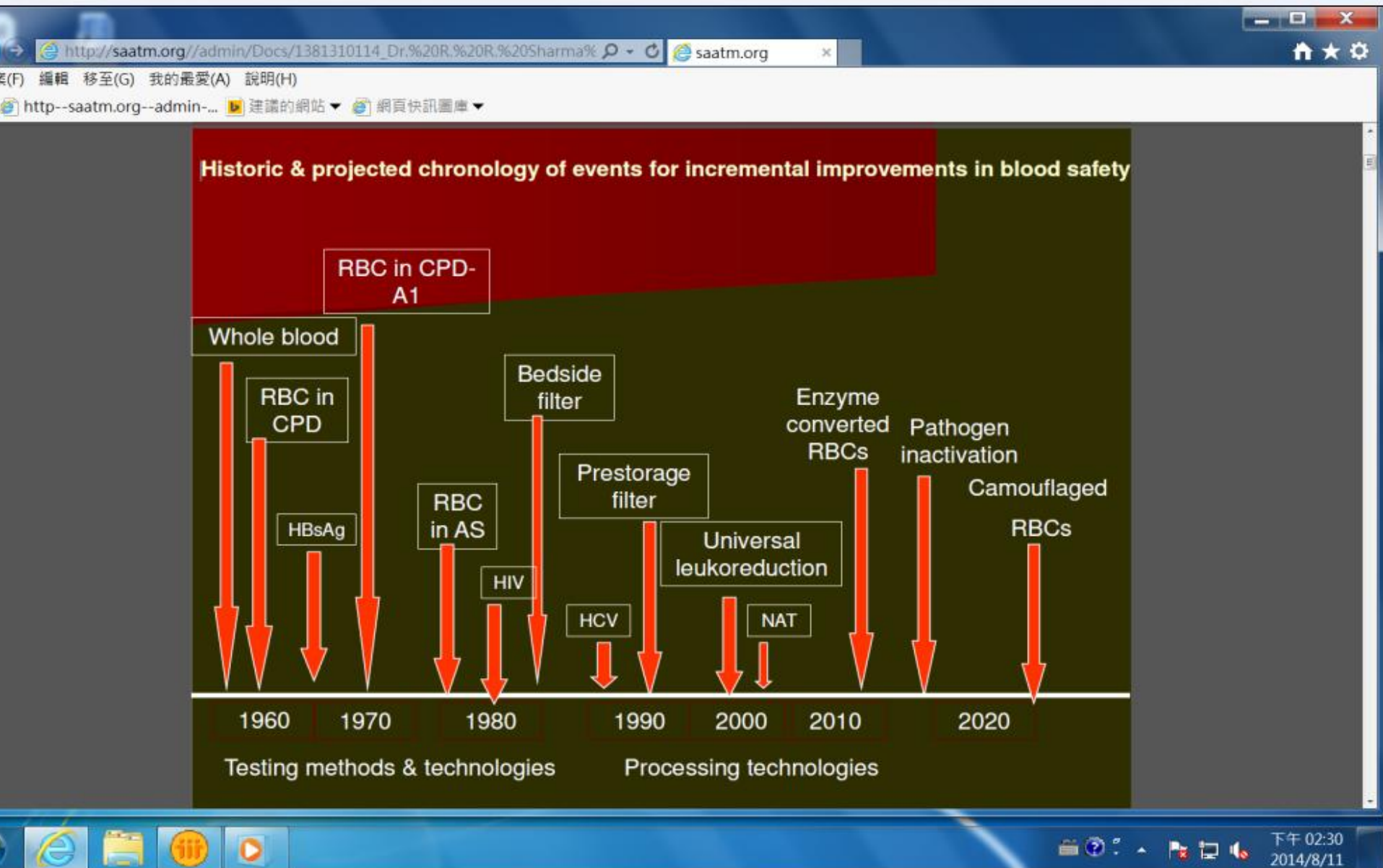


Prestorage leukoreduction blood product

臺中捐血中心

演講者:林啟靈 醫師



Classification of Transfusion-related Adverse Reactions and Estimated Incidence

Immunological		Incidence*	Non-immunological		Incidence*
Acute (<24 hours)	Haemolytic transfusion reactions	ABO/Rh mismatch 1:40,000 ^c	Massive transfusion complications		Variable ^{c,d}
		Acute	Non-immune mediated haemolysis (physical or chemical destruction of blood)		Rare ^c
		Fatal	Transfusion associated sepsis (for clinically apparent reactions)	Platelets	At least 1:75,000 ^a
	Febrile non-haemolytic transfusion reactions	0.1%–1% of transfusions with universal leucocyte depletion ^c		Red cells	At least 1:500,000 ^b
	Allergic reactions	Mild (urticarial) 1%–3% of transfusions ^c	Transfusion-associated circulatory overload (TACO)		Less than 1% of patients ^c
		Severe (anaphylaxis) 1:20,000–1:50,000 ^{b,c}			
	Transfusion-related acute lung injury (TRALI)		1:1,200–1:190,000 ^c		

Delayed (>24hours)	Delayed haemolytic transfusion reaction		1:2,500–1:11,000 ^{c,d}	Iron overload	Iron overload requiring chelation therapy	May occur after 10–20 RBC units ^e
	Post-transfusion purpura		Rare ^c		Iron overload with organ dysfunction	May occur after 50-100 RBC units ^c
	Transfusion-associated graft versus host disease (TA-GVHD)		Rare ^c	Transfusion-transmissible infections	For incidence rates refer to risk estimates for transfusion-transmissible infections	
	Alloimmunisation	RBC antigens	1:100 ^c			
		HLA antigens	1:10 ^c			
Transfusion-related immune modulation (TRIM)		Not known ^c				

Leukocyte content of whole blood average two billion(2×10^9)Leukocyte per 500 ML of whole blood.

during blood component preparation :

90% of leukocytes fractionate with the red blood cell(RBC_s)

8% is retained within platelet concentrates

2% are present in plasma

Proven Benefits of Leukoreduction

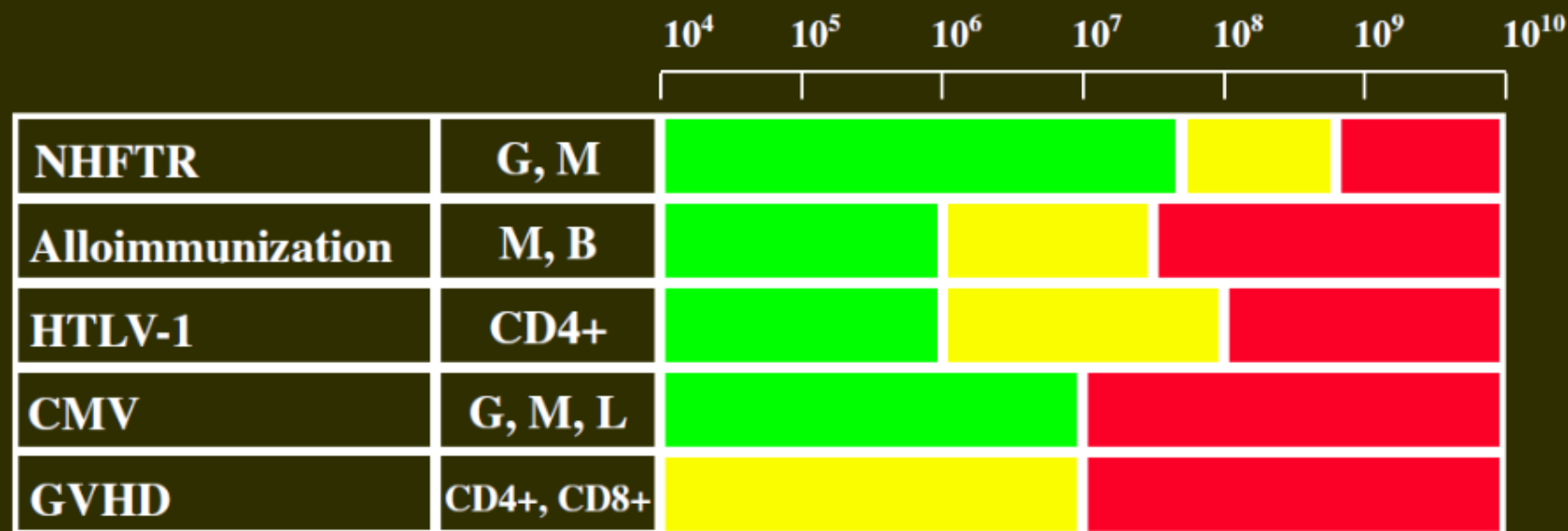
- Reduced febrile transfusion reactions
- Reduced HLA alloimmunization
reduced platelet refractoriness
- Reduced CMV transmission

UNIVERSAL LEUKOREDUCTION(2)

Canada, Austria ,France, Great britian, Ireland, Norway, Netherland, Portugal, Spain, Japan, Germany, are already implementing universal leukocyte reduction of their blood supplies

Leukodepletion - How far

■ Transfusion Reaction (WBC-associated)



 : High occurrence
  : Unknown
  : Preventable

AMERICAN ASSOCIATION OF BLOOD BANK

leukocyte content in a blood component unit should be less than 5×10^6 /unit after leukoreduction (3log reduction 99.9%) with a minimum Of 85% **red cell recovery in 95% of the units tested.**

EUROPEAN COUNCIL GUIDELINES are a little more stringent in terms of residual leukocyte content and require it to be less than 1×10^6 /unit

Type of Leukocyte Filters

Table 2. Leukocyte Reduction Filters

Generation	Pore Size	Mechanism	Purpose
First	170–260 μm	Screen filter	No leukocyte filtration; “standard” blood filter
Second	20–49 μm	Screen filter	Microaggregate filter; leukocyte filtration < 90%
Third	Not applicable	Adhesion filter	Adsorption filter; leukocyte filtration > 99.9%

Prestorage vs. bedside

Bedside filtration
reduction in
Allosensitization to HLA
lowering of the rate of
refractoriness to platelet
transfusion

prestorage
in addition:
reduction of febrile non-
hemolytic transfusion
reactions by prevention
of cytokine accumulation

FEBRILE NONHEMOLYTIC TRANSFUSION REACTION


Incidence

0.5% in patients receiving a first blood transfusion

60% in chronically transfused patients

FNHTR

(Febrile non-hemolytic transfusion reaction)



The occurrence of $\geq 1^{\circ}\text{C}$ rise in temperature above 37°C , associated with transfusion, for which no other is identifiable.

FNHTR MECHANISM

- A. recipient **antibodies reacting donor leukocyte** and stimulating the release of **cytokine** from the donor cell

- B. passive transfer of **cytokine that accumulate** in whole blood derived platelet concentrates during **storage.**

- 1)The amounts of IL- 1, IL-8, and TNF alpha increased during the storage period.
- 2)Filtered units had lower concentrations of IL-1, IL-6, IL-8, and TNF alpha after 2 weeks of storage than did the control and WBC-rich units.
- 3)The amounts of cytokines in filtered units did not increase during the study period.
- 4)CONCLUSION: Prestorage filtration seems to diminish the amount of IL-1, IL-6, IL-8, and TNF alpha RBCs during storage.

- * IL-8 and IL-1 beta accumulated in the supernatants of stored RBCs despite cold storage conditions.
- * WBC filtration early in storage prevented the accumulation of IL-8

Transfusion

Volume 35, Issue 3, pages 199–203, March 1995

Febrile Transfusion Reaction

DAYS OF STORAGE OF PLATELET CONCENTRATES (range)	IL-1B(pg/ml) median(range)	IL-6(pg/ml) median
NOT LEUKOCYTE REDUCE		
• 1 DAY	0	1
• 3 DAYS	4	64
• 5 DAYS	14	540
• 10 DAYS	106	1314
• LEUKOCYTE REDUCED		
• 1 DAY	0	2
• 3 DAYS	0	8
• 5 DAYS	0	6
• 10 DAYS	0	5
•	Heddle N Eng J Med 1994	

Effect of Prestorage Leukocyte Reduction on the Rate of FNHTRs

Authors	Non-LR RBCs	LR-RBCs	Non LR- Plts ~~~~~	LR- Plts ~~~~~
Yazar et al. ¹ ~~~~~	0.33%	0.19% (p<0.001)	0.45%	0.11%(p<0.001)
Paglino et al. ² ~~~~~	0.34%	0.18%(p<0.001)	2.18%	0.15%(p<0.001)
King et al. ³	0.37%	0.19%(p=0.0008)	NA	NA

1. Transfusion 2004;44:10-15,
3. Transfusion 2004;44:25-29

2. Transfusion 2004;44:16-24

Table 1. . FNHTR before and after transition to leukoreduced RBC inventory

Date	RBC transfusions	Percentage of leukoreduced RBCs	Total TR [*] (%)†	Allergic TR (%)†	FNHTR (%)†
July-December 1994	16,246	4.0	91 (0.56)	24 (0.15)	60 (0.37)
July-December 2001	19,916	99.5	79 (0.40)	34 (0.17)	37 (0.19)
p value			0.024	0.59	0.0008

* Total TRs including allergic, FNHTRs, as well as other reactions associated with RBCs (e.g., acute and delayed hemolytic TRs).

† Reactions as a percentage of total units transfused.

Transfusion⁺

[Volume 44, Issue 1, pages 25–29, January 2004⁺](#)

Prevention of HLA alloimmunization and platelet refractoriness

- .donor antigen presenting cell are able to present HLA class I and II antigen to recipient T-cell. Which result in host anti-HLA antibody production
- . it is confirmed that prestorage leukoreduction was highly effective at lowering HLA alloimmunization

HLA Alloimmunization

Cause of **platelet refractoriness**

.Alloimmunization

--**HLA antibody** (70-80%)

--**platelet antibody** (20-30%)

Non-immune causes

--consumption:sepsis.DIC.GVHD

--Sequestration:splenomegaly

--Drug-related

HLA Alloimmunization

Animal study: 8 weekly infusions in rabbits

Filtration	platelet survival	refractory state
Prestorage LR	54.7 hr	33%
Post-storage LR	31 hr	67%
No LR	18.5hr	96%

B lajchman Blood 1992;79:1731

Table 2. Number of newly detected RBC alloantibodies in transfused patients with AML during two periods with different types of RBC transfusions

Antigen	Non-WBC-reduced transfusion recipients 1978–1989	WBC-reduced transfusion recipients 1990–2001
Number	195	215
K	6	4
E	8	2
C	2	0
Jk ^a	1	0
S	1	0
c	3	0
Jk ^b	1	0
Kp ^a	0	1
Total	22	7

Transfusion⁴

[Volume 43, Issue 7](#), pages 945–952, July 2003⁴

Transmission of leukocyte associated viruses (eg cytomegalovirus)

Transfusion-associated CMV infection is a significant morbidity and mortality in Immune-compromised patients and especially in **organ transplant** recipients

Prevent of leukocyte-transmitted infections

.leukoreduction can reduced the transmission
Of leukocyte-borne viruses.such as **CMV**.

And Epstein barr virus(**EBV**)

.most studies focus on CMV transmission.since it
can be associated **with high morbidity and
mortality** for **immunosuppressed** patients

CMV Transmission

- * CMV can be transmitted by transfusion
- * CMV resides in WBC
- * CMV transmission can be reduced by removing WBC(leukoreduction/filtration)
- * removal of WBC is equally effective as screening for antibody

CMV transmission

	Not filtered	filtered	p value
CMV infection	9/24	0/30	
	21%	0%	0.005

Lancet 1989 ;3 June:1228-1231

Leukoreduction in Cardiac Surger

Preoperative and Demographic Variables and Results for Transfusion Recipients* (*US Study*)

	Not Leukocyte-Reduced, 1997 (n = 171)	Leukocyte-Reduced, 1998 (n = 159)	Percent Chang
Variables			
Age (y)	70 ± 10	69 ± 11	—
Weight (kg)	77 ± 15	81 ± 18	—
Ejection fraction (%)	47 ± 14	47 ± 13	—
Female patients (%)	49	48	—
Emergency cases (%)	11	14	—
Urgent cases (%)	51	51	—
Elective cases (%)	38	35	—
Units of RBC transfusions, day 1	3.6 ± 2.8	3.6 ± 3.5	—
Hematocrit value			—
Preoperative	39 ± 4.9 (0.39 ± 0.05)	39 ± 4.3 (0.39 ± 0.04)	—
Postoperative	29 ± 4.2 (0.29 ± 0.04)	29 ± 3.7 (0.29 ± 0.04)	—
Discharge	30 ± 3.3 (0.30 ± 0.03)	30 ± 3.3 (0.30 ± 0.03)	—
Results			
Length of stay (d)	15.1 ± 22.1	12.4 ± 12.6	-18
Total charges (\$)	46,000 ± 56,800	40,900 ± 37,300	-11
Total costs (\$)	29,900 ± 36,300	28,200 ± 25,100	-6
Hours in the intensive care unit	118 ± 385	81 ± 162	-31
Hours of ventilator use	80 ± 35	33 ± 120	-59
Days of antibiotic therapy	6.7 ± 22	4.6 ± 10	-31
Days with fever	6.9 ± 11	5.4 ± 6	-22
Deaths during hospitalization (%)	5.3	3.2	-40

* Data are given as mean ± 1 SD unless otherwise indicated.

Am J Clin Pathol 2002;118:376-381

In the absence of definitive evidence-based studies, **pretransfusion medication** to prevent transfusion reactions should not be encouraged

Transfusion

Volume 48, Issue 11, pages 2274–2276, November 2008

We did not find evidence to support the use of premedications in minimizing
transfusion-related reactions

we question the need for this practice in settings where leukoreduction is used.↵

Journal of Pediatric Oncology Nursing **May 2, 2014**↵

Cost Analyses of the Use of Leukoreduced Transfusions

Study	Sample Size	Study Design	Control Arm	Treatment Arm	Outcomes	Cost Savings
Blumberg <i>et al.</i> ²⁴	N = 169	Retrospective cohort	<u>BMT</u> : ABO-unmatched/ non-LR allogeneic blood <u>Acute Leukemia</u> : ABO-unmatched/ non-LR allogeneic blood & ABO-ID /non-LR allogeneic blood	<u>BMT</u> : ABO-Identical/LR allogeneic blood <u>Acute Leukemia</u> : ABO-ID/LR allogeneic blood	Reduced resource consumption and costs of care with use of LR products	<u>BMT</u> : Mean hospital costs decreased by \$26,000/ patient <u>Acute Leukemia</u> : Mean hospital costs decreased by \$14,000/ patient
Jensen <i>et al.</i> ²⁵	N = 197	Randomized, controlled trial	Non-LR whole blood	LR whole blood	Decreased hospital costs, frequency of post-operative	\$4,480 decrease in hospital costs/patient

Transfusion Alternatives in Transfusion Medicine

Volume 4, Issue 5, Article first published online: 28 JUN 2008

Table 2

Cost Analyses of the Use of Leukoreduced Transfusions

Blumberg <i>et al.</i> ⁹	N = 330	Implementation trial	Non-LR allogeneic blood	LR allogeneic blood	Decreased costs of care with use of LR transfusions	Mean cost savings of \$1,700 /patient with the use of LR allogeneic blood (unadjusted for inflation)
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adverse effects of leukoreduction

- * loss of blood cell
- * Hypotensive reaction(ACE inhibitors)
- * RED EYE SYNDROME

- * Hypotensive reactions can occur with blood products that are LR before storage
- * these reactions that may be occurring more frequently now that **ACE inhibitors** are so commonly prescribed.

Transfusion

[Volume 44, Issue 9,](#) pages 1361–1366, September 2004

The pathophysiology of HyTRs is not fully understood. Circumstantial evidence supports the hypothesis that increased bradykinin (BK) levels, as seen with the use of negatively charged leukoreduction filters and the use of ACEi, is a major contributor to the pathophysiology of HyTR.

Transfusion

Volume 55, Issue 7, pages 1668–
1674, July 2015

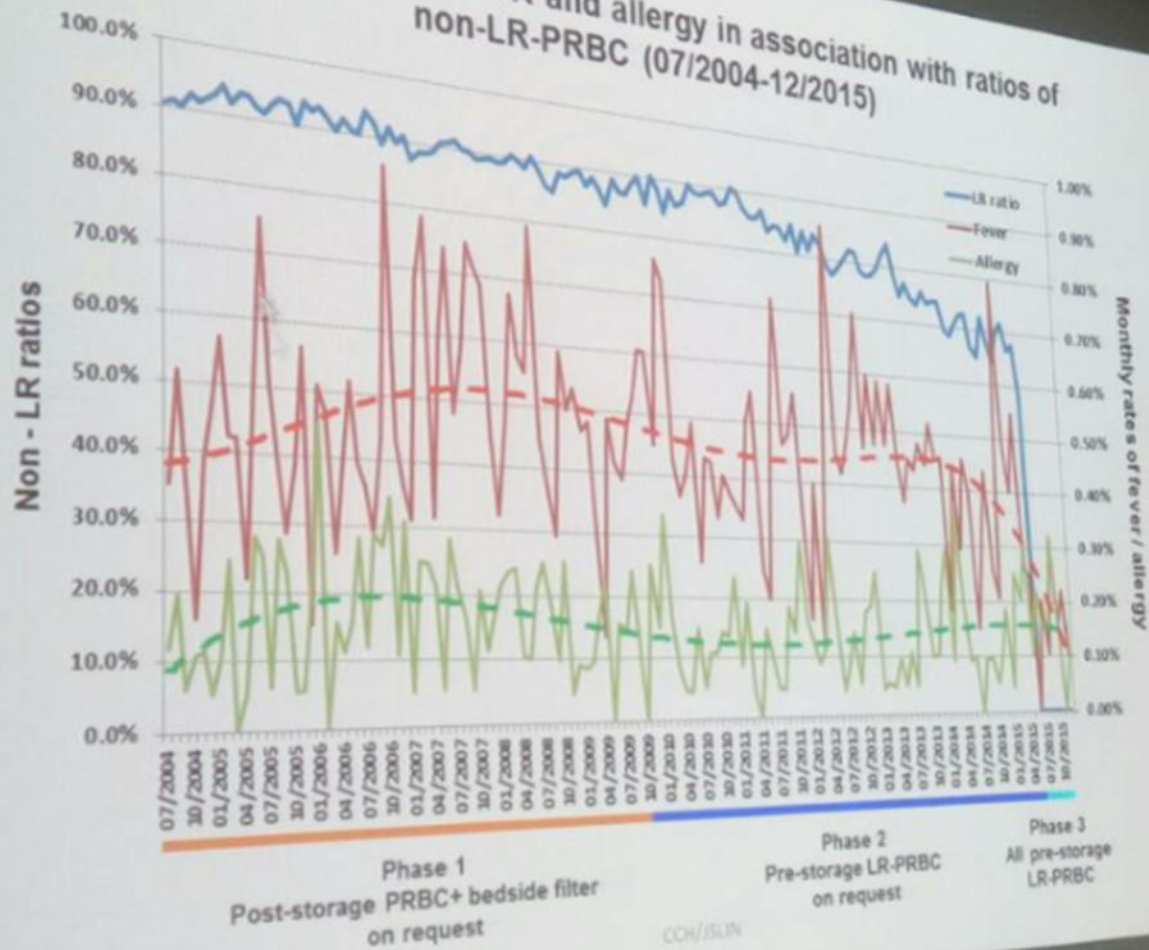
紅血球濃厚液

時程/ 減白紅血球濃厚液	總輸血人 次	PRBC輸血 人次	非減白 率(%)	NHFR		Allergy	
				人次	發生率%	人次	發生率%
2004.07-2009.10 貯存後減白 (床邊)	194876	120687	90.3	568	0.47	193	0.16
2009.11-2015.05 貯存前減白 (捐中供應)	204513	141878	79.8	622	0.44	194	0.14
2015.06-2015.12 100%貯存前減白 (捐中供應)	19940	13330	0	21	0.16	21	0.16

CON/SUN

2016/2/19

Monthly rates of NHFTR and allergy in association with ratios of non-LR-PRBC (07/2004-12/2015)





Collection Date Unit Number EXPIRES

滅除白血球之
紅血球濃厚液



- 注意事項：
1. 儲存於1-8℃。
2. 輸血時，請使用有過濾器之輸血管路。
3. 請留意含和輸血可能發生的風險。

本品品為500ml全血製備。

抗凝劑：☒ CPD-SAGM
☐ CPDA-1

台灣血液基金會台灣中區血中心
台北市中區路3段134號30號



O+

製備日期: 2012/07/09

有效期限: 2012/08/20

See
card



This product may contain a ...
PROPERLY IDENTIFY INTERGOV. HOLDING.

Collection/Processing
I.D. Label Here

BPFB 1150694

Manufactured for:
Pall Corporation
Port Washington, NY 11050, USA

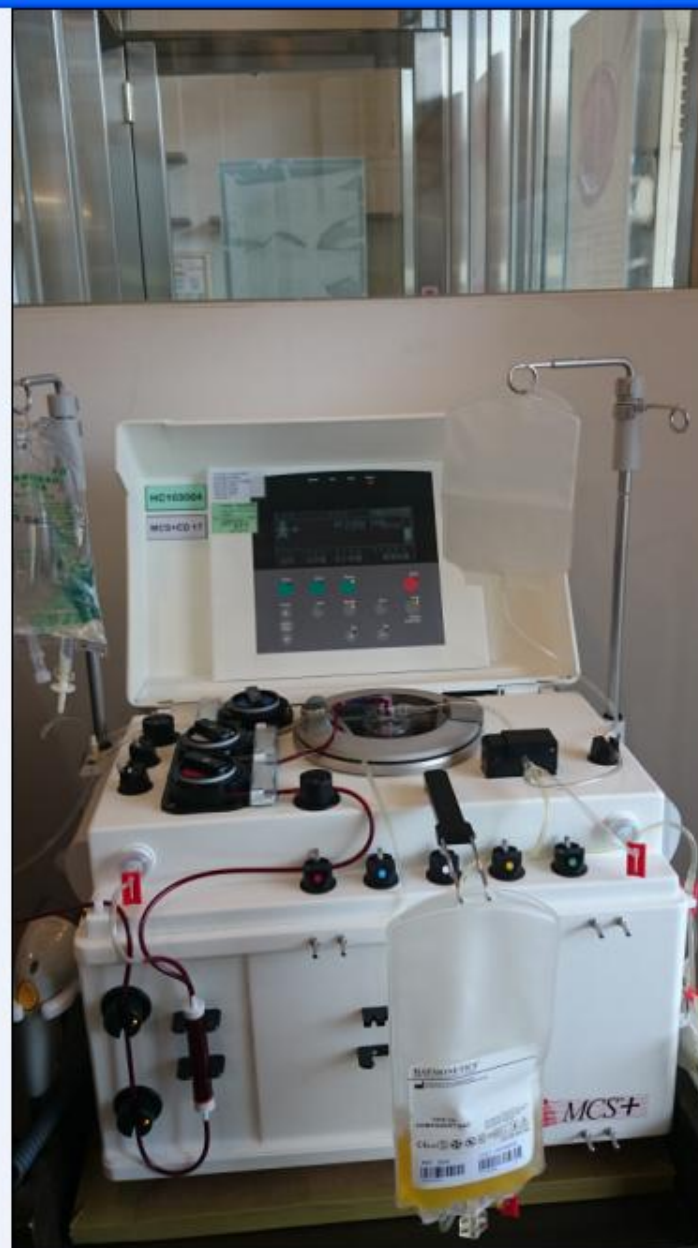


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Summary – Leukoreduction

Table 1. Adverse Effects Associated with Donor Leukocytes

Definitive

- Nonhemolytic febrile transfusion reactions
- Transmission of leukocyte-associated viruses
 - Cytomegalovirus, Epstein-Barr virus, human T cell leukemia virus type 1
- Alloimmunization

Probable

- Immunomodulatory effects
 - Cancer recurrence
 - Postoperative infections

Potential

- Reperfusion injury
- Transfusion storage time for red blood cells and platelets
- Transfusion-related acute lung injury
- Transfusion-associated graft-versus-host disease
- Reactivation of human immunodeficiency virus

Table 4. Advantages of Universal Leukocyte Reduction

Definitive

- Decreased nonhemolytic febrile transfusion reactions
- Decreased platelet refractoriness because of alloimmunization
- Decreased cytomegalovirus transmission

Probable

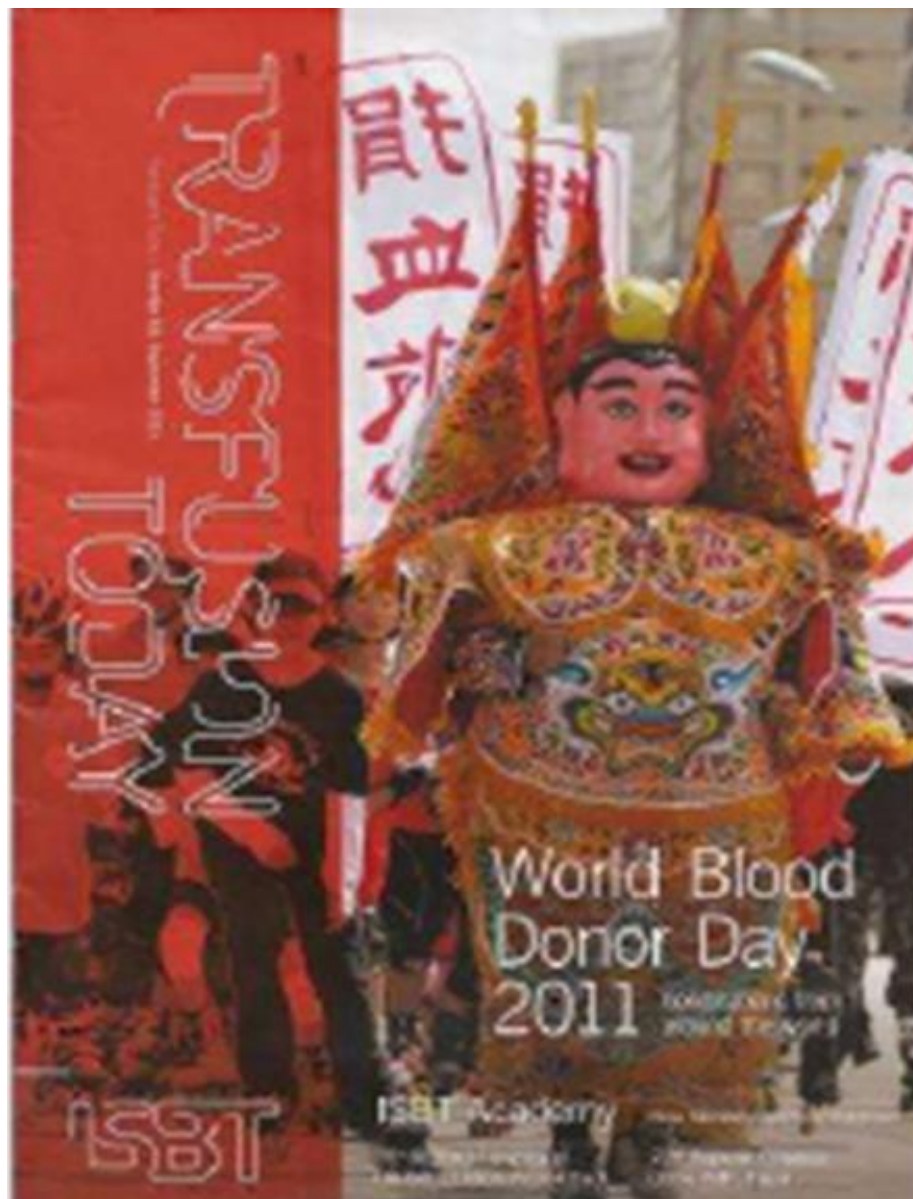
- Decreased allergic reactions
- Decreased postoperative infections

Potential

- Reduction or elimination of new variant Creutzfeldt-Jakob disease
- Decreased reperfusion injury
- Decreased transfusion-related acute lung injury
- Improved storage conditions for red blood cells and platelets

➤ 中央健康保險局中區業務組統計

年/季	項目		健保編號	抽審醫令量	核減醫令量	核減比率
103/Q4	減白	RBC	93019C	195	0	0
		血小板	93023C	45	3	6.7
	非減白	RBC	93001C	3025	51	1.7
		血小板	93007C	119	4	3.4
		Total		3384	58	1.7



Thanks for your attention