	8‡
No. not evaluated for other reasons	0	4§
No. (%) who completed the follow-up	135 (94)	120 (91)

*Three hundred twenty-nine patients with acute myeloid leukemia were admitted to participating hematology units during the study period. Of these, 53 were not randomized: 37 had secondary leukemia, 10 had received a transfusion before the diagnosis of acute myeloid leukemia, 4 did not meet the age criteria, and 2 declined to give consent.

†Disseminated intravascular coagulation developed on the day of admission in one patient who was admitted with fever (temperature, >38°C), which continued until death, and he died of cerebral hemorrhage on day 5, when his morning platelet count was 13,000 per cubic millimeter. The remaining eight patients were alive at discharge.

‡All eight patients were alive at discharge.

§Two patients died within 24 hours after admission (one of cerebral hemorrhage and one of cardiac arrest), and two patients received a nonmyeloablative course of chemotherapy.

P. Rebulla et al, NEJM 1997

TABLE 2. CHARACTERISTICS OF THE PATIENTS.

	THRESHOLD, 10,000 PLATELETS/mm³ (N=135)	THRESHOLD, 20,000 PLATELETS/mm³ (N=120)
Male sex — %	53	52
Age — yr		
Median	51	49
Range	16–70	17–70
FAB classification of AML — no. of patients (%)*		
M0	7 (5.2)	5 (4.2)
M1	41 (30.4)	24 (20.0)
M2	28 (20.7)	37 (30.8)
M4	27 (20.0)	31 (25.8)
M5	21 (15.6)	17 (14.2)
M6	1 (0.7)	1 (0.8)
M7	1 (0.7)	0
Undefined	9 (6.7)	5 (4.2)
Days of hospitalization		
Median	29	28
Range	3–64	4–54
Pretransfusion platelet count/mm³		
Median	9000	14,000
Range	1000–89,000	0–64,000
No. of platelet transfusions/patient		
Mean ±SD	7.05±4.56	8.97±5.17†
Median	6	8
Range	1–22	2–27
No. of red-cell units transfused/patient		
Mean ±SD	9.57±5.18	9.07±4.58
Median	9	8
Range	3–48	2–27

*FAB denotes French–American–British, and AML acute myeloid leukemia.

†P = 0.001 for the difference between groups.

P. Rebulla et al, NEJM 1997

TABLE 3. CHARACTERISTICS OF PLATELET CONCENTRATES.

VARIABLE	THRESHOLD, 10,000 PLATELETS/mm³	THRESHOLD, 20,000 PLATELETS/mm³
Platelet concentrates (%)		
Selected by HLA type	4.8	4.6
Transfused within 2 days of storage	79.9	78.1
Prepared by apheresis	50.5	42.0
Processed to reduce the number of leukocytes	45.0	44.6
Irradiated	40.0	38.7
Platelet count in apheresis concentrates (cells×10⁻⁹/unit)		
Median	280	290
Range	110–588	130–610
Platelet count in nonapheresis concentrates (cells×10⁻⁹/pool)		
Median	217	217
Range	140–555	140–505

P. Rebulla et al, NEJM 1997

TABLE 4. MAJOR END POINTS OF THE TRIAL.

END POINT	THRESHOLD, 10,000 PLATELETS/mm³ (N=135)	THRESHOLD, 20,000 PLATELETS/mm³ (N=120)
Patients with major bleeding episodes — no. (%)	29 (21.5)	24 (20.0)
1 episode	21 (15.6)	18 (15.0)
2 episodes	7 (5.2)	3 (2.5)
3 episodes	0	3 (2.5)
4 episodes	1 (0.7)	0
>4 episodes	0	0
Total days in hospital	4006	3330
Days with major bleeding episodes — no. (%)	123 (3.1)	65 (2.0)
Complete remission — no. of patients (%)	76 (56.3)	76 (63.3)
Death — no. of patients (%)	18 (13.3)	9 (7.5)
Infection	12	7
Cardiac failure	2	0
Acute renal failure	0	1
Trauma	1	0
Disseminated intravascular coagulation	1	0
Apoplectic stroke	0	1
Intestinal infarction	1	0
Cerebral hemorrhage	1	0

P. Rebulla et al, NEJM 1997

REASONABLY WELL (?) DEFINED TRIGGERS

Platelet Transfusion for Patients With Cancer: Clinical Practice Guidelines of the American Society of Clinical Oncology

By Charles A. Schiffer, Kenneth C. Anderson et al., JCO 2001;19:1519

- Objective
- Outcomes
- Evidence
- Values
- Benefits/Harms/Cost
- Recommendations
- Validation
- Sponsor: ASCO

PDF file: www.asco.org

Estimation of the Lower Limits of Manual and Automated Platelet Counting

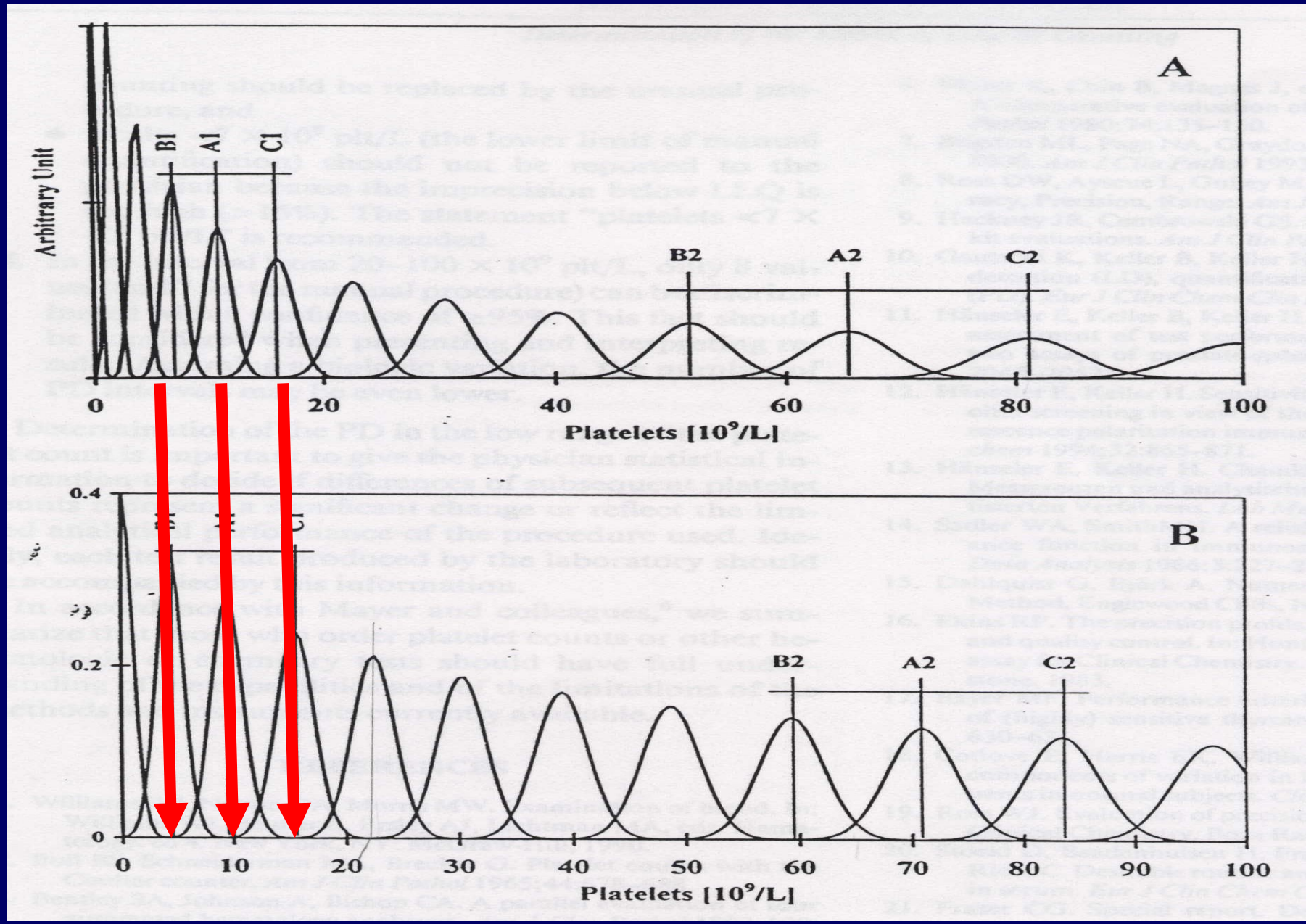
EDGAR HÄNSELER, PHD,[1] JÖRG FEHR, MD,[2] AND HERBERT KELLER, MD, PHD[1]

Most evaluators of automated or manual methods for platelet counting focus on characteristics such as imprecision, linearity, and carry over. The limits of the analytical procedure are usually not assessed. The limits of the different techniques are neither discussed in the literature nor do manufacturers of analytical systems supply these data.

A new procedure is presented to assess the performance of the manual as well as the automated platelet count. This procedure allows, with defined statistical confidence (eg, 95%), the determination of (1) the limit of platelet detection (LD) at which signals of platelets can be discriminated from the system noise; (2) the lower limit of quantification (LLQ), at which a certain imprecision is not surpassed; and (3) the power of definition (PD) that defines the number of values that can be discriminated in a certain interval. For each value, the PD allows calculation of the two adjacent (lower and higher) values that are significantly ($P \geq 0.95$) different.

For the manual count, LD was found to be 1.6×10^9 plt/L and the LLQ 6.9×10^9 plt/L. For the automated count with the Technicon H1, LD was 4.3×10^9 plt/L and LLQ 13.8×10^9 plt/L ($CV_{max} = 15\%$).

The PD in the range 20 to 100×10^9 plt/L is 8 for the automated and 7 for the manual count. (Key words: Platelet count; Measuring interval; Limit of detection; Lower limit of quantification; Power of definition) Am J Clin Pathol 1996;105:782–787.

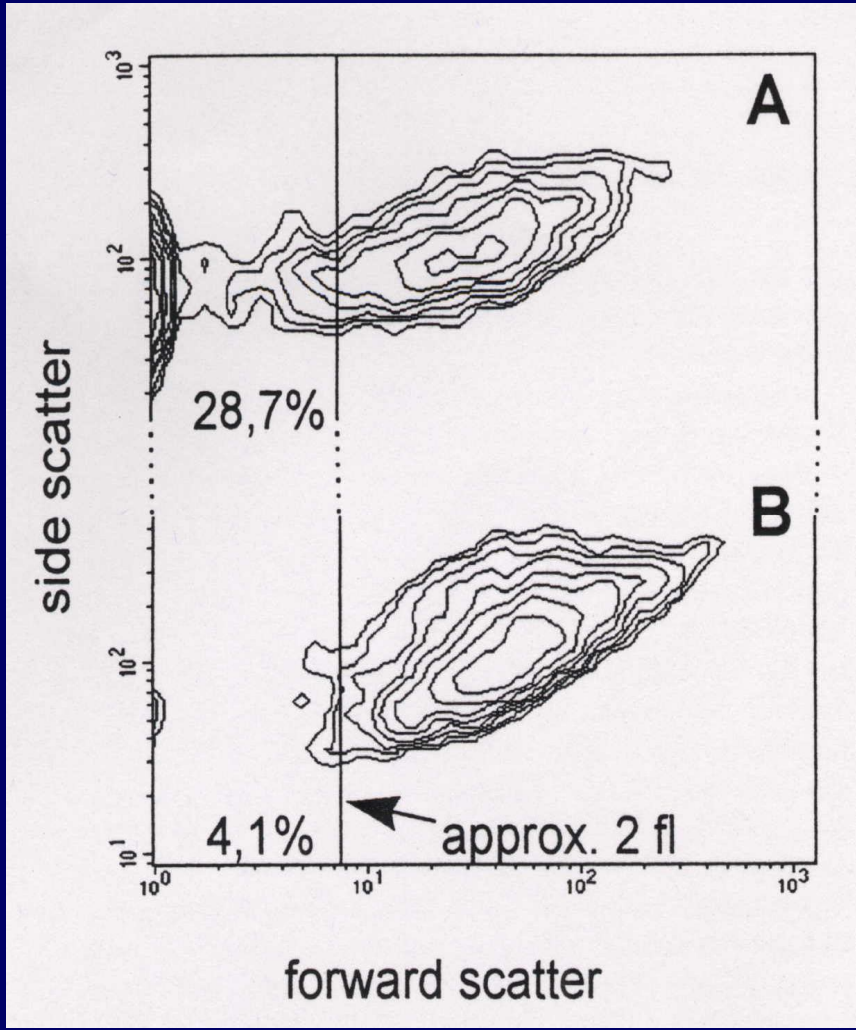


Hanseler et al, Am J Clin Pathol 1996

Difficulties in determining prophylactic transfusion thresholds of platelets in leukemia patients

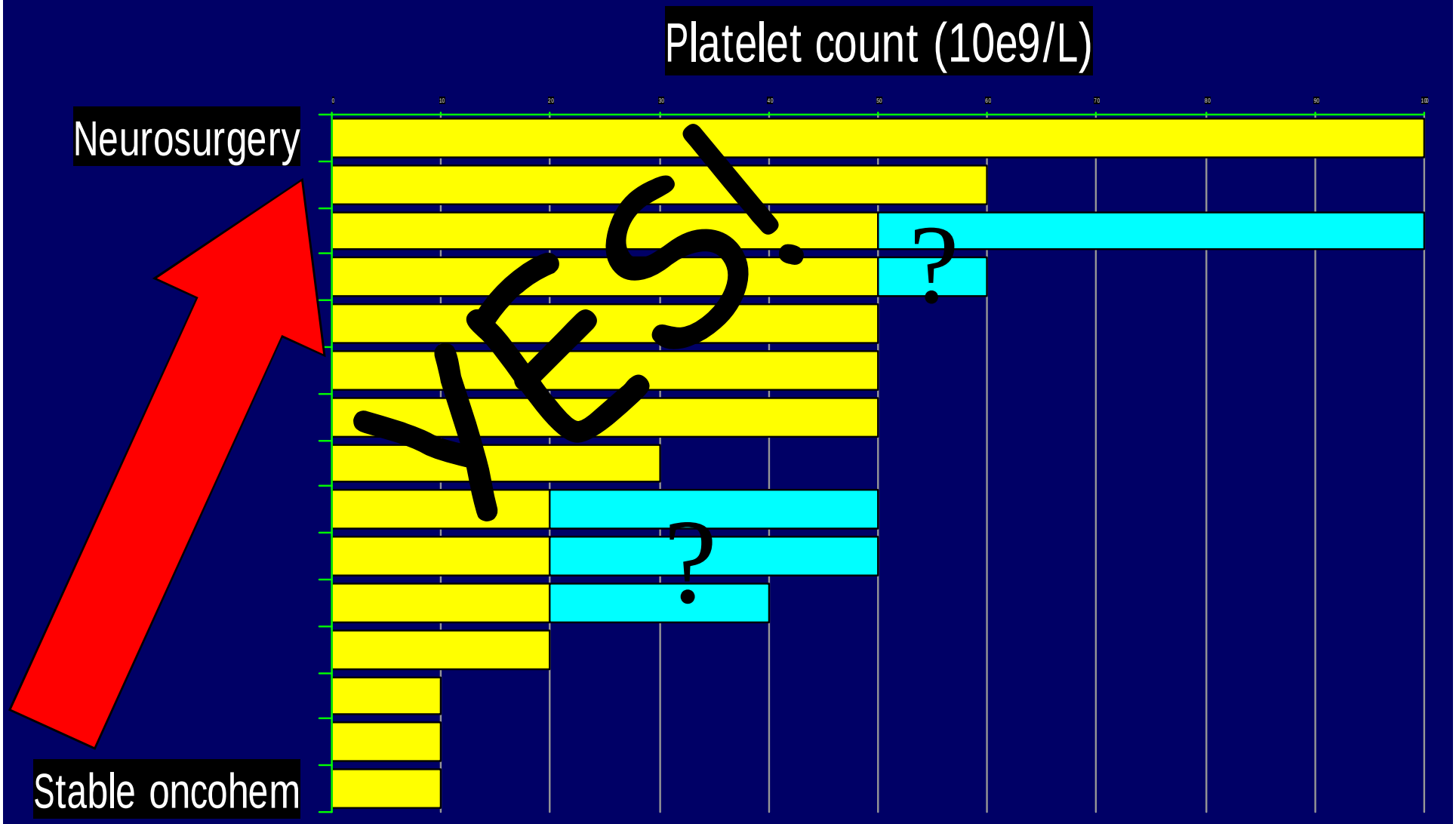
Springer et al, Blood 1998; 92: 2183

Fig. 1. Flow cytometric analysis of platelets and platelet-derived microparticles in a patients with acute myelogenous leukemia (A) and a normal individual (B) using anti-CD61 and anti-CD42b antibodies.



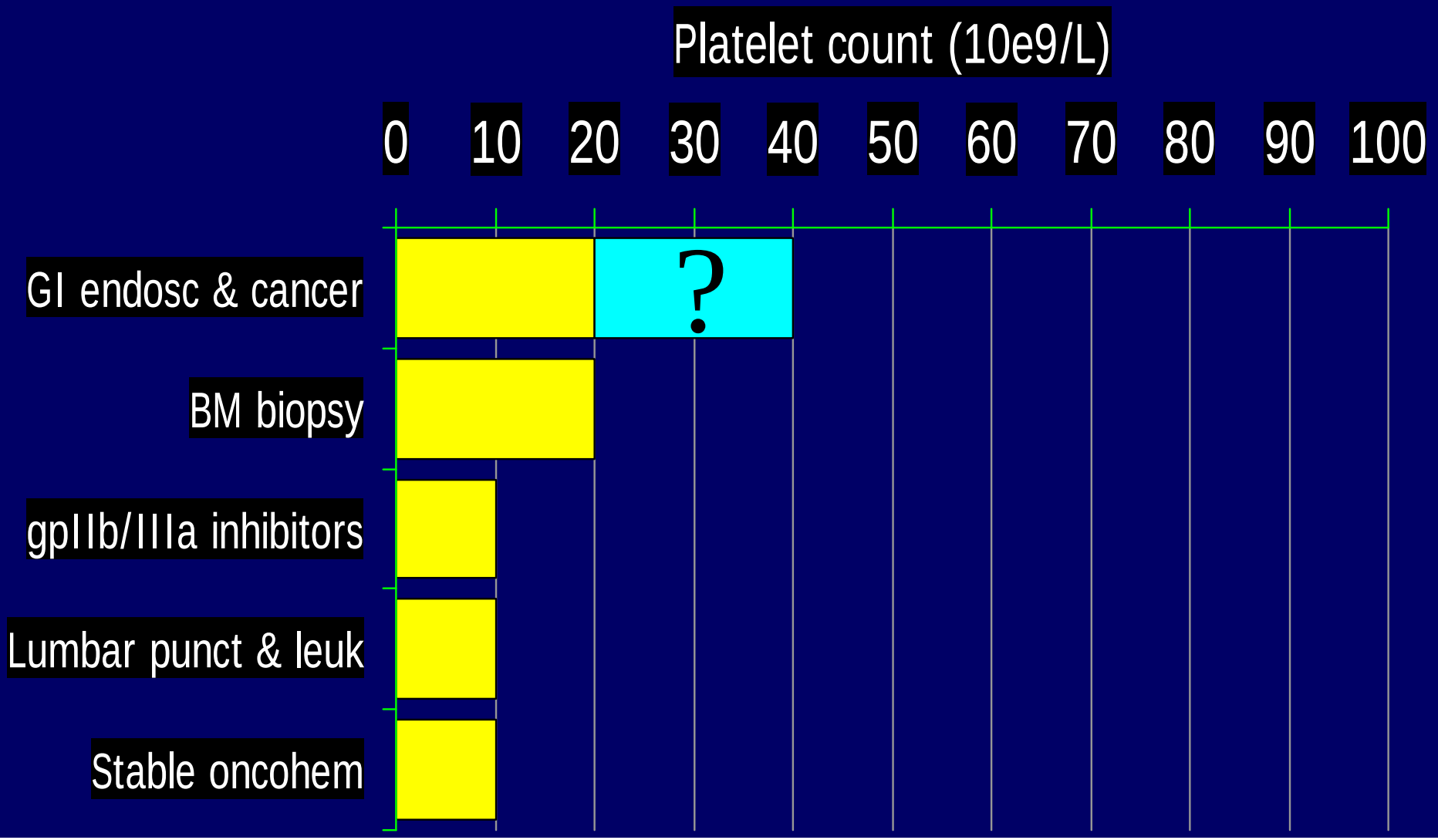
… the existence of platelet-derived microparticles (or membranes) that can improve hemostasis.

The Platelet Transfusion Trigger Chart



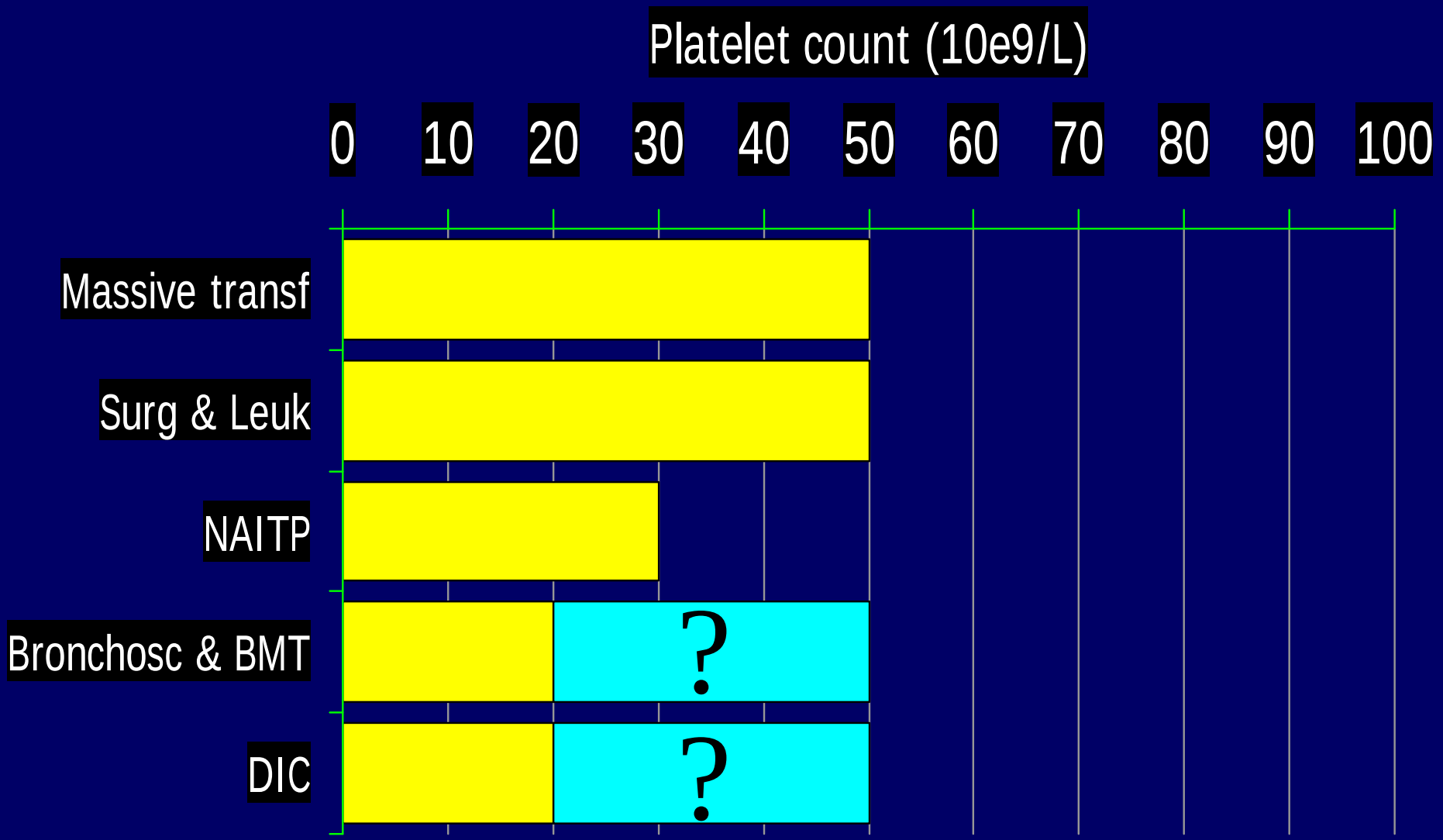
The Platelet Transfusion Trigger Chart

Platelet counts: 10,000 - 20,000



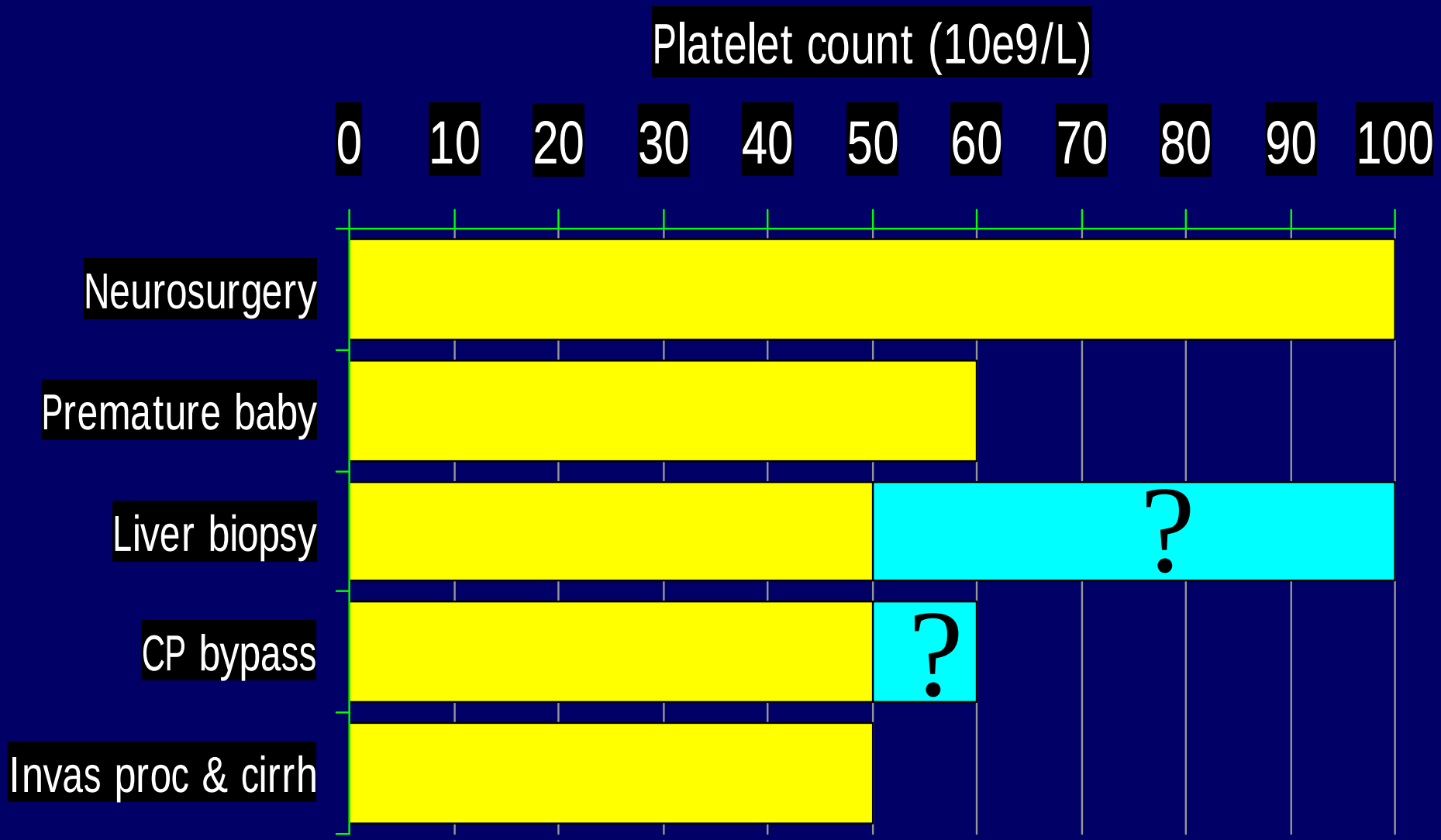
The Platelet Transfusion Trigger Chart

Platelet counts: 20,000 - 50,000

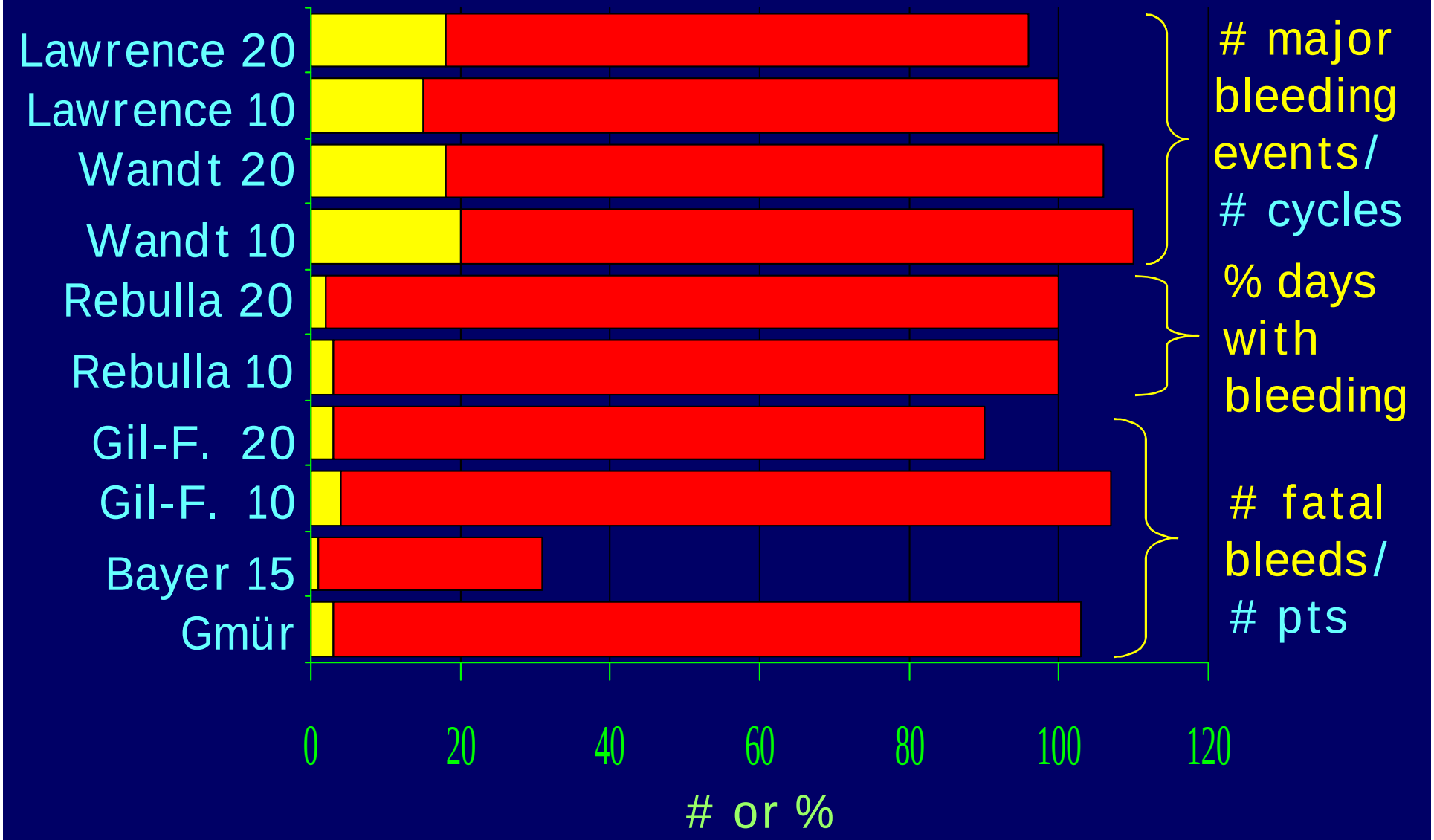


The Platelet Transfusion Trigger Chart

Platelet counts: 50,000 - 100,000



or % BLEEDING EVENTS in trials testing the 10,000 vs 20,000 platelet transfusion triggers



When things go wrong: platelet refractoriness

Refractoriness to platelet transfusion from random donors

- Alloimmune refractoriness: 5 vs 15% of hematology recipients of leuko-reduced vs non leuko-reduced blood components
- Anti-HLA antibodies: 13% of cardiac surgery recipients of 1 transfusion

Platelet alloantibodies in transfused patients

Volker Kiefel, Claudia König, Hartmut Kroll, and Sentot Santoso

Transfusion 2001; 41:766-770

TABLE 1. Diagnoses of patients

Diagnosis	Number
Systemic hematologic diseases (n = 187)	
Acute leukemia	43
Myeloproliferative syndromes	25
Myelodysplastic syndromes	36
Hodgkin's disease	10
Other lymphomas	73
Severe aplastic anemia	18
Solid tumors	14
Thrombocytopenia (various causes)	33
Total	252

Volker Kiefel et al. Transfusion 2001; 41:766-770

TABLE 2. Frequencies of platelet-specific and HLA class I antibodies

Antibody specificity	Female	Male	Total
HLA	56	37	93
HLA + HPA-5b	5	1	6
HPA-5b	4	0	4
HLA + HPA-5a	2	0	2
HPA-1a	1	0	1
HLA + HPA-1b	1	3	4
HLA + HPA-1b + HPA-5b	1	0	1
HLA + HPA-2b	0	1	1
HLA + HPA-1b + HPA-2b	0	1	1
Total	70 (56.5%)	43 (33.6%)	113 (44.8%)

Kiefel et al, Transfusion 2001;41:766-770

TABLE 3. GP specificities of sera with broad reactivities against platelet GPs

GP specificity	Number of sera
IIb/IIIa	4
IIb/IIIa + Ia/IIa	2
IIb/IIIa + Ib/IX	1
IIb/IIIa + Ia/IIa + Ib/IX	3
Total	10

Volker Kiefel et al. Transfusion 2001; 41:766-770

TABLE 4. Relation between rate of immunization and previous pregnancies in female patients

	Immunized	
Previous pregnancy	No	Yes
No	23	7
Yes	15	21

Volker Kiefel et al. Transfusion 2001; 41:766-770

Provision of platelet support to refractory patients

- HLA-matched donors
  - large number (>5,000) of HLA typed donors
  - difficult identification of compatible donors for patients with uncommon HLA types
  - low CCI in 20-40% of cases
- Cross-match compatible donors
  - large number of platelet concentrates from random donors
  - long screening time

Q Our blood supplier provides us with HLA-matched platelet-pheresis products when we have a refractory HLA-alloimmunized patient. The HLA-matched product is sometimes in the blood center's inventory, but we usually have to wait two or three days to receive the first product. Also, occasionally the donation fails and we don't get any product. Would it be better if the blood center crossmatched platelet-pheresis units for us?

AABB News 2000; 20, 4

Our experience

In 1999 we discontinued the use of HLA-matching and started a platelet cross-matching program for platelet recipients refractory to random donors.

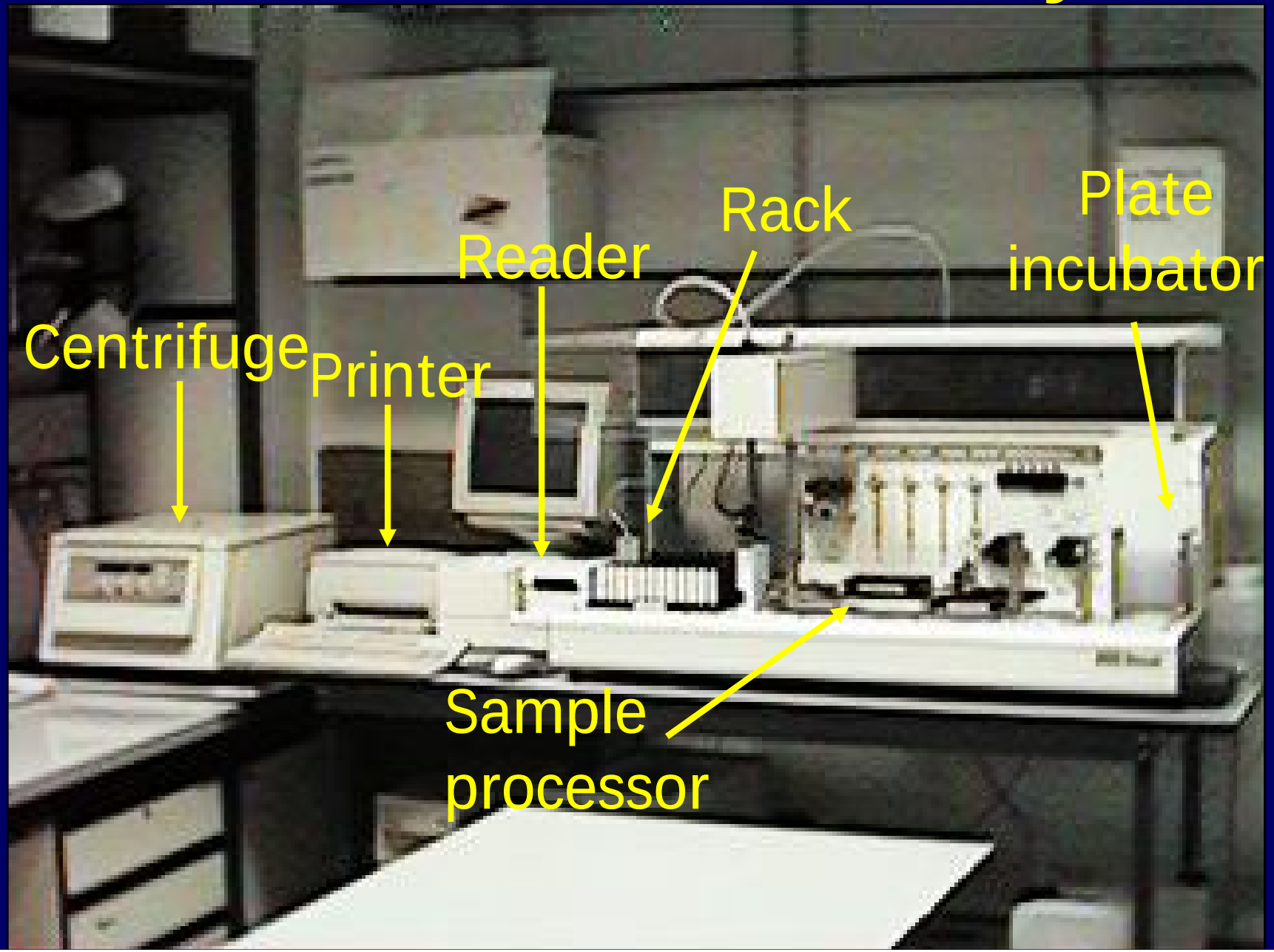
Aim of the study

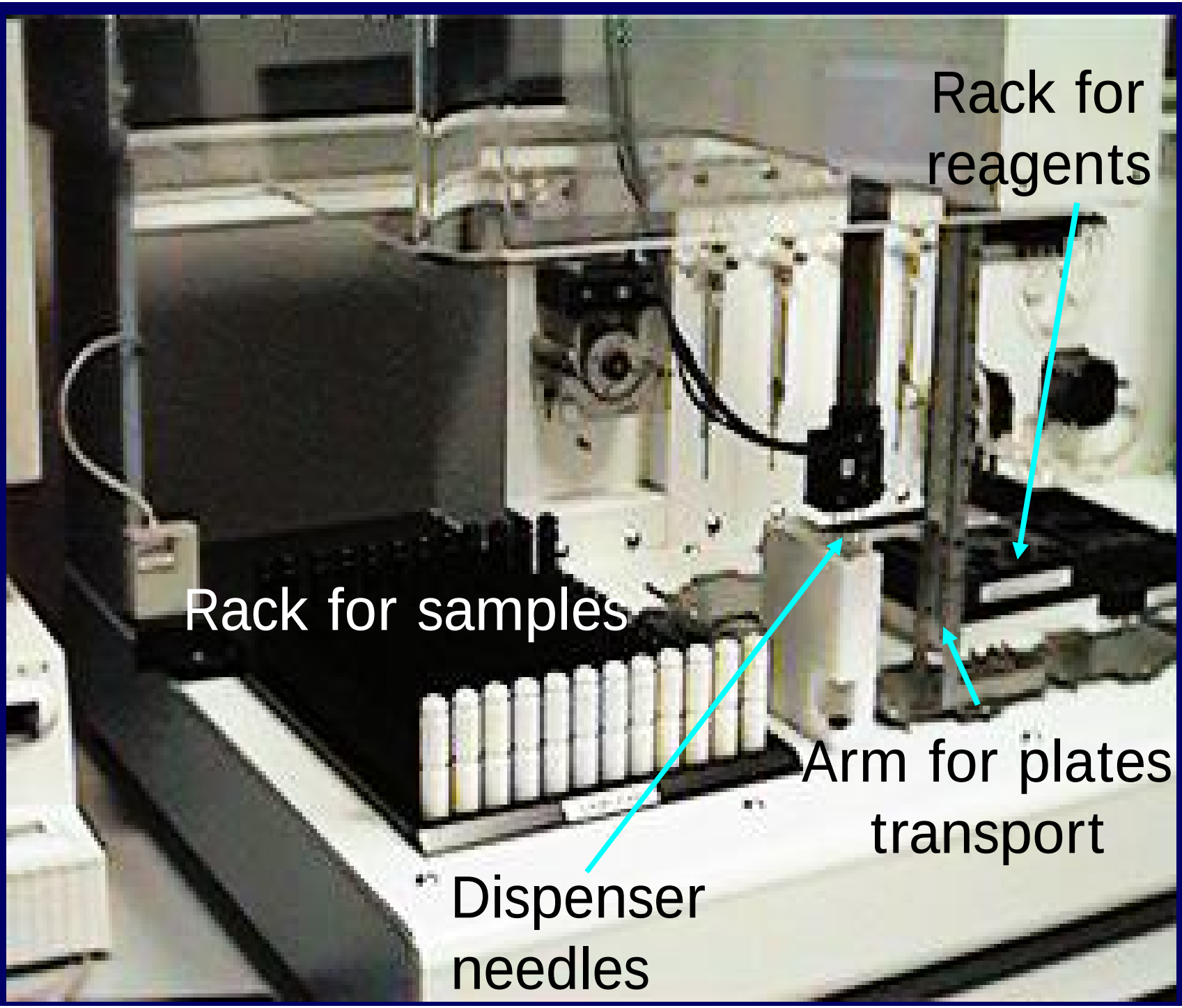
Evaluation of pre- and post-transfusion platelets counts in consecutive refractory and HLA allo-immunized hematology patients transfused in 33 months after implementation of the new policy.

Elements of our semi-automated platelet cross-matching system

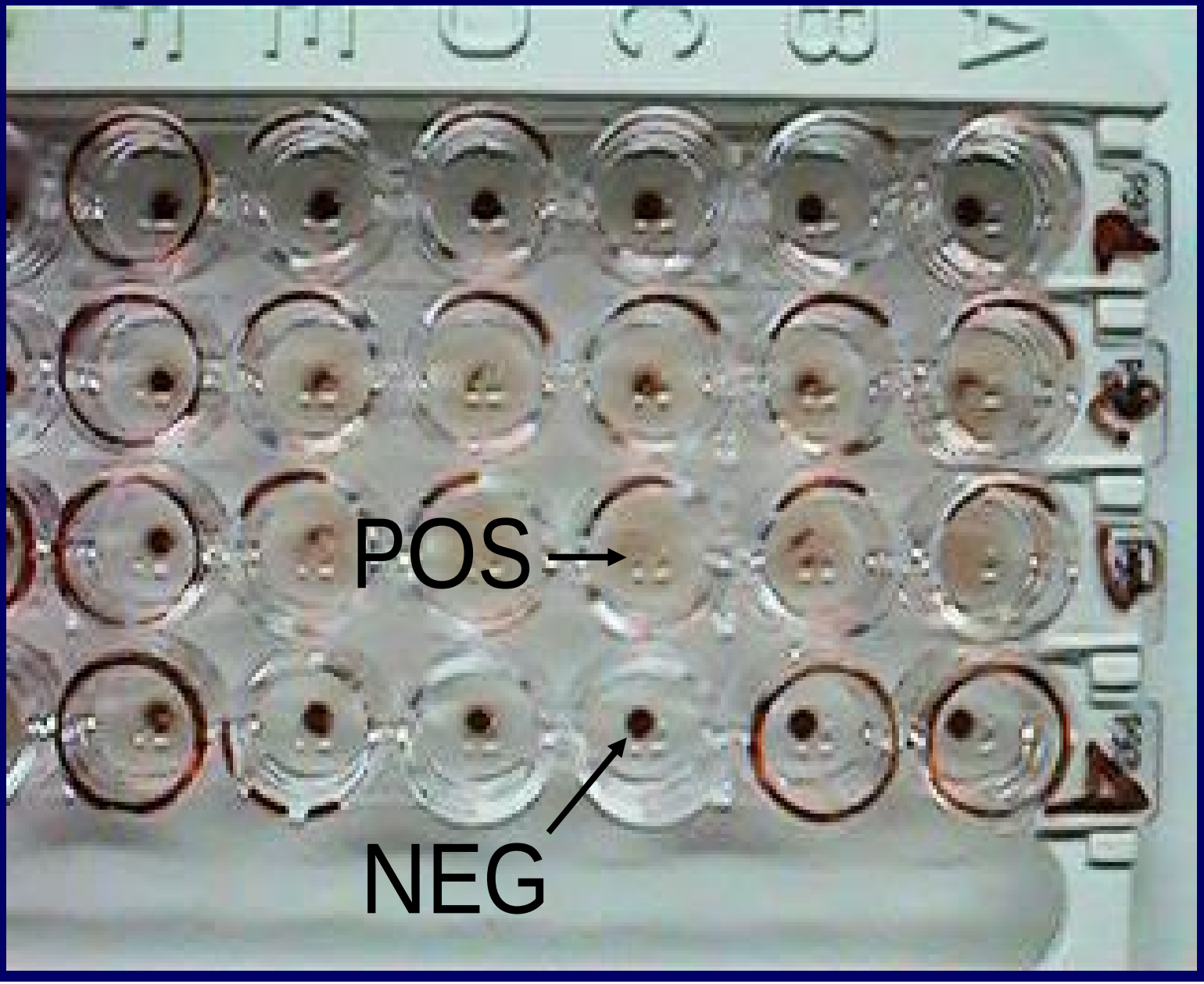
- Semi-automated instrument (originally ABS Precis → since 2003 Galileo, Immucor: sample processor, incubator, automated plate reader)
- Immunoadherence assay (Capture-P Immucor)

The semi-automated system




Rack for reagents
Rack for samples
Arm for plates transport
Dispenser needles

Test results



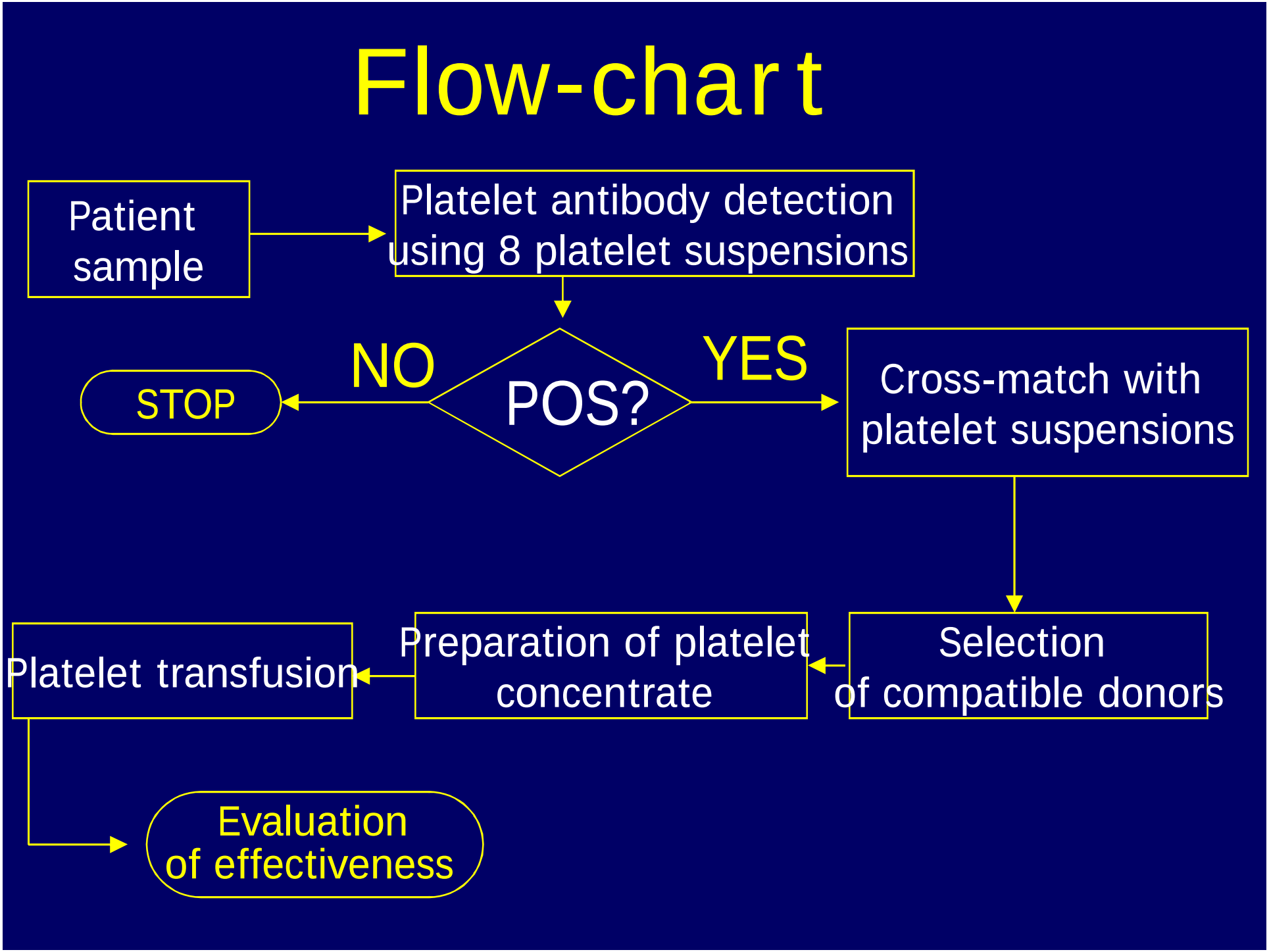
Selection of cross-match compatible platelets to refractory patients

- Random platelet supensions are obtained from supernatants of complete blood count (CBC) samples routinely collected (we collect approx 100 whole blood donations per day).
- CBC samples are used fresh or stored overnight.
- Buffy-coats from cross-match negative donors are pooled to obtain platelet concentrates (BC-PC)


Use of sedimented CBC
samples for cross-match


Platelet suspensions obtained by
CBC sample sedimentation

Flow-chart

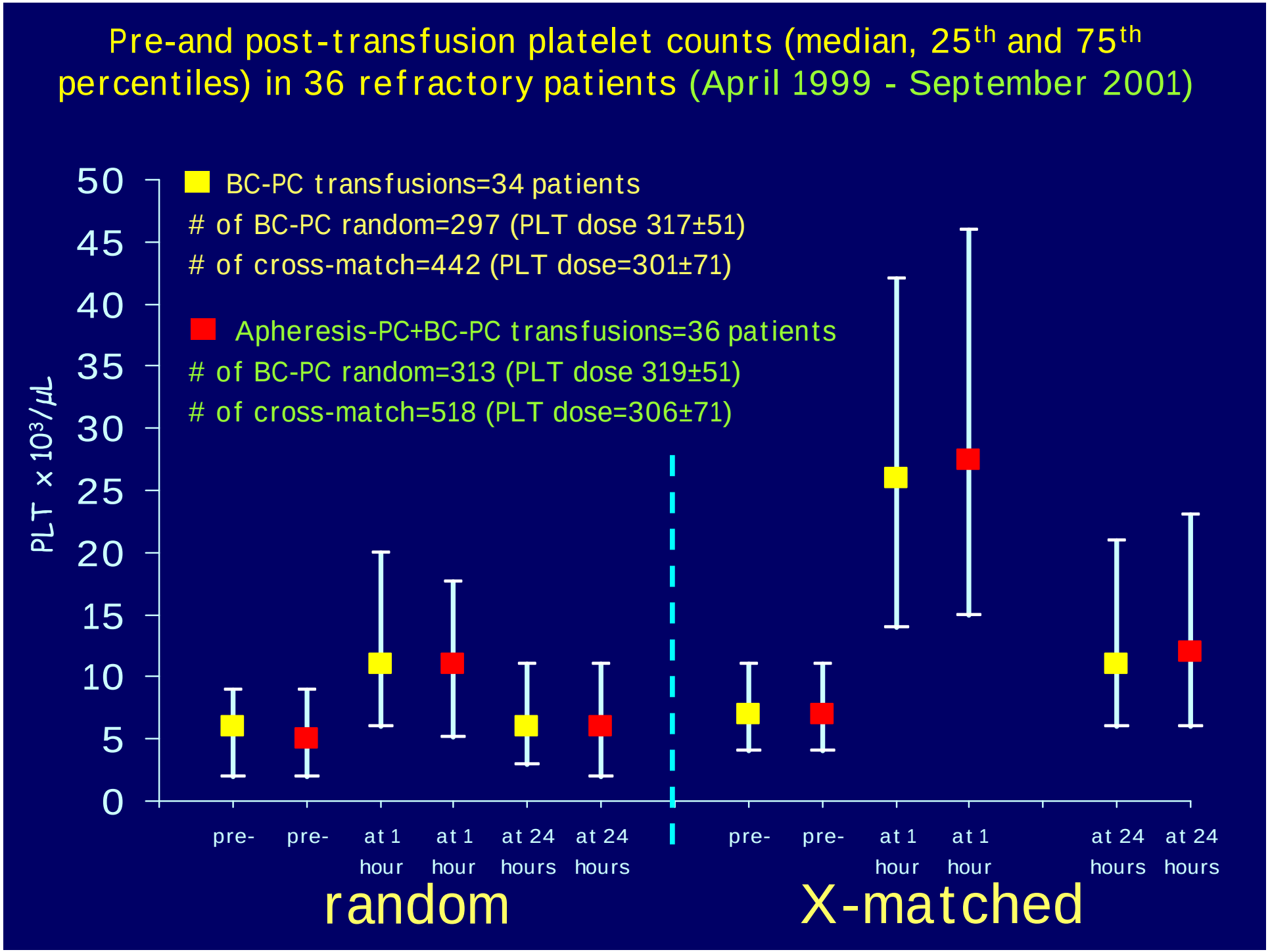

Patient sample
Platelet antibody detection using 8 platelet suspensions
POS?
NO
STOP
YES
Cross-match with platelet suspensions
Selection of compatible donors
Preparation of platelet concentrate
Platelet transfusion
Evaluation of effectiveness

		Standard platelets *n* = 6057 vol = 455 ± 46ml		WBC-reduced platelets *n* = 3144 vol = 408 ± 43 ml	
Year	**Donations per pool (*n*)**	Platelets (10^9)	WBC (10^6)	Platelets (10^9)	WBC (10^6)
1999-2000	6	347 ± 54	163 ± 116	336 ± 52	0·35 ± 0·27
2001	5	287 ± 40	75 ± 62	288 ± 45	0·50 ± 0·50

	MEN	WOMEN
# refractory patients (%)	13 (32·5)	27 (67·5)
Age (years, mean ± SD)	61±15	56±15
# of days from 1st transfusion to detection of refractoriness (mean ± SD)	219±180	119±187
# of patients that died during the study (%)	8 (61·5)	10 (37·0)
Pretransfusion platelet counts (10^9/l) of last three random donor platelet transfusions	4·9 ± 2·7 (*n* = 39)	4·6 ± 3·5 (*n* = 81)
1 h post-transfusion platelet counts (10^9/l) of last three random donor platelet transfusions	5·3 ± 4·0 (*n* = 7)	9·5 ± 9·3 (*n* = 22)
24 h post-transfusion platelet counts (10^9/l) of last three random donor platelet transfusions	4·7 ± 2·8 (*n* = 18)	4·3 ± 3·6 (*n* = 52)

No. of blood components transfused before and after detection of refractoriness (DR)

	Before DR		After DR	
Blood component	Standard (%)	WBC-reduced (%)	Standard (%)	WBC-reduced (%)
RBCs	553 (31·8)	205 (11·8)	54 (5·5)	315 (32·3)
Platelets	681 (39·2)	300 (17·2)	36 (3·7)	569 (58·4)
Total	1234 (71·0)	505 (29·0)	90 (9·3)	884 (90·7)

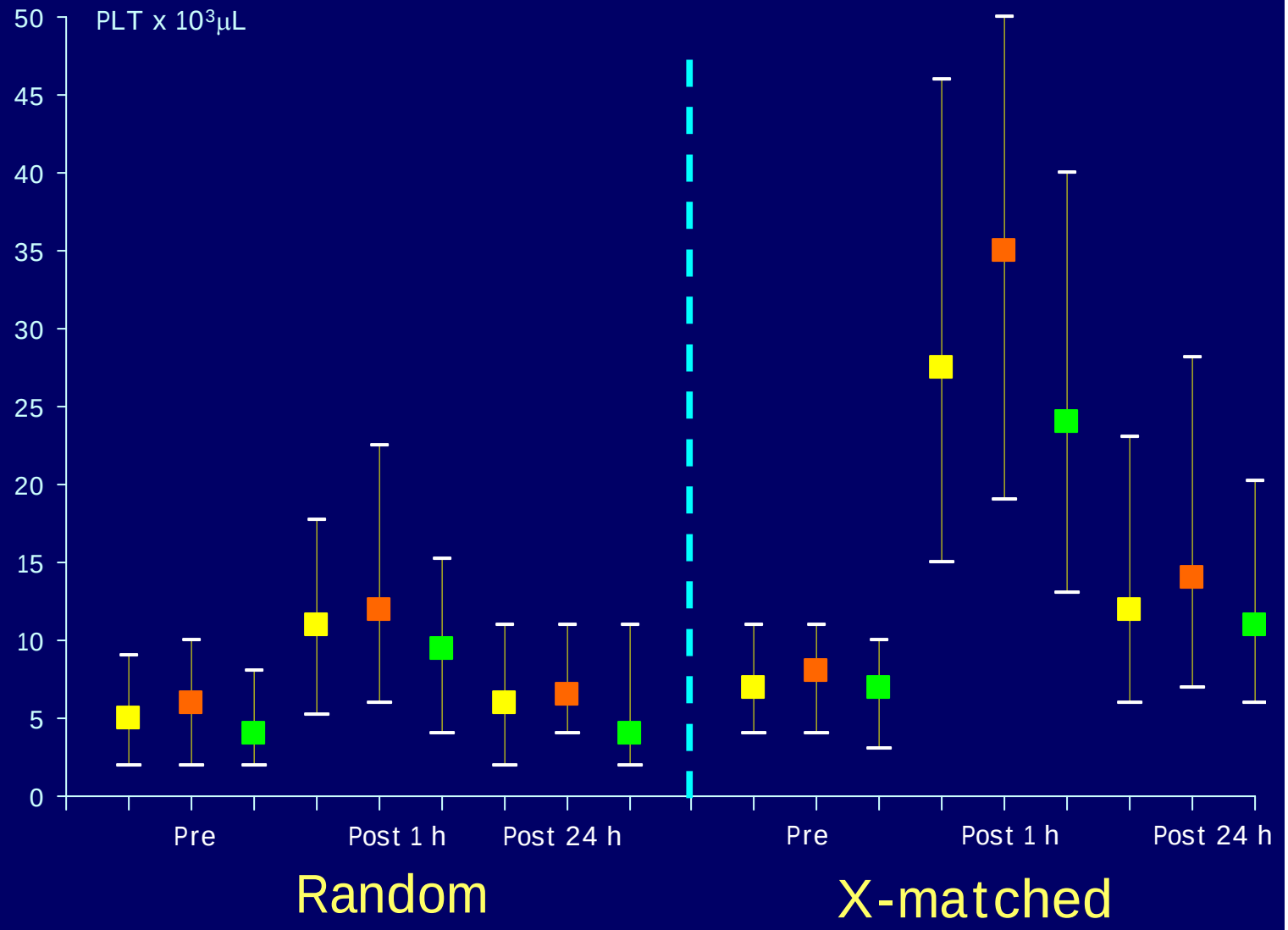

Pre-and post-transfusion platelet counts (median, 25th and 75th percentiles) in 36 refractory patients (April 1999 - September 2001)
BC-PC transfusions=34 patients
# of BC-PC random=297 (PLT dose 317±51)
# of cross-match=442 (PLT dose=301±71)
Apheresis-PC+BC-PC transfusions=36 patients
# of BC-PC random=313 (PLT dose 319±51)
# of cross-match=518 (PLT dose=306±71)
PLT x 10³/μL
50
45
40
35
30
25
20
15
10
5
0
pre-
pre-
at 1 hour
at 1 hour
at 24 hours
at 24 hours
pre-
pre-
at 1 hour
at 1 hour
at 24 hours
at 24 hours
random
X-matched

Pre-and post-transfusion platelet counts (median, 25th and 75th percentiles) in 36 refractory patients (April 1999 - September 2001)

All patients
random pool= 313
PLT dose= 319 ± 51
x-match= 518
PLT dose= 306 ± 71

19 Patient without detrimetal factors
random pool= 148
PLT dose 321 ± 54
x-match= 217
PLT dose=322 ± 72

17 Patients with detrimental factors
random pool= 165
PLT dose 320 ± 54
x-match = 301
PLT dose = 295 ± 69



Effective transfusions in refractory patients (April 1999 - September 2001)

Patients with detrimental factors

of PLT transfusions = 301

# of transfusions with 1 h post-PLT counts = 190 (63.1%)

# of 1 h post-PLT counts ≥10,000 μL = 159 (83.7%)

Δ ≥10,000 μL = 121 (63.7%)

Patients without detrimental factors

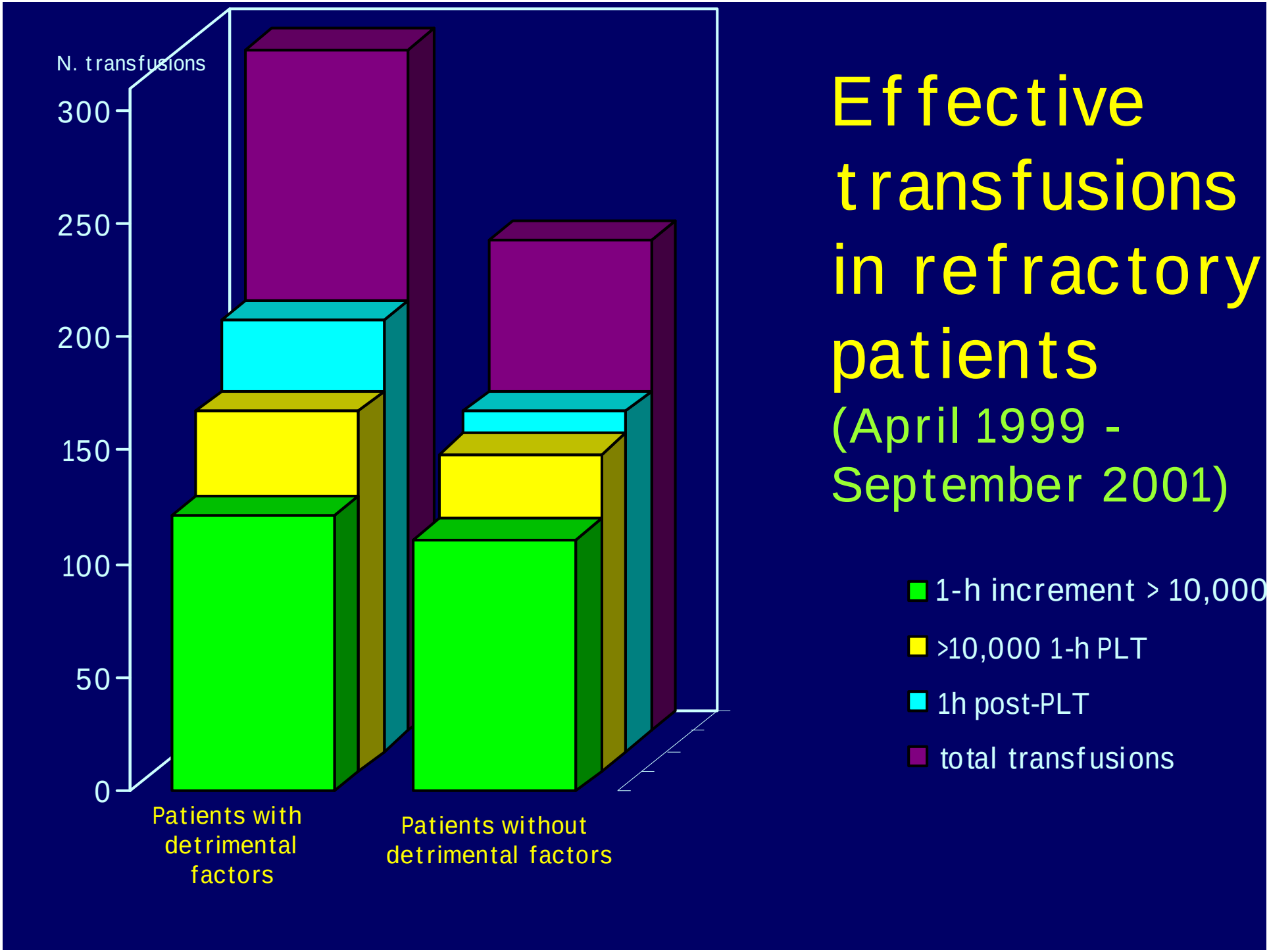
of PLT transfusions = 217

# of transfusions with 1 h post-PLT counts = 150 (69.1%)

# of 1 h post-PLT counts ≥10,000 μL = 140 (93.3%)

Δ ≥10,000 μL = 111 (74%)

Δ = (1 h PLT count post-transfusion) - (PLT count pre-transfusion)


N. transfusions
300
250
200
150
100
50
0
Patients with detrimental factors
Patients without detrimental factors
Effective transfusions in refractory patients
(April 1999 - September 2001)
1-h increment > 10,000
>10,000 1-h PLT
1h post-PLT
total transfusions

Technical time (minutes) to cross-match one patient serum with 90 platelet suspensions

Semi-automated system	160
Manual	
PSIFT	557
Immunoadherence	225

No. of effective transfusions(*) and no. of antibody detection kit wells used in refractory patients (1-18) to select cross-match neg platelets (April 1999 - September 2001)

Pt.	# wells	#effective/total transfusions	Pt.	# wells	#effective/total transfusions
1	268	5/11	10	444	2/5
2	117	13/15	11	134	0/2
3	1,082	11/23	12	340	6/7
4	15	5/5	13	129	1/1
5	127	2/2	14	1,965	30/45
6	271	1/4	15	1,198	14/16
7	1,487	24/52	16	891	4/20
8	1,430	17/35	17	1,713	15/31
9	857	9/25	18	308	0/2

(*) ($\Delta \geq$ 10,000 PLTs/μL)

No. of effective transfusions(*) and no. of antibody detection kit wells used in refractory patients (19-36) to select cross-match neg platelets (April 1999 - September 2001)

Pt.	# wells	#effective/total transfusions	Pt.	# wells	#effective/total transfusions
19	970	5/7	28	1,112	14/37
20	258	2/2	29	3,634	15/47
21	693	2/10	30	889	3/7
22	429	3/6	31	1,505	9/17
23	786	2/21	32	654	9/11
24	287	0/2	33	870	2/15
25	70	2/2	34	154	2/2
26	268	0/4	35	524	0/7
27	1,020	2/14	36	246	1/6

(*) ($\Delta \geq$ 10,000 PLTs/μL)

Reagent cost of platelet crossmatch in 40 refractory patients

(April 1999 - December 2001)

- Total cost of wells used for the refractory patients: US$105,530
- Total # of 'effective' transfusions ($\Delta \geq 10{,}000$ PLTs/μL): 236/348 evaluable at 1 h

- Plastic well cost per 'effective' transfusion: US$ 447

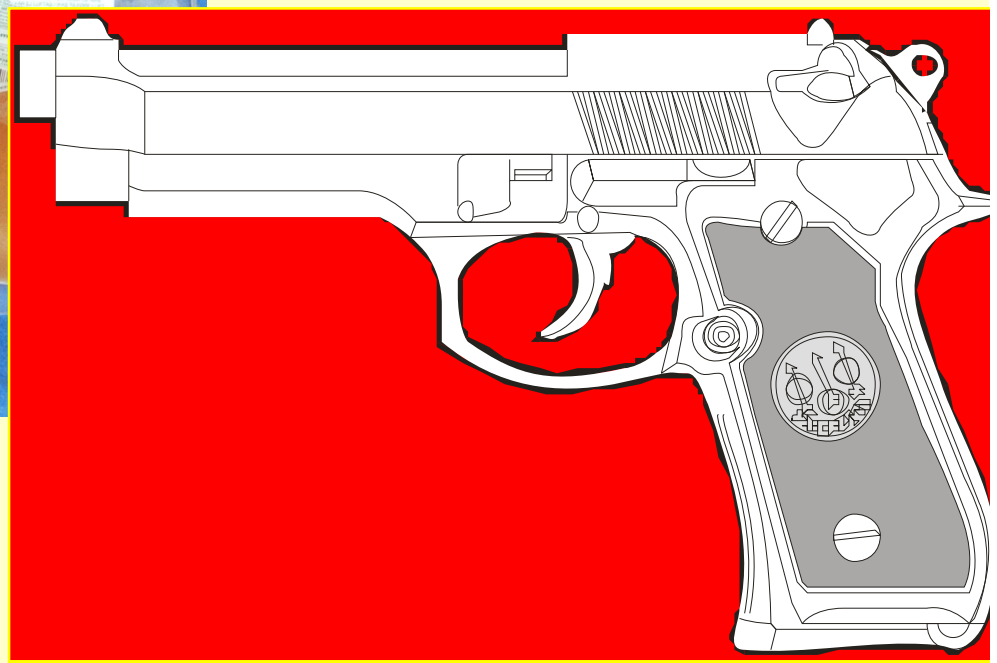
Conclusions

The platelet cross-matching program was able to select effective platelets in two thirds of 569 transfusions given to 40 consecutive refractory patients during 33 months of study

DO NOT TRANSFUSE

When bleeding prophylaxis is not recommended *(ASCO guidelines)*

- Severe thrombocytopenia in myelodysplasia and aplastic anemia
  - ➔ ‘ … many of these patients can be observed without prophylactic transfusions …’
- Refractory patients for whom matched platelets are not available
  - ➔ ‘ … the Panel recommends that such patients be transfused only for hemorrhagic events.’
- Thrombotic thrombocytopenic purpura
  - ➔ ‘ … risks of precipitating thromboses.’



The trigger
is only one part of the gun

Prophylactic platelet transfusion for haemorrhage after chemotherapy and stem cell transplantation (Review)

By Stanworth SJ, Hyde C, Heddle N, Rebulla P, Brunskill S, Murphy MF
The Cochrane Library 2004, issue 4, Wiley & Sons

- There is no reason to change current practice but uncertainty about the practice of prophylactic [platelet] transfusion therapy should be recognised .....

Art no. CD004269.pub2

Key factors for effective platelet support in oncology and hematology

- Platelet concentrates of good quality from carefully selected blood donors
- Patient monitoring and laboratory evaluation (signs of hemorrhage and anti-HLA antibody detection)
- Prompt treatment of refractoriness