The transfusion of blood and blood components

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Blood components

- Red Blood Cells
  - 42 d at 2-6°C
- Platelets
  - 5-7 d at 20-24°C
- (Fresh Frozen) Plasma
  - 12 months at -40°C

Red Blood Cells for transfusion prepared from 450 mL whole blood (I)

- Terminology:
  - Packed Red Cells
  - Erythrocyte concentrates
- Volume: about 180 mL RBC + 100 mL crystalloid storage solution (+/- 10%)
- Hematocrit: 55-80%
- Hemoglobin: >45-50 g
- Storage: 42 d at 4 +/- 2° C

Red Blood Cells for transfusion prepared from 450 mL whole blood (II)

- Shelf life based on:
  - Hemolysis < 0.8%
  - Post-transfusion survival >75% at 24 h
- RBC main modifications during storage:
  - ATP & DPG decline, pH fall
  - Membrane rigidity, microvesciculation
- Effect: 1 g/dL Hb increase in average adult recipient (about 3 g/dL in children)

Red Blood Cells for transfusion prepared from 450 mL whole blood (III)

- ABO & Rh compatibility
  - Blood grouping +/- cross-matching
  - Irregular RBC abs detection in the recipient
  - Type & Screen
- Further processing
  - Filtration (> 99.9% WBC removal)
  - Washing (removal of plasma protein, electrolytes, antibodies)
  - Gamma irradiation at 2,500 cGy (WBC inactivation)
  - Cryopreservation at -80°C (long term storage)

Klein et al: Red blood cell transfusion in clinical practice
Lancet 2007;370:415

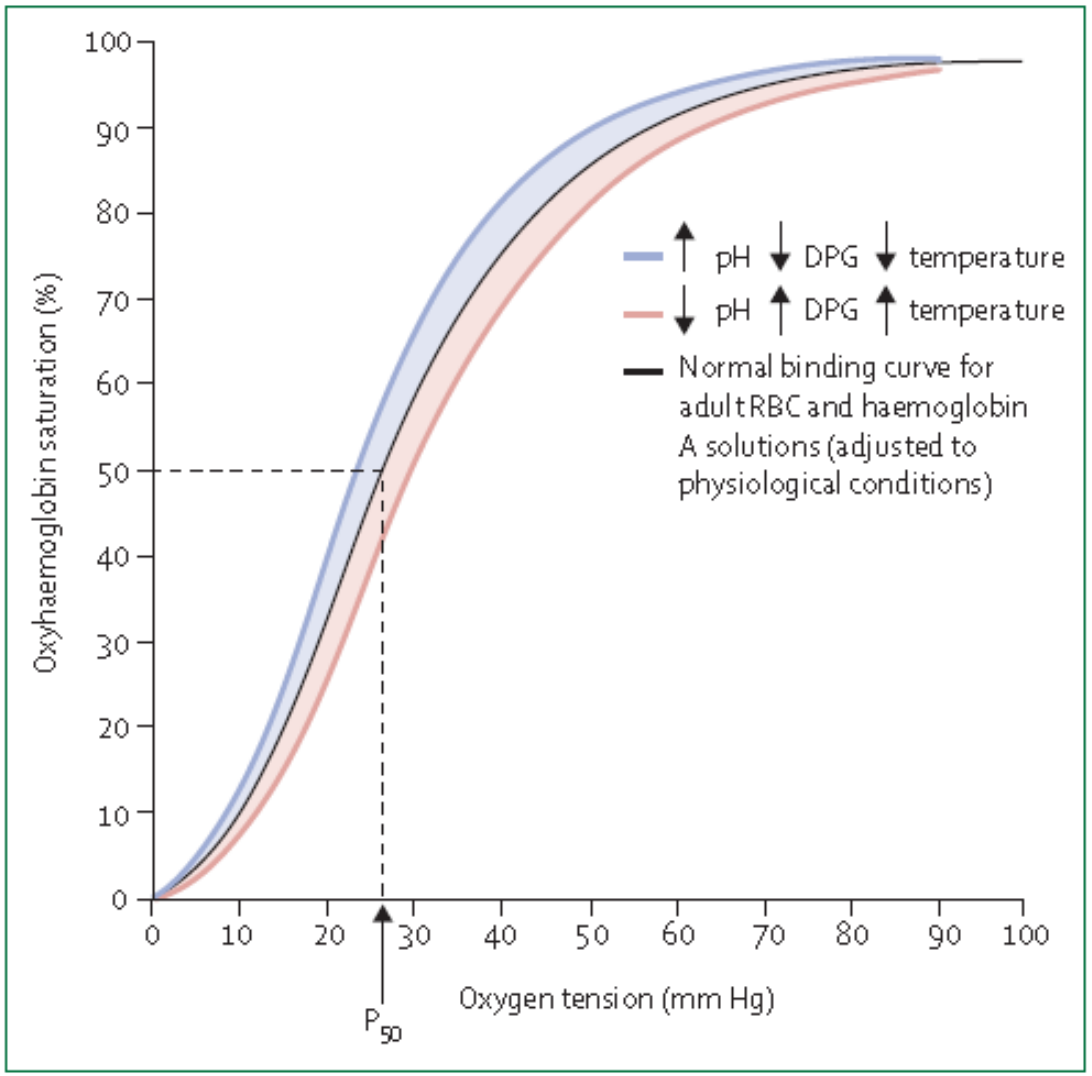


***Figure 1*: The oxygen-haemoglobin dissociation curve**
P50=the oxygen tension at which oxyhaemoglobin is 50% saturated.

Klein et al: Red blood cell transfusion in clinical practice
Lancet 2007;370:415

Panel: Oxygen delivery and consumption

$CaO_2 = (Hb \times 1{\cdot}34 \times SaO_2) + (PaO_2 \times 0{\cdot}003)$

$DO_2 = \text{cardiac output} \times CaO_2$

$VO_2 = \text{cardiac output} \times (CaO_2 - CvO_2)$

$VO_2 = \text{cardicac output} \times ([Hb \times 1{\cdot}34 \times (SaO_2 - SvO_2) + (PaO_2 - PvO_2) \times 0{\cdot}003])$

CaO_2 = Arterial oxygen content
CvO_2 = Venous oxygen content

DO_2 = Oxygen delivery
VO_2 = Oxygen consumption

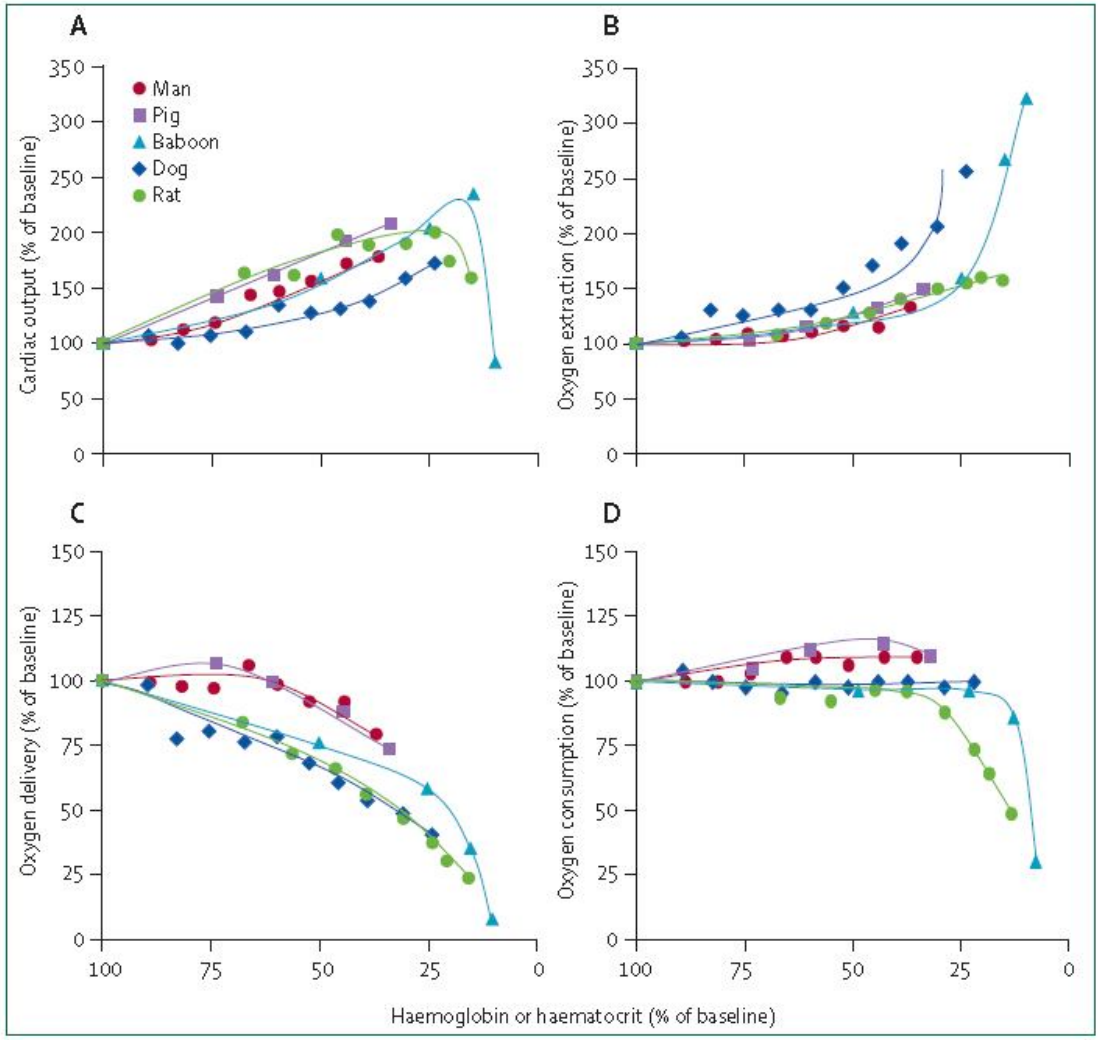


Figure 2: **Relative changes in cardiac output (A) oxygen extraction (B), oxygen delivery (C), and oxygen consumption (D) as haemoglobin concentration decreases in humans, pigs, baboons, dogs, and rats**
The combined increases in cardiac output and oxygen extraction allow maintainance of oxygen consumption until low haemoglobin levels. At extremely low haemoglobin levels, cardiac output and oxygen consumption can fall, indicating the exhaustion of the compensatory mechanisms. Data are from the original articles,[41-45] the curves were approximated.

Blood transfusion

- Hemovigilance
- Risks
- Adverse events
- Reactions

Emovigilanza

I principali programmi di emovigilanza in Europa

Francia: Hemovigilance network

(Transfusion 2002; 42: 1356-1364)

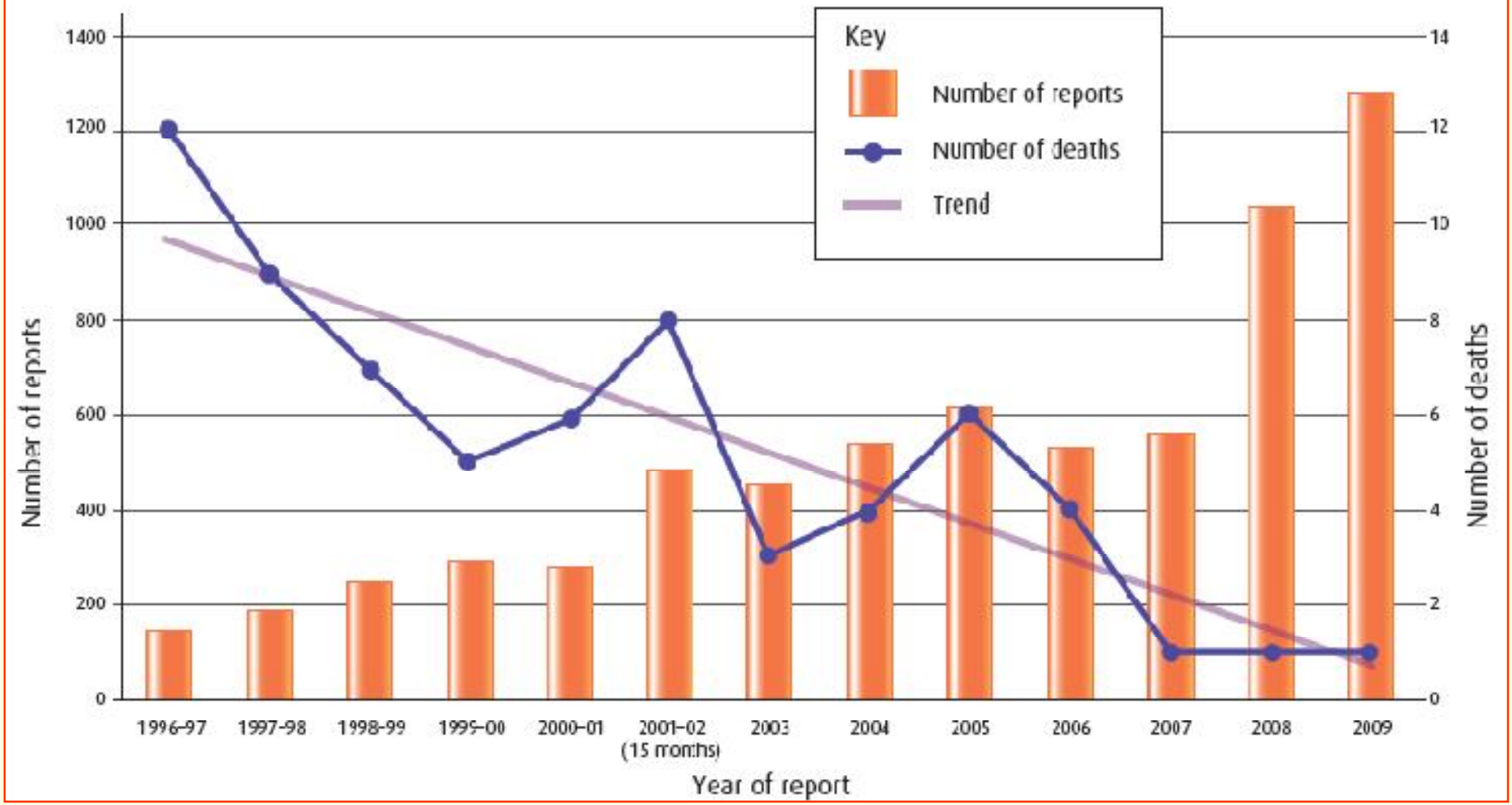
UK: Serious Hazards of transfusion (SHOT)

http//www.shot.demon.co.uk

SHOT Report - 2009

Figure 1

Total reports and total deaths definitely due to transfusion between 1996 and 2009

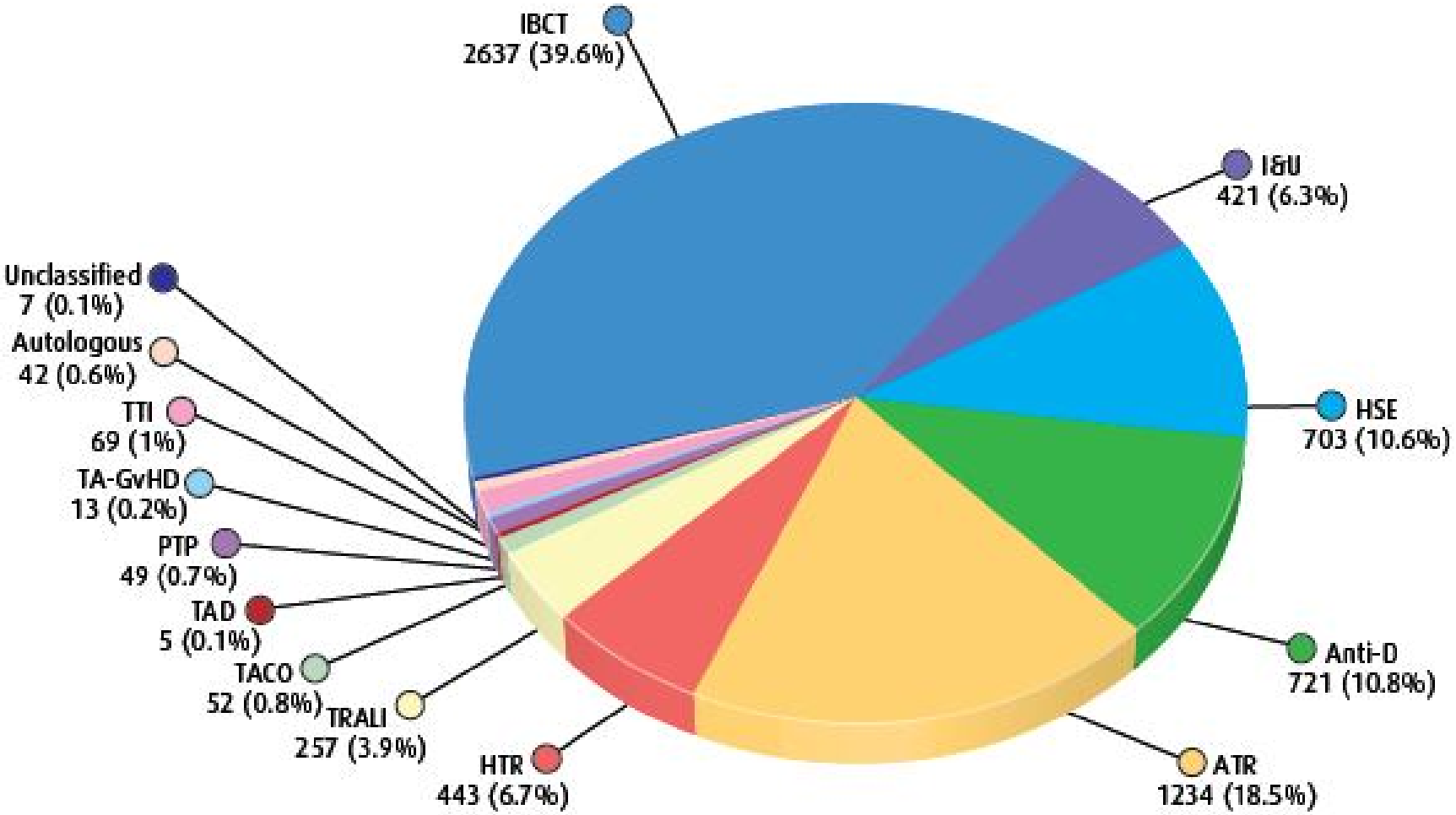


SHOT Report Glossary

- IBCT: incorrect blood component transfused
- I&U: inappropriate and unnecessary transfusion
- HSE: handling and storage errors
- Anti-D related events
- ATR: acute transfusion reaction
- HTR: hemolytic transfusion reaction
- TRALI: transfusion related acute lung injury
- TACO: transfusion associated circulatory overload
- TAD: transfusion associated dyspnoea
- PTP: post-transfusion purpura
- TA-GvHD: transfusion associated graft vs host disease
- TTI: transfusion-transmitted infection
- Near miss events

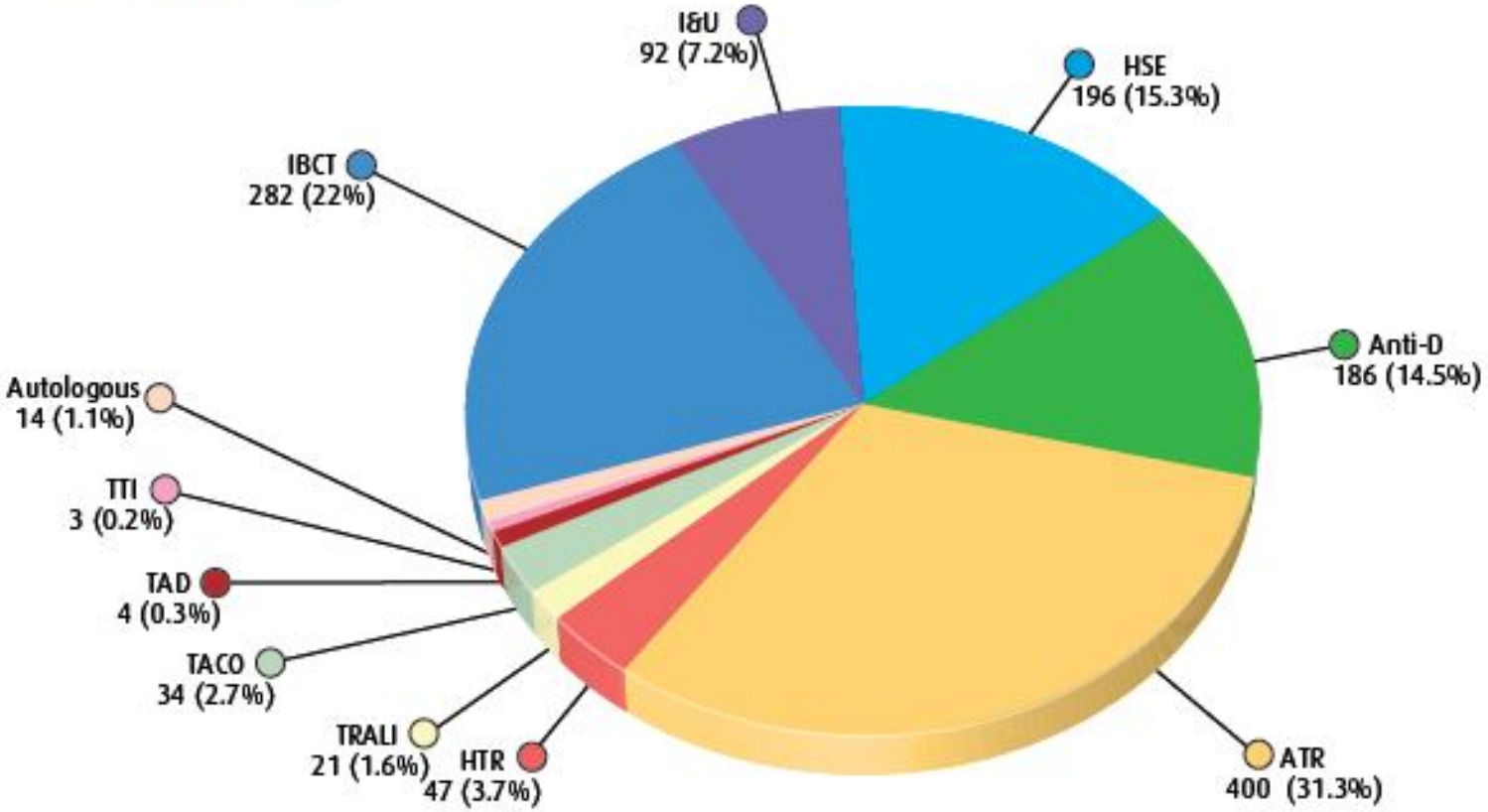
SHOT Report – 1996-2009

Figure 5
Cumulative numbers of cases reviewed 1996–2009 *n* = 6653



SHOT Report - 2009

Figure 4
Cases reviewed *n* = 1279



Clinical versus laboratory errors

Of the total 1279 errors, 230 originated primarily in the hospital transfusion laboratory (149 IBCT, 38 anti-D and 43 handling and storage errors) which is 18% of the total reports, the same proportion as in 2008. Laboratory errors also accounted for 149 of 282 cases of IBCT, i.e. 53% of IBCT reports, compared with 50% in 2008.

SHOT Report - 2009

7. Incorrect Blood Component Transfused (IBCT)

Definition

The category Incorrect Blood Component Transfused (IBCT) comprises all reported episodes where a patient was transfused with a blood component that was intended for another patient or which was incorrect in terms of its specification.

DATA SUMMARY

Total number of cases	282

Implicated components	
Red cells	220
FFP	17
Platelets	26
Other *(specify)*	
Unknown	19

Mortality/morbidity	
Deaths due to transfusion	0
Deaths in which reaction possibly contributed	3
Major morbidity	4

Gender	
Male	132
Female	145
Unknown	5

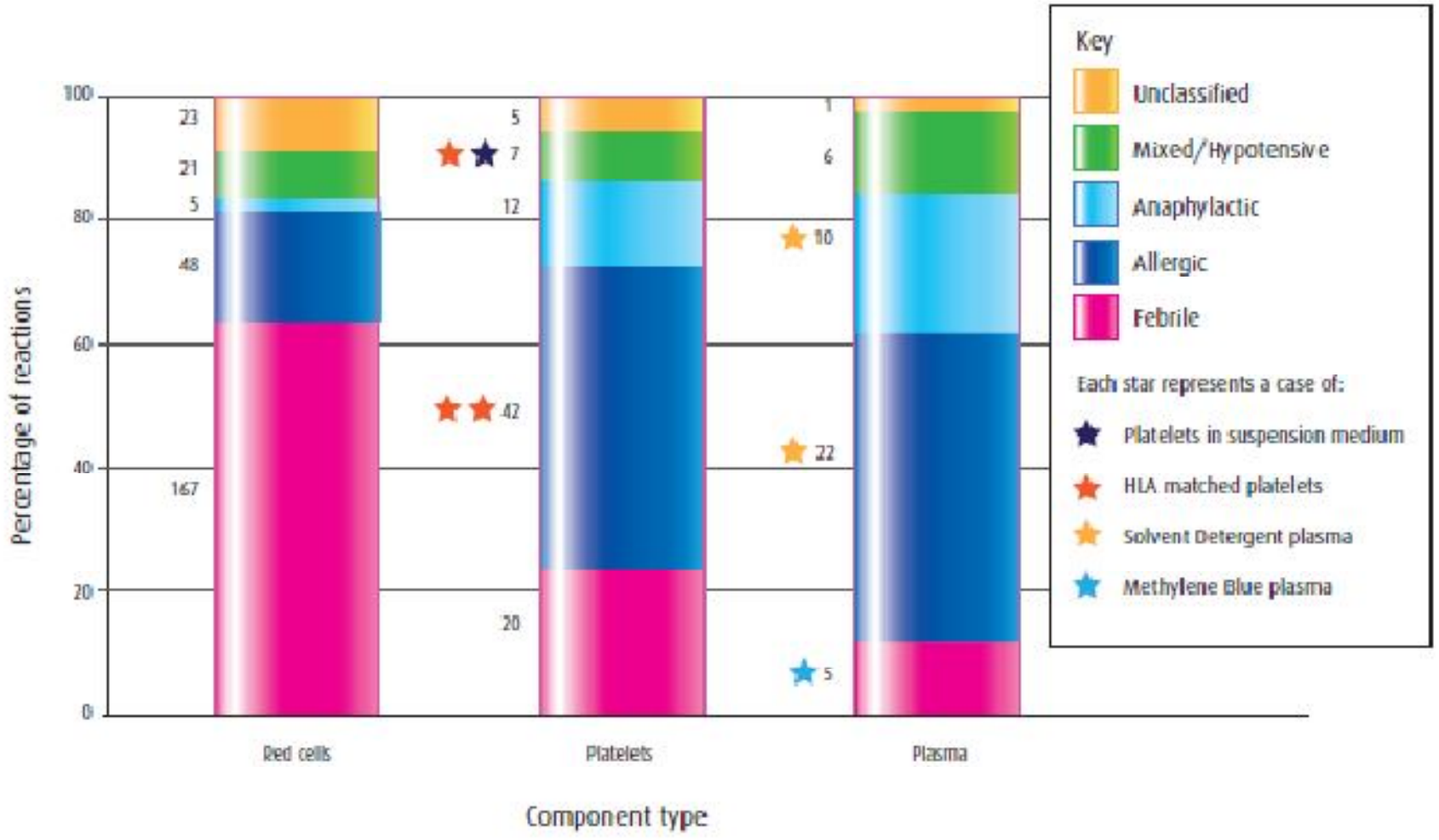
Age	
18 years+	242
16 years+ to 18 years	3
1 year+ to 16 years	21
28 days+ to 1 year	9
Birth to 28 days	7
unknown	
Total	282

Emergency vs. routine and core hours vs. out of core hours	
Emergency	60
Routine	189
Not known	33
In core hours	82
Out of core hours	45
Not known/applicable	155

Where transfusion took place	
ED	4
Theatre	9
ITU/NNU/HDU/Recovery	14
Wards	76
Community	1
Outpatient/day unit	10
Not known	168

SHOT Report - 2009

Figure 12
Reaction by component type (excluding 6 reactions which could not be attributed to a particular component)



Complicanze della trasfusione

Classificazione:

- Non Infettive
  - acute
    - immunologiche
    - non immunologiche
  - ritardate
    - immunologiche
    - non immunologiche
- Infettive

Complicanze non Infettive

Acute (Immediate, < 24 h)

Immunologiche

	Incidenza[1]	Gravità/ Mortalità
AHTR (RT Emolitiche Acute)	**1: 38.000-1: 70.000**	**1:1.000.000**
FNHTR (RT Febbrili Non Emolitiche)	**1: 17-1:200**[2] **1: 3-1:100**[3]	**non grave**
Allergiche (orticarioidi)	**1: 33-1:100**	**non grave**
Anafilattiche (anafilattoidi)	**1: 20.000-1: 50.000**	**grave**
Edema polmonare acuto non cardiogeno (TRALI)	**1: 5.000-1: 190.000**	1: 30.000-1: 1.140.000

(1) AABB Technical Manual 14th Edition
(2) relativa alla trasfusione di RBC
(3) relativa alla trasfusione di piastrine, incluse non immunologiche

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Complicanze non Infettive

Acute (Immediate, < 24 h)

Non Immunologiche

	Incidenza[1]	Gravità/ Mortalità
(Pseudo)emolitiche	**rara**	**N.D**
Ipotensione associata ad ACE inibitori	**variabile**	**N.D**
Sovraccarico circolatorio	**< 1:100**	
Metaboliche **(Trasfusione Massiva)**	**N.D**	**N.D**

(ipotermia, tossicità da citrato, iperpotassiemia)

(1) AABB Technical Manual 14th Edition

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Complicanze non Infettive

Ritardate

Immunologiche

	Incidenza[1]	Gravità/ Mortalità
Reazui Emolitiche Ritardate	1: 5.000 - 1: 11.000	non grave
Alloimmunizz. Eritrocitaria	1: 100	/
Alloimmunizz. anti-HLA	1: 10	/
Refrattarietà (trasf. piastrinica)	5 – 15%	/
PTP (Porpora Post Trasfusionale)	rara	variabile
TA-GVHD (Graft versus host disease posttrasfusionale)	rara	90-100%
Immunomodulazione	N.D.	/

(1) AABB Technical Manual 14th Edition

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Complicanze non Infettive

Ritardate

Non Immunologiche

Sovraccarico di ferro

Incidenza

dopo >100 unità di RBC

Gravità/ Mortalità

co-morbidità

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TABLE 2. Costs to reduce noninfectious hazards*

Cost drivers	Patient bar code	Unified online database	TRALI: exclusion and/or HLA testing of high-risk donors	Total
Incremental cost/unit	$10-$20	$3-$6	$1-$2	$14-$28
× 27 million units†	$392 million	$90 million	$40 million	$432 million
Number of major events (hemovigilance data)†				295
Cost per event avoided				$1.5 million

* Adapted from S. Dzik as presented at Consensus Conference.
† Data from Stains by et al.[32]

TRANSFUSION 2007;47:2338-2347.

Complicanze infettive

TABLE 1. Risk per unit of selected transfusion-transmitted pathogens

Pathogen	Component	United States	Canada	Europe
HIV	All	1:2,000,000	1:7,800,000	1:900,000-5,500,000*
HCV	All	1:2,000,000	1:2,300,000	1:2,000,000-4,400,000*
HBV	All	1:277,000	1 in 153,000	1:77,000-1,100,000*
WNV	All	1:350,000	Rare	No reported cases
HTLV-I and/or -II	RBCs and/or PLTs	1:3,000,000	1:4,300,000	Not tested
Bacterial transmission	RBCs	1:40,000-1:5,000,000		
Bacterial sepsis	PLTs	1:59,000 single-donor	1:41,000 single-donor	1:11,000 (pooled)
Malaria	RBCs	1:1,000,000-1:5,000,000	Three cases in 10 years	11 cases in 10 years

* Variation between low and medium endemic areas. Modified from Bihl et al.[21]

TRANSFUSION 2007;47:2338-2347.

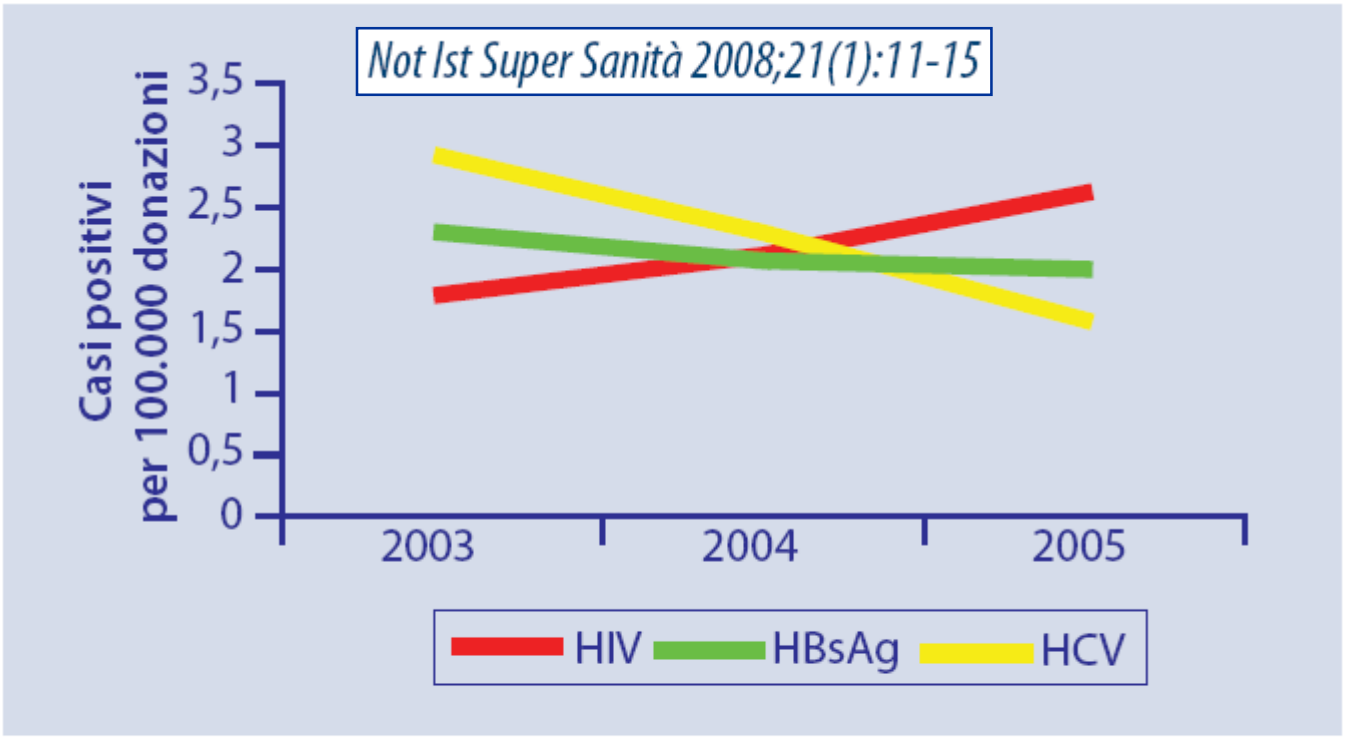

Figura 1 - Incidenze in Italia negli anni 2003-2005 (per 100.000 donazioni)

V. Piccinini, F. Vulcano, S. Palmieri et al.

SUMMARY (*Italian surveillance system of transfusion transmitted infections (SMITT) in the year 2005*) - In Italy, the Istituto Superiore di Sanità (Italian National Institute of Health) coordinates the surveillance system for the screening of the infectious disease markers in blood donations. The system collects data from the Italian Transfusion Services (TS), in collaboration with the regional coordinating centers. 2005 data were sent by 63.4% of the TS with a 75.4% coverage of the total donations. Incidence (I) and prevalence (P) (x100,000 donations) were calculated: for HIV (I = 2.6; P = 18.5), HBsAg (I = 2.0; P = 284.2), HCV (I = 1.6; P = 199.1) and *Syphilis* (I = 7.1; P = 116.9). The surveillance system is an efficient instrument for monitoring blood supply safety.

Key words: donor's surveillance, incidence, prevalence, infectious markers

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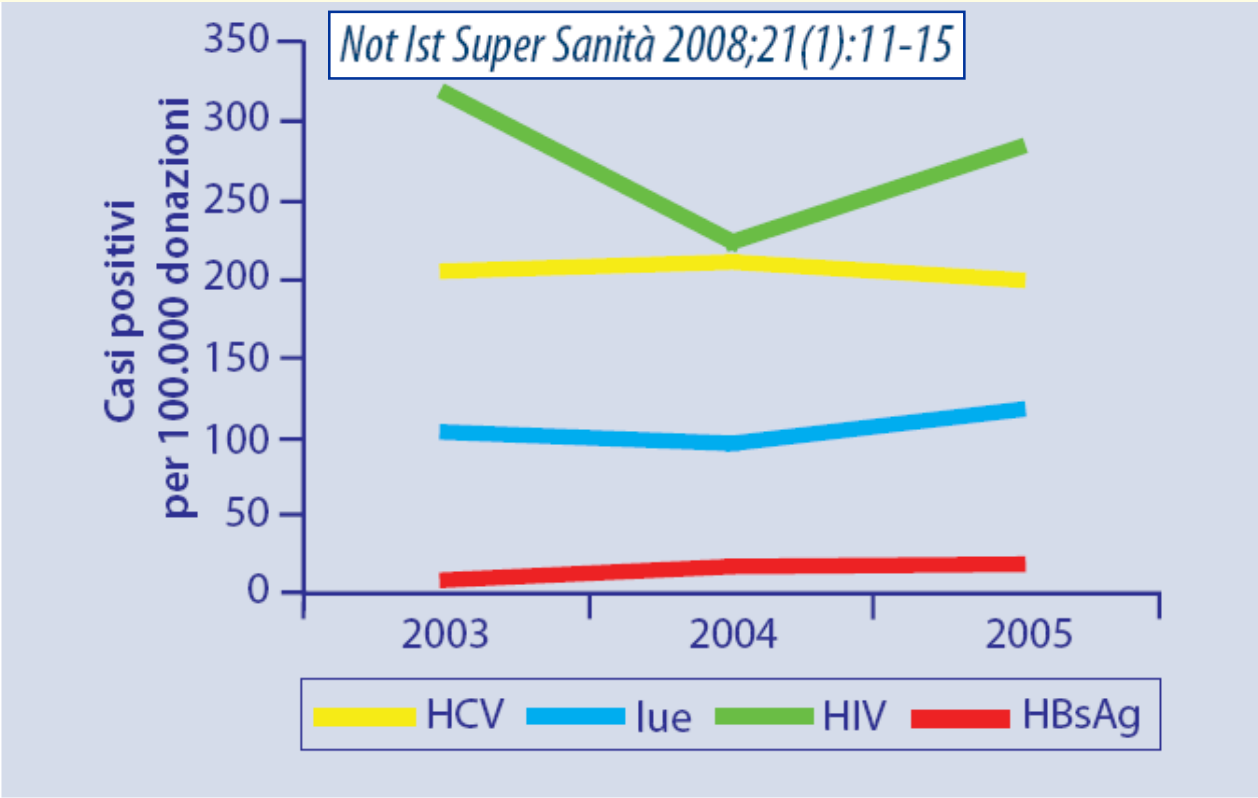

Figura 3 - Prevalenze in Italia negli anni 2003-2005 (per 100.000 donazioni)

V. Piccinini, F. Vulcano, S. Palmieri et al.

SUMMARY (*Italian surveillance system of transfusion transmitted infections (SMITT) in the year 2005*) - In Italy, the Istituto Superiore di Sanità (Italian National Institute of Health) coordinates the surveillance system for the screening of the infectious disease markers in blood donations. The system collects data from the Italian Transfusion Services (TS), in collaboration with the regional coordinating centers. 2005 data were sent by 63.4% of the TS with a 75.4% coverage of the total donations. Incidence (I) and prevalence (P) (x100,000 donations) were calculated: for HIV (I = 2.6; P = 18.5), HBsAg (I = 2.0; P = 284.2), HCV (I = 1.6; P = 199.1) and *Syphilis* (I = 7.1; P = 116.9). The surveillance system is an efficient instrument for monitoring blood supply safety.

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Not Ist Super Sanità 2008;21(1):11-15

V. Piccinini, F. Vulcano, S. Palmieri et al.

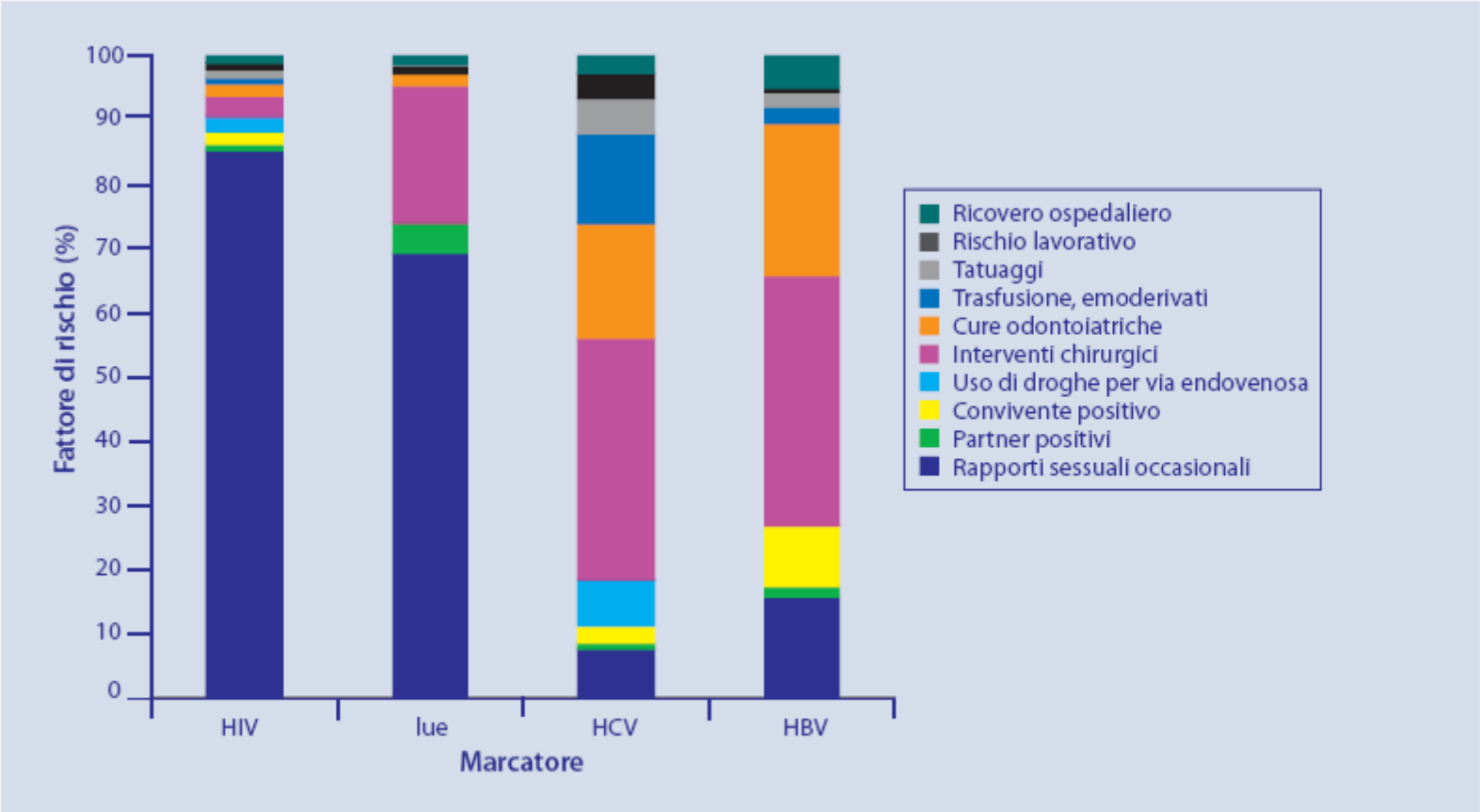

Figura 5 - Distribuzione dei possibili fattori di rischio noti per infezione

Compiti del reparto in caso di reazione trasfusionale acuta

Infermiere:

- interrompere la trasfusione
- mantenere la via endovenosa pervia
- controllare i segni vitali del paziente
- controllare i documenti di assegnazione dell'unità trasfusa e l'identità del paziente
- avvisare il medico curante

Medico:

- prestare le cure immediate
- segnalare la complicanza al Centro trasfusionale (D.M. 25 gennaio 2001 Art.15)
- inviare l'unità interrotta e i campioni del paziente al Centro trasfusionale
- se necessario avvisare il rianimatore

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Il ruolo del Centro trasfusionale in caso di reazione trasfusionale acuta

Escludere/identificare tempestivamente la reazione trasfusionale emolitica acuta

In caso di AHTR dovuta ad errore trasfusionale
il Centro trasfusionale deve:

- chiarire la dinamica dell'errore
- verificare se ci sono altri pazienti a rischio
- assicurare emocomponenti compatibili se necessari
- riportare dettagliatamente l'incidente alla Direzione Sanitaria
- in caso di danno importante al paziente, congelare i campioni per eventuali indagini medico-legali

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Reazione trasfusionale emolitica acuta (AHTR)

Eziologia:

incompatibilità eritrocitaria

emolisi acuta (prevalentemente intravascolare)
mediata da immunocomplessi fissanti il complemento

Emocomponenti implicati:

sangue intero, concentrati eritrocitari (plasma, o piastrine che contengono anticorpi diretti contro antigeni presenti sui globuli rossi del ricevente)

Fattori di rischio: sesso femminile, gruppo 0

AHTR

Sintomatologia

Esordio: febbre (↑ T>1°C) dopo 10-15 mL di sangue trasfuso, brividi, dolore, nausea, rossore, dispnea

Evoluzione/Complicanze: insufficienza renale e DIC (ipotensione, tachicardia, sanguinamento diffuso, oliguria, anuria)

Paziente anestetizzato: emoglobinuria, ipotensione, sanguinamento diffuso

Emolisi intravascolare

Caratterizza prevalentemente la reazione trasfusionale emolitica acuta

Anticorpi di classe IgM o IgG (sottoclassi 1 e 3) capaci di attivare la cascata del complemento.

Cascata enzimatica completa = emolisi intravascolare.

Segni:

emoglobina libera plasmatica.

Sistemi gruppoematici implicati : ABH, Lewis, P, Rh, Kidd, Kell, Vel.

Emolisi extravascolare

Caratterizza prevalentemente la reazione trasfusionale emolitica ritardata

Eliminazione selettiva degli eritrociti sensibilizzati da anticorpi IgG e/o frazione C3b del complamento, da parte dei macrofagi del sistema reticoloendoteliale che hanno recettori specifici per Fc delle IgG e C3b.

Meccanismo analogo a quello "fisiologico" con il quale vengono eliminati eritrociti vecchi.

Sistemi gruppoematici implicati: Rh, Kell, Kidd, Duffy, MNS, ecc.

Segni: iperbilirubinemia indiretta

Table 1-9. Cytokines Implicated in Hemolytic Transfusion Reactions

Terminology	Biologic Activities
Proinflammatory Cytokines TNF, IL-1	Fever Hypotension, shock, death (synergy) Mobilization of leukocytes from marrow Activation of T and B cells Induction of cytokines (IL-1, IL-6, IL-8, TNF-α, MCP) Induction of adhesion molecules Induction of procoagulants
IL-6	Fever Acute-phase protein response B-cell antibody production T-cell activation
Chemokines IL-8	Chemotaxis of neutrophils Chemotaxis of lymphocytes Neutrophil activation Basophil histamine release
MCP-1	Chemotaxis of monocytes Induction of respiratory burst Induction of adhesion molecules Induction of IL-1
Anti-Inflammatory Cytokines IL-1 receptor antagonist	Competitive inhibition of IL-1 type I and II receptors

IL = interleukin; MCP = monocyte chemoattractant protein; TNF = tumor necrosis factor.

Popovsky et. Al. 1996

AHTR

Trattamento (rianimatore)

- terapia dell'ipotensione (Dopamina a basso dosaggio)
- terapia dell'insufficienza renale: (furosemide) mantenimento di una perfusione renale adeguata (monitorare e mantenere output delle urine a 100mL/h per 18-24h)
- terapia della DIC (quando necessario)

AHTR Il ruolo del Centro Trasfusionale e la diagnosi di laboratorio

1° fase immediata, controllo di:

- ➔ errore "amministrativo"
- ➔ emoglobina libera plasmatica

confronto visivo tra campione del paziente pre e post-trasfusione (apprezza conc. di Hb=20-50mg/dL, pari a emolisi intravascolare di 5-10 mL di globuli rossi in un paziente adulto)

- ➔ anticorpi adesi alle emazie trasfuse (DAT) (confronto pre-post)
- ➔ *(emoglobinuria)*

In caso di positività di almeno uno di questi elementi, la reazione emolitica non può essere esclusa e le indagini devono proseguire immediatamente fino a chiarimento del caso

AHTR Il ruolo del Centro Trasfusionale e la diagnosi di laboratorio

2° fase

➔ test pretrasfusionali (AB0, Rh, ricerca di alloabs-eritrocitari, DAT, compatibilità) su campioni del paziente pre e post-trasfusione, su un segmento dell'unità restituita e su quello conservato a norma di legge

➔ identificare eventuali anticorpi irregolari presenti nel siero o adesi alle emazie (eluato)

Test aggiuntivi:

controllo ematocrito ed emoglobina del paziente (pre-vs post-), dosaggio aptoglobina (pre- vs post-), dosaggio bilirubina (picco a 5-7 ore)

N.B.: i test negativi debbono essere ripetuti

AHTR

Prevenzione

- procedure scritte per prelievo e trasfusione
- mezzi informatizzati per l'identificazione del paziente, dei suoi campioni di sangue e delle unità assegnate
- doppio controllo di gruppo del paziente pretrasfusione
- metodi sensibili per lo screening anticorpale sui campioni di sangue del paziente (e del donatore)
- addestramento degli operatori

AHTR

Test predittivi del significato clinico degli anticorpi

in vitro:

- sottoclassi IgG (pericolose IgG1 e IgG3)
- range termico
- emolisine
- test interazione emazie - monociti (rosette o fagocitosi)
- test dell'antiglobulina diretto con stimolazione mediante mitogeni e citochine

in vivo:

- monitoraggio emolisi in vivo
- monitoraggio della sopravvivenza delle cellule trasfuse (test citofluorimetrici: dopo tx di >10 mL di sangue)

Table 1-6. Specificities Associated With Intravascular or Extravascular Hemolysis

Blood Group System	Intravascular Hemolysis	Extravascular Hemolysis
ABO, H	A, B, A1, H	
Lewis	Le^a, Le^b	
P	P, P + P_1 + Pk (Tj^a)	P_1
I/i	I, i	
Rh	D, E, c*	All
Lewis	Le^a, Le^b	
Duffy		Fy^a, Fy^b†
MNS	U	M, S, s, Mi,‡ N‡
Lutheran		Lu^b
Kell	K	K, k, Kp^a, Kp^b, Js^a, Js^b†
Kidd	Jk^a	Jk^a, Jk^b, Jk3†
Cartwright		Yt^a
Diego		Di^a, Di^b
Scianna		Sc1, Sc2
Colton		Co^a, Co^b
Dombrock		Do^a, Do^b
Vel	Vel	Vel
Gerbich		Ge
Lan		Lan
Sid		Sd^a‡

* Potentially any specificity can cause intravascular hemolysis.
† Potentially any specificity can cause extravascular hemolysis.
‡ Only some antibodies of this specificity are reported to cause hemolysis.

Popovsky et. Al. 1996

Emolisi acuta non immuno-mediata
(pseudoemolitica)

Segni e sintomi

emoglobinemia o emoglobinuria in assenza di altri sintomi o evidenze di laboratorio (DAT negativo)

Eziologia:

trasfusione di unità di globuli rossi emolizzata

Possibili cause:

lisi termica (cong-scong., riscaldamento eccessivo)
lisi osmotica (soluzioni ipotoniche, farmaci)
lisi meccanica (aghi, pompe, CEC)

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Reazione trasfusionale emolitica ritardata (DHTR)

Eziologia:

incompatibilità eritrocitaria (risposta anamnestica), emolisi extravascolare

Sintomatologia:

4-15 giorni dopo la trasfusione: febbre, anemmizzazione improvvisa e ingiustificata (o mancato incremento dell'Hb postrasfusionale), modesto ittero (↑ bilirubina indiretta)

Sistemi gruppoematici implicati:

Rh, Kell, Kidd, Duffy, ecc.

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DHTR

Il ruolo del Centro Trasfusionale: diagnosi di laboratorio

➔ DAT su campioni del paziente pre e post-trasf.

➔ ricerca di alloabs e prova di compatibilità su campioni di sangue del paziente pre e post-trasf.

➔ identificazione degli abs irregolari rilevati nel siero del paziente o adesi alle emazie trasfuse (eluato)

DHTR

Prevenzione

- ➔ selezionare unità compatibili
- ➔ mantenere i record dei pazienti immunizzati, rispettare la compatibilità anche per anticorpi pregressi
- ➔ allegare alla cartella clinica del paziente immunizzato una segnalazione che riporti specificità e caratteristiche degli anticorpi identificati

Reazione trasfusionale febbrile non emolitica (FNHTR)

Eziologia

- **Immunologica:** anticorpi contro i leucociti del donatore (HLA)

Principale causa delle reazioni ai concentrati eritrocitari

- **Non immunologica:** accumulo di mediatori della febbre (citochine) nell'unità conservata

Principale causa delle reazioni ai concentrati piastrinici

Sintomatologia

brividi, febbre (↑ T>1°C), rigor, malessere, dolori, vomito

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FNHTR

Indagini di laboratorio:

- Ricerca di anticorpi leucopiastrinici
- *Ricerca di citochine nel surnatante dell'unità (non di routine)*

Trattamento:

antipiretici, terapia steroidea

Prevenzione:

- FNHTR immunologica: emocomponenti leucodepleti
- FNHTR non immunologica

- concentrati piastrinici freschi (< 4 giorni)
- concentrati piastrinici filtrati prima della conservazione
- rimozione del surnatante prima della trasfusione

Reazione trasfusionale allergica (orticarioide)

Eziologia

- anticorpi presenti nel plasma del paziente diretti contro allergeni trasfusi (determinanti antigenici delle proteine plasmatiche del donatore o altro)
- trasfusione di mediatori della reazione allergica

Sintomatologia:
prurito, orticaria, eruzione cutanea, rossore

Indagini di laboratorio: nessuna

Trattamento/Prevenzione: antistaminici
La trasfusione può essere temporaneamente sospesa e ripresa se i sintomi regrediscono rapidamente

Reazione trasfusionale anafilattica o anafilattoide

Eziologia:

spesso ignota, anticorpi del ricevente (IgE) contro allergeni trasfusi (proteine plasmatiche del donatore, altre sostanze), anticorpi di classe IgG o IgE anti-IgA (di norma in pazienti IgA carenti). Trasfusione passiva di IgE del donatore.

Sintomatologia:

Esordio: 1 min.-2-3 ore da inizio trasfusione. Sintomi: cutanei (prurito generalizzato, orticaria, eritema diffuso), gastrointestinali (nausea, crampi, dolori, diarrea), respiratori (edema laringe e faringe, cianosi, sensazione di morte imminente, dispnea, oppressione), cardiovascolari (tachicardia, ipotensione, shock).

Donatella Riccardi
2000-2003

Reazione trasfusionale anafilattica o anafilattoide

Indagini di laboratorio:

- dosaggio IgA (1:900 IgA carenti),
- anticorpi anti- IgA (presenti nel 17-40% degli IgA carenti)

Trattamento:

dipende da gravità e sintomatologia. (Epinefrina, rimpiazzo dei liquidi, corticosteroidi, terapia intensiva)

Prevenzione:

- emocomponenti lavati (approccio empirico, nei soggetti a rischio)
- plasma da donatore IgA carente (ove indicato)

Transfusion Related Acute Lung Injury (TRALI)

1. Diagnosis
2. Radiology
3. Histology
4. 1-hit vs 2-hit pathogenesis
5. Blood donors & antibodies
6. Animal models
7. Frequency and severity
8. Treatment
9. Differential diagnosis
10. Prevention

TABLE 1. Recommended criteria for TRALI and possible TRALI

1. TRALI criteria
   a. ALI
      i. Acute onset
      ii. Hypoxemia
         Research setting:
            $PaO_2/FiO_2 \leq 300$,
            or $SpO_2 < 90\%$ on room air
         Nonresearch setting:
            $PaO_2/FiO_2 \leq 300$
            or $SpO_2 < 90\%$ on room air
            or other clinical evidence of hypoxemia
      iii. Bilateral infiltrates on frontal chest radiograph
      iv. No evidence of left atrial hypertension (i.e., circulatory overload)
   b. No preexisting ALI before transfusion
   c. During or within 6 hr of transfusion
   d. No temporal relationship to an alternative risk factor for ALI
2. Possible TRALI
   a. ALI
   b. No preexisting ALI before transfusion
   c. During or within 6 hr of transfusion
   d. A clear temporal relationship to an alternative risk factor for ALI

Kleinman et al

Ten TRALI issues

2. Radiology

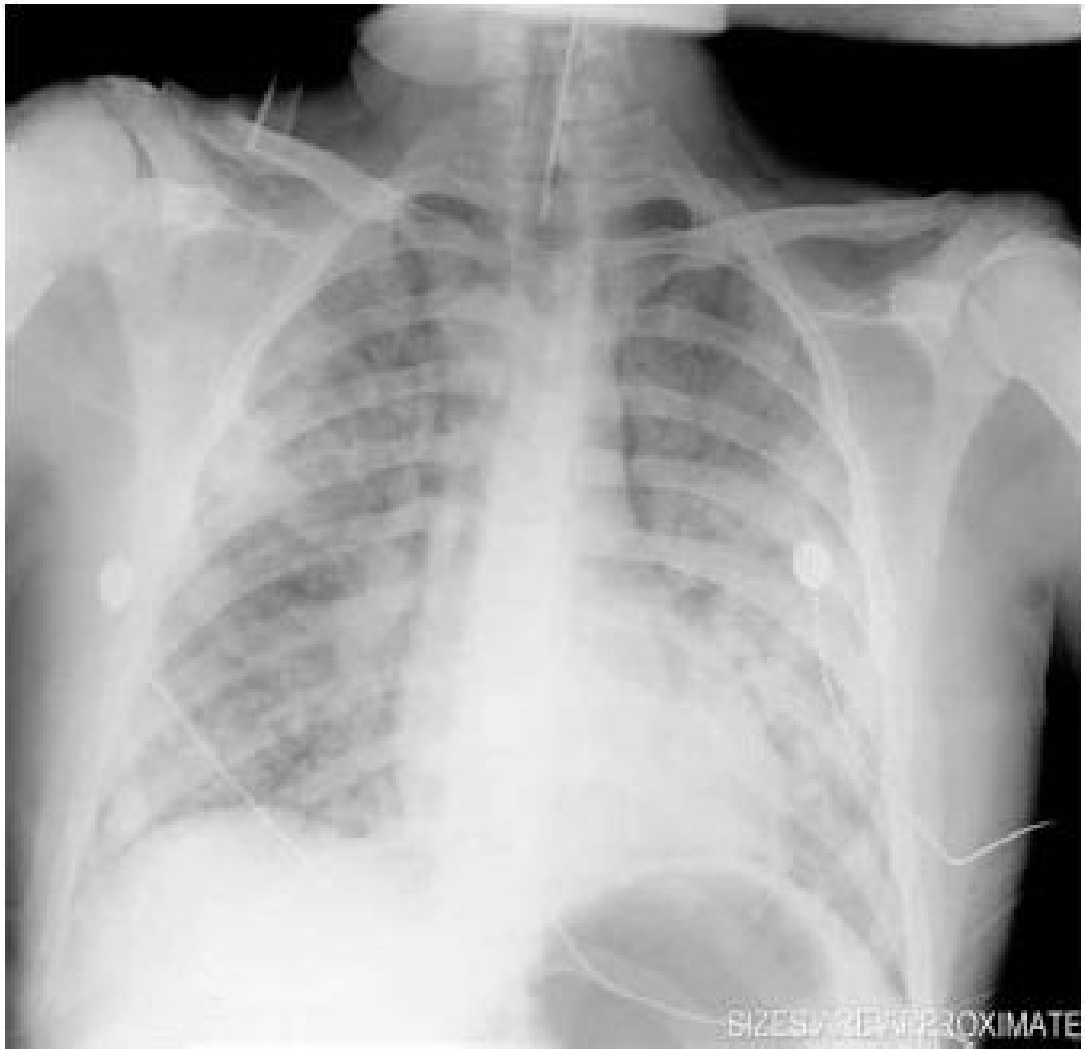


Fig. 1. The radiograph demonstrates heavy bilateral pulmonary infiltrates consistent with pulmonary edema 1 h after the infusion of the offending unit of cryo-poor plasma.

Cruz et al, J Clin Apher 2008

Ten TRALI issues

3. Histology

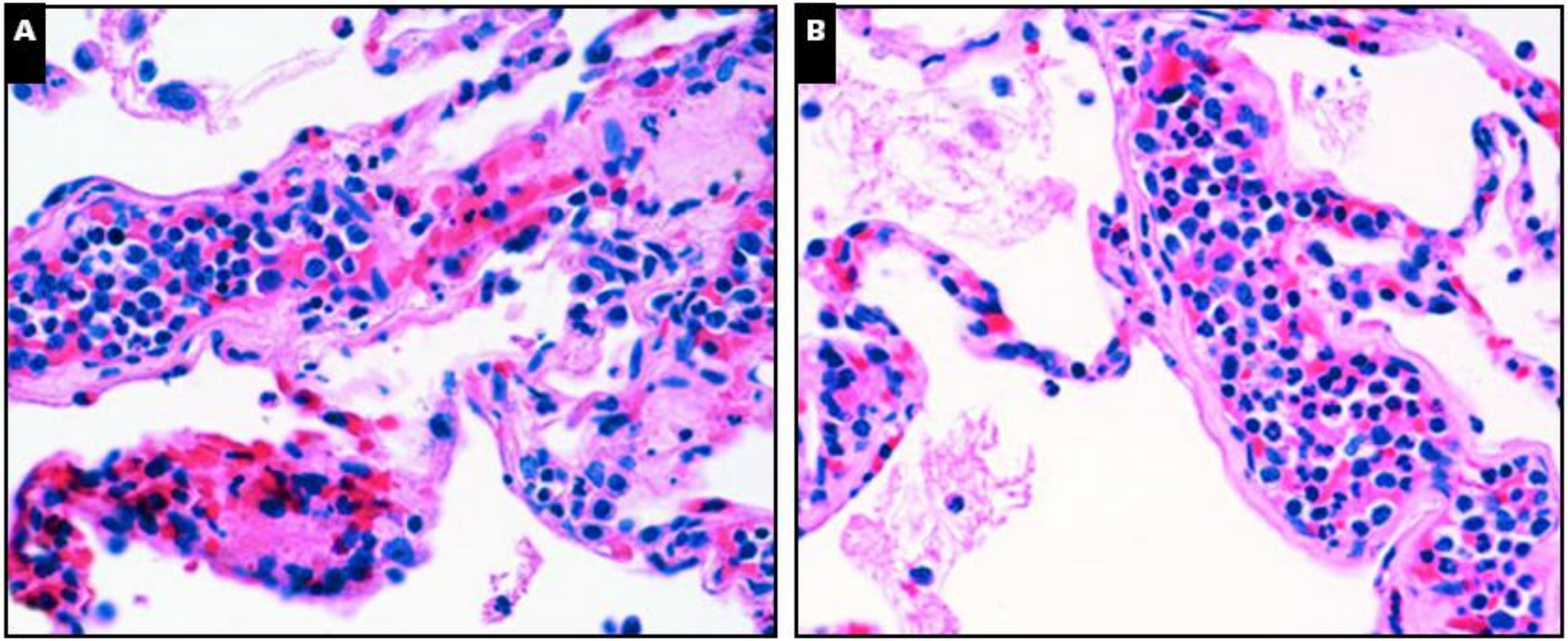


Image 1 A complete autopsy was performed on a patient who died with the clinical diagnosis of transfusion-related acute lung injury. The most significant finding was pulmonary edema (combined lung weight of 2,780 g) (**A**) with neutrophilic aggregates in the pulmonary vasculature (**B**, H&E, ×180).

Cherry et al, Am J Clin Pathol 2008

Pulmonary pathology of rapidly fatal transfusion-related acute lung injury reveals minimal evidence of diffuse alveolar damage or alveolar granulocyte infiltration

Constance Danielson, Richard J. Benjamin, Mark M. Mangano, Charles J. Mills, and Dan A. Waxman

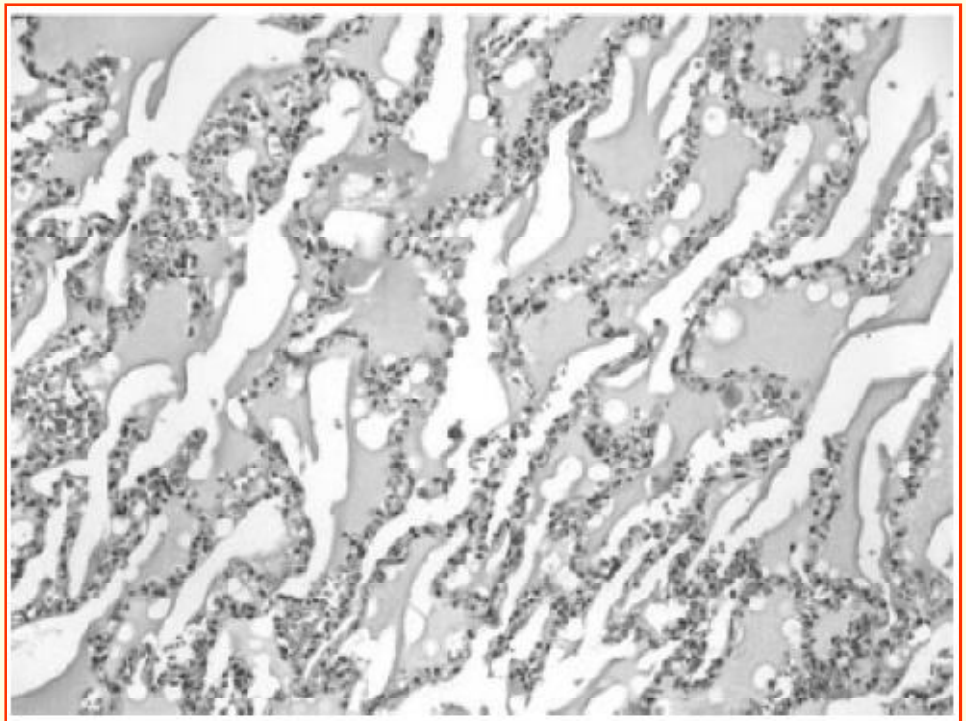


Fig. 1. 100-fold magnification of a hematoxylin and eosin–stained section of parenchymal lung tissue from Patient 1. Patchy pulmonary edema is evident as eosinophilic proteinaceous alveolar material. Although the alveolar capillaries are markedly congested with PMNs and RBCs, there is no WBC accumulation within the alveolar spaces.

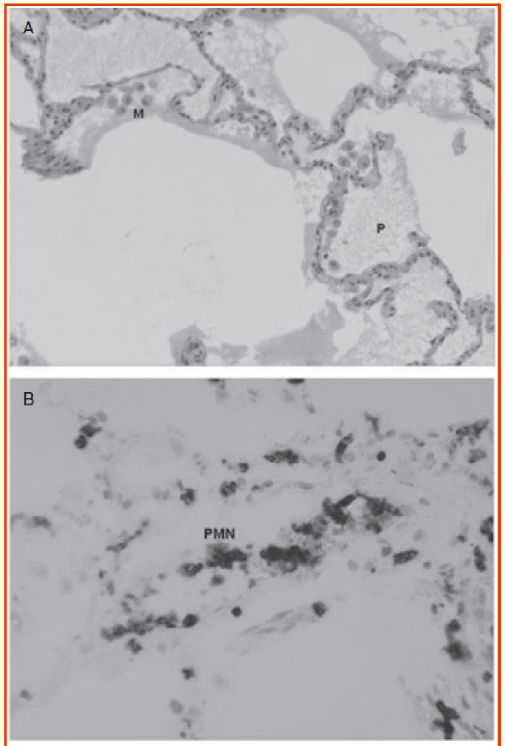


Fig. 2. (A) 200-fold magnification of a hematoxylin and eosin–stained section of parenchymal lung tissue from Patient 2. The alveolar spaces are filled with eosinophilic proteinaceous (P) material and isolated activated macrophages (M). Intravascular accumulation of RBCs and granulocytes is noted. No evidence of hyaline membranes, interstitial inflammation, or alveolar infiltration by PMNs is seen. Immunohistochemical staining with CD15 antibodies (B) reactive with PMNs at 400-fold magnification reveals aggregations of intravascular PMN in alveolar capillaries without extravasation into alveolar spaces.

doi: 10.1111/j.1537-2995.2008.01879.x
TRANSFUSION **;**:**–**.

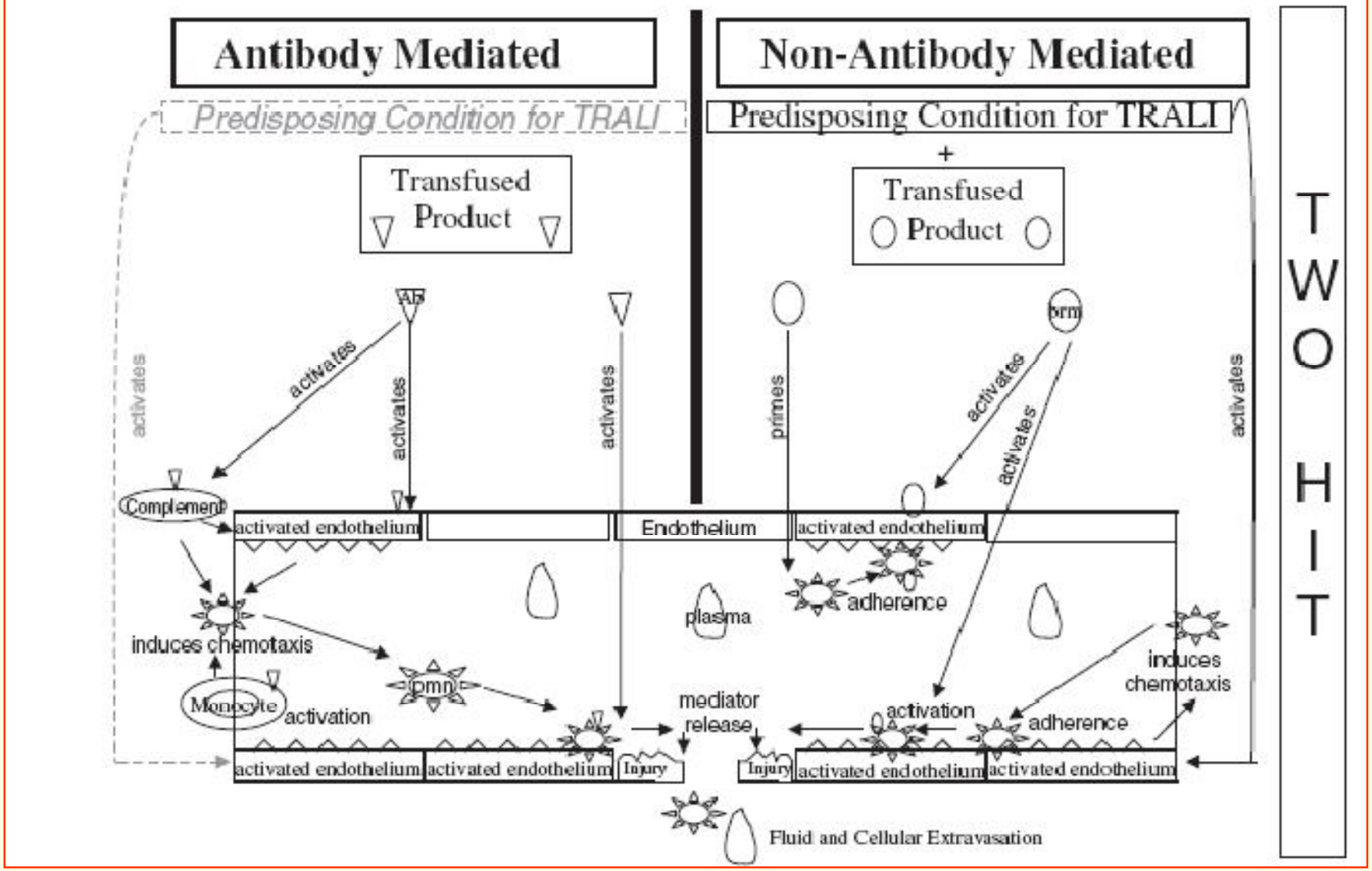
Ten TRALI issues

4. 1-hit vs 2-hit pathogenesis

TRALI pathogenesis

- Antibody mediated
  - Abs in transfused product activate PMN and pulmonary endothelial cells
  - Outcome: capillary damage, fluid extravasation
- Non antibody mediated
  - Biological Response Modifiers (‘2° hit’, lipids?) activate primed PMN in predisposed patient with activated pulmonary endothelium
  - Outcome: capillary damage, fluid extravasation

Journal of Intensive Care Medicine / Vol. 23, No. 2, March/April 2008



Java et al, 2008

bjh review

2007 Blackwell Publishing Ltd, *British Journal of Haematology*, **136**, 788–799

The pathogenesis of transfusion-related acute lung injury (TRALI)

Jürgen Bux[1] and Ulrich J. H. Sachs[2]

[1]*DRK-Blood Service West of the German Red Cross, Hagen, and* [2]*Institute for Clinical Immunology and Transfusion Medicine, Justus Liebig-University, Giessen, Germany*

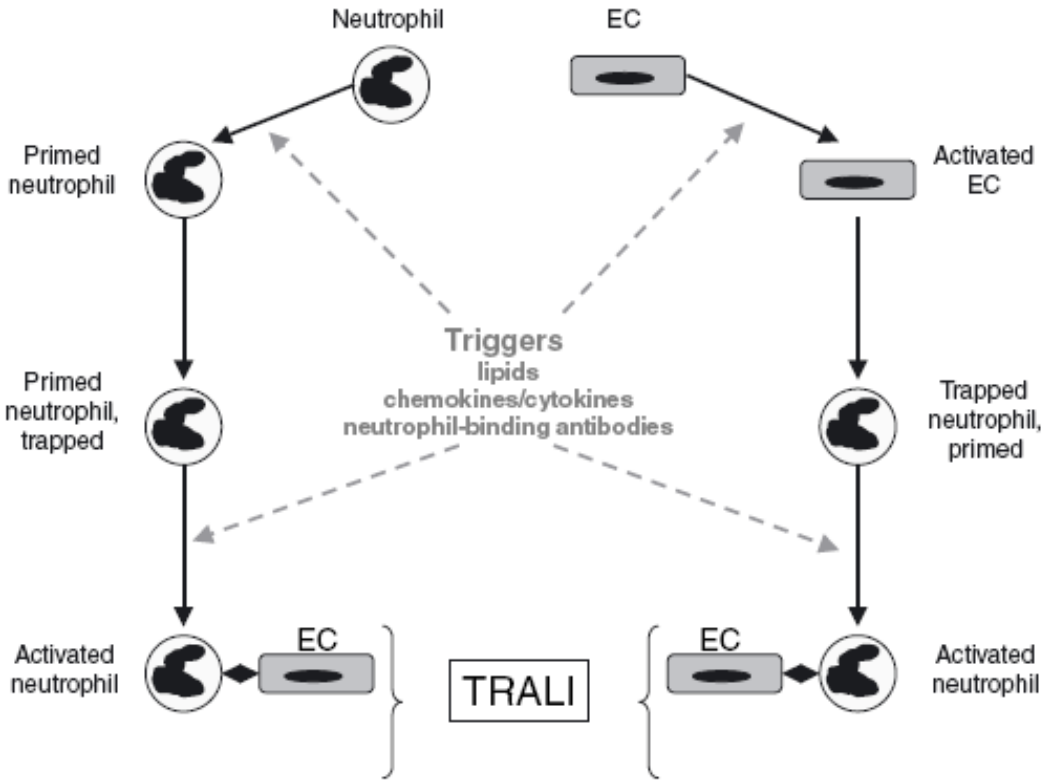


Fig 2. Possible pathomechanism of transfusion-related acute lung injury (TRALI). Neutrophils and pulmonary cells are key players in TRALI. Activation of each cell type may lead to TRALI. On the one hand, neutrophils may become primed, most probably as a result of endogenous triggers, such as those present during infections. Primed cells are trapped in the lungs' microvasculature, where they experience activation via substances present in the blood component, e.g. antibodies or bioactive lipids. On the other hand, an activated endothelial cell can induce neutrophil trapping within the lungs, where they are primed and finally activated because of triggers present in the blood component. In either case, neutrophil/endothelial cell interaction is necessary to finally induce TRALI.

Ten TRALI issues

5. Blood donors & antibodies

Transfusion-related acute lung injury (TRALI) in the Netherlands in 2002-2005

Wiersum-Osselton JC, Porcelijn L, van Stein D, Vlaar AP, Beckers EA, Schipperus MR.

TRIP Landelijk Hemovigilantie Bureau, Den Haag. j.wiersum@tripnet.nl

OBJECTIVE: To determine the number of reported cases of transfusion-related acute lung injury (TRALI) in the Netherlands in 2002-2005 and to determine how many cases were associated with incompatibility between leukocyte-reactive antibodies in the donor plasma and leukocytes or antigens in the recipient. DESIGN: Retrospective national case review. METHOD: Cases of TRALI reported in 2002-2005 were assessed according to the national clinical definition of TRALI, and the relationship between TRALI and transfusion was assessed. Additional clinical details were requested from the treating hospital as necessary. The results of leukocyte serological tests from donors and recipients were linked to clinical cases. For cases with positive leukocyte serological tests, the relevant blood components and the sex of the donor were recorded. RESULTS: Of the 46 cases reported, 6 had insufficient information. 8 cases did not meet the definition or had another more likely diagnosis. There was a trend toward an increase in the number of reports: 12 cases were reported in 2005, corresponding with 1:60,000 blood components.

Of the 40 evaluable cases, 32 (80%) met the definition of TRALI and were deemed to be definitely (n = 16), probably (n = 5) or possibly (n = 11) related to transfusion. Severity ranged from moderate to life-threatening, and there was one TRALI-related death.

Leukocyte serology was fully investigated in 18 cases: 13 (72%) had leukocyte incompatibility and in 5 cases exclusively fresh frozen plasma from a female donor was implicated

The SAUQUIN TRALI Study

Vox Sanguinis 2008;95(suppl 1) abs 4C-S26-04

- Jan 2005 – Jul 2007: total 53 cases
- HLA & HNA abs tested in 258 donors (39% women) and 48 investigated recipients (5.4 donors/case)
- 69 donors (45 women, 24 men) involved in 36 cases had positive abs screening
- In 12/20 (60%) TRALI cases with proven incompatibility at least 1 of implicated blood products was female FFP

Ten TRALI issues

6. Animal models

TRALI animal models

- Ex-vivo: Isolated perfused rat lung *(Silliman)*
  - lipopolysaccharides
- Ex-vivo: Isolated perfused rabbit lungs
  - Anti HNA-5b *(Seeger)*
  - mAb mouse anti-HNA-2a *(Sachs)*
- In-vivo: Intavenously injected mice
  - MHC I mAb *(Looney, Strait)*
- Support 2-hit model and role of neutrophils

Ten TRALI issues

7. Frequency and severity

Ten-year SHOT Report

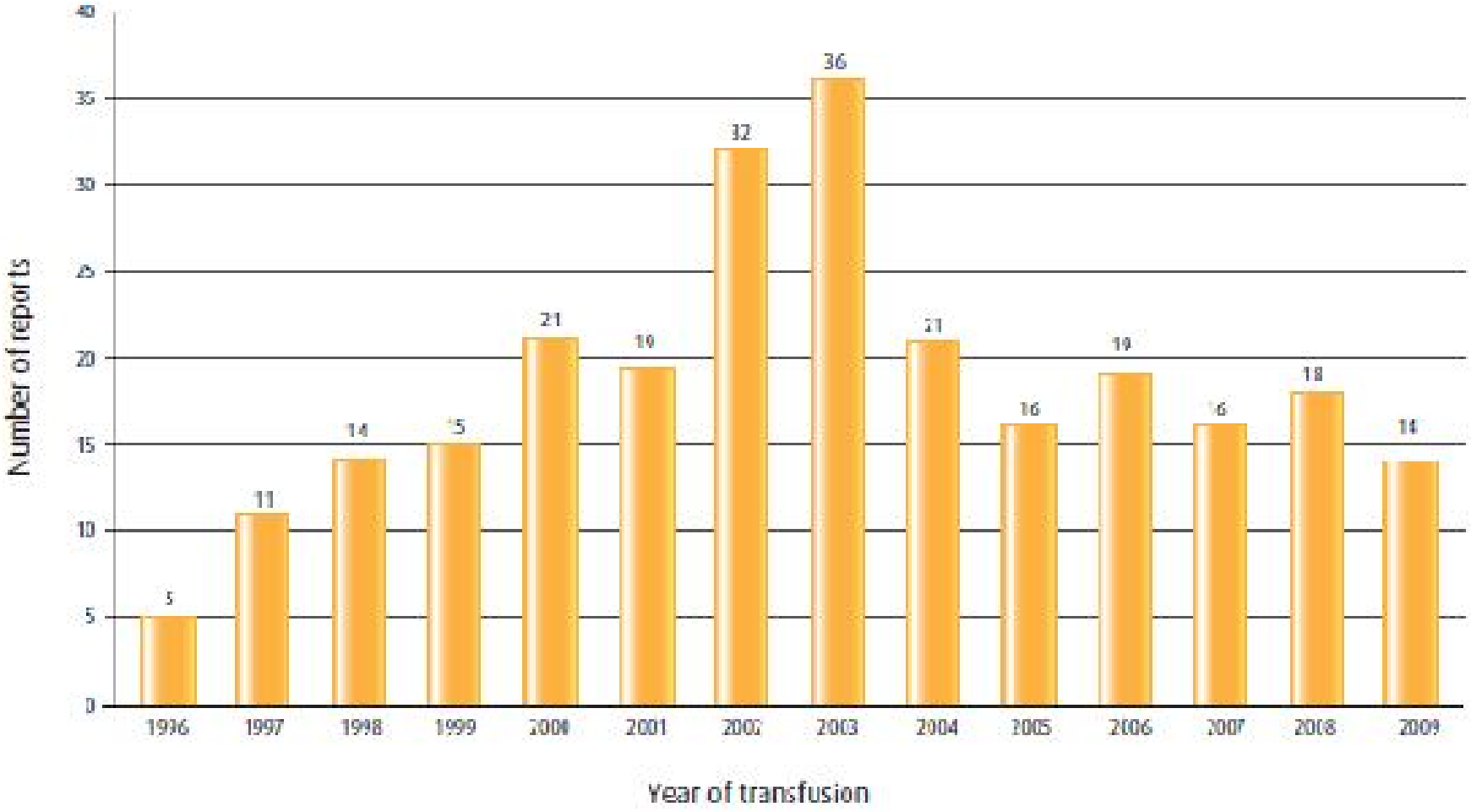
Table 3. Frequency of Reported Serious Hazards of Blood Transfusion in the UK (not all incident types are included)

Event	Number of incidents reported	Frequency of reported events per 100 000 components issued
IBCT	1832	7
ABO-incompatible transfusions (all components—included in IBCT)	249	1
Death as a result of IBCT	20	0.07
TRALI	162	0.6
Fatal TRALI	36	0.1
ATR	267	1
TTI (including bacterial)	49	0.2
Total adverse reactions/events	2630	10
Total transfusion-related deaths	100	0.4

Transfusion Medicine Reviews, Vol 20, No 4 (October), 2006: pp 273-282

SHOT Report - 2009

Figure 18
TRALI by year of transfusion *n* = 257



ARC-Estimated risk of TRALI in recipient fatalities (2003-2005)

TABLE 4. Estimated risk of TRALI in recipient fatalities (2003-2005)

Involved component	Number of probable TRALI reactions	Number of total components distributed*	Rate per 10^6 distributed components	OR (95% CI)†
RBCs	7	17,692,062	0.40 (1:2,527,437)	
Plasma	24	4,864,144	4.93 (1:202,673)	12.5 (5.4-28.9)
Apheresis PLTs	5	1,602,862	3.12 (1:320,572)	7.9 (2.5-24.8)
Whole-blood PLTs	1	2,157,883	0.46 (1:2,157,883)	1.2 (0.1-9.5)
Cryoprecipitate	1	1,235,089	0.81 (1:1,235,089)	2.0 (0.2-16.6)

* Represents the total number of components distributed within the Red Cross system, including allogeneic, autologous, and directed donations.

† OR and 95 percent CI relative to RBC transfusions.

Eder et al, Transfusion 2007

Mild TRALI cases

TABLE 1. Clinical and laboratory features of three cases of mild TRALI

Variables	The salesman	The dancer	The new mother
Patient characteristics			
Age (years)	38	79	21
Cardiac disease	AVR, pericardial effusion	Ischemic cardiomyopathy	No
INR	2.9	1.9	Normal
Transfusion indication	Preprocedure INR correction	Preprocedure INR correction	Hct 22%
Transfusion reaction details			
Product implicated	FFP	FFP	RBC
Inital symptoms	Chills, dyspnea	Chills, dyspnea	Chills, dyspnea
BP (mmHg)	160/70	160/60	130/70
Pulse rate (bpm)	128	90	140
RR (per min)	40	Not available	28
T/rise in T (°C)	38.9 (+2.2)	37.8 (+1.8)	39 (+2.0)
O_2 sat (%)	92	92	88
Examination	No stridor, wheeze, rales, urticaria	No stridor, wheeze, rales, urticaria	No stridor, wheeze, rales, urticaria
CXR	Not done	Not done	Not done
Supplemental O_2	Yes	Yes	Yes
WBC count before/after (4.5×10^9-11×10^9/L)	7.5/7.3	6.4/2.7	8.4/7.3
Platelet count (150×10^9-350×10^9/L)	321	168	269
Brain natriuretic peptide (0-450 pg/ml)	Not done	Not done	428
HLA findings			
Recipient HLA type	A3, Ax; B7, B51	A3, A30; B44, B49	A2, A3; B35, B39
Donor PRA Class I	59%	95%	77%
Donor PRA Class II	78%	86%	Not tested
Donor antibody specificity	Anti-B7	Multiple	Anti-A2
HLA crossmatch	Incompatible T & B	Incompatible T & B	Incompatible T

Davis et al, Transfusion 2008

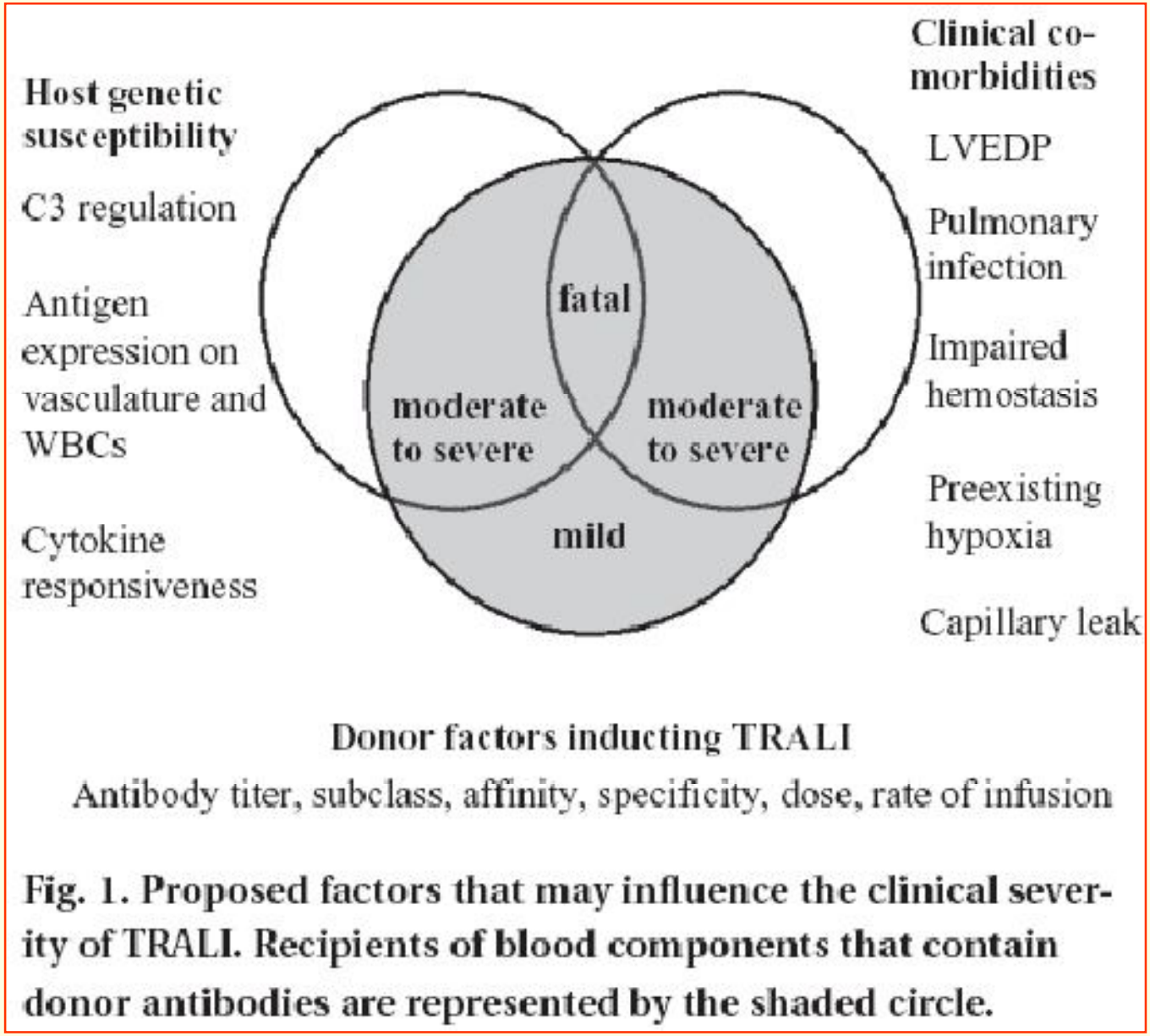


Fig. 1. Proposed factors that may influence the clinical severity of TRALI. Recipients of blood components that contain donor antibodies are represented by the shaded circle.

Davis et al, Transfusion 2008

bjh review

2007 Blackwell Publishing Ltd, *British Journal of Haematology*, **136**, 783–799

The pathogenesis of transfusion-related acute lung injury (TRALI)

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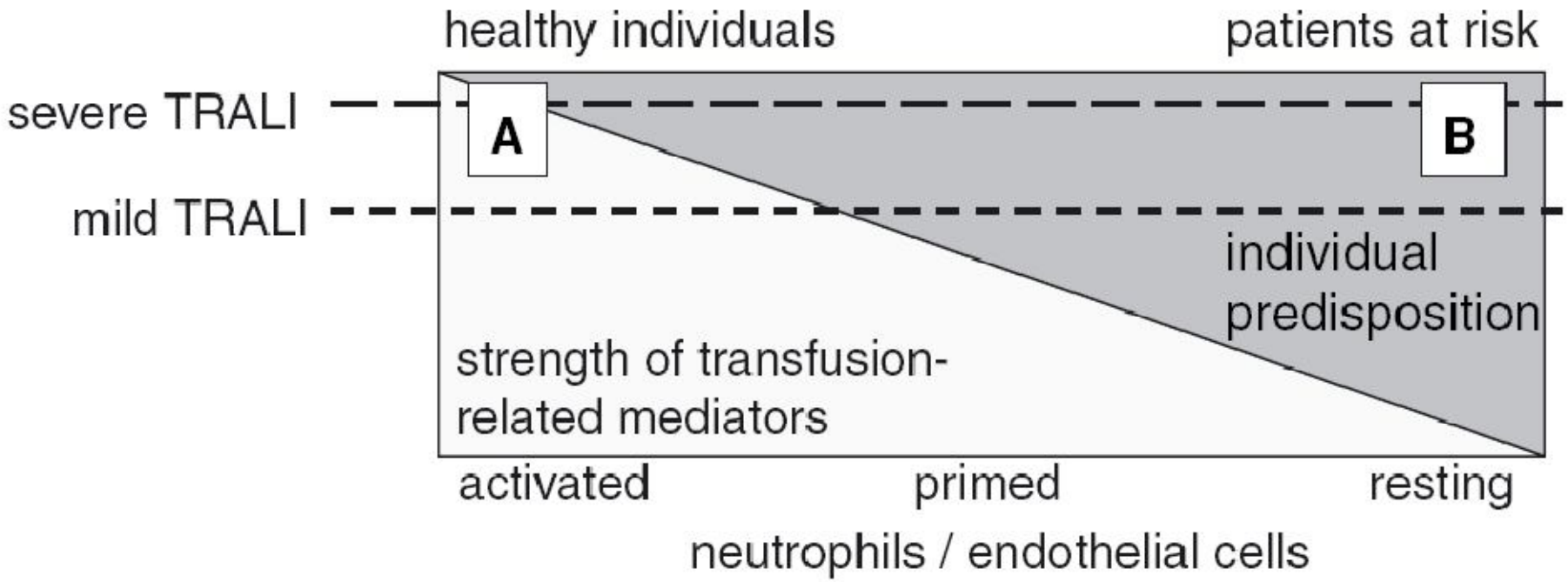


Fig 3. Threshold model of transfusion-related acute lung injury (TRALI). The TRALI threshold model proposes that a certain threshold must be overcome to induce a TRALI reaction.

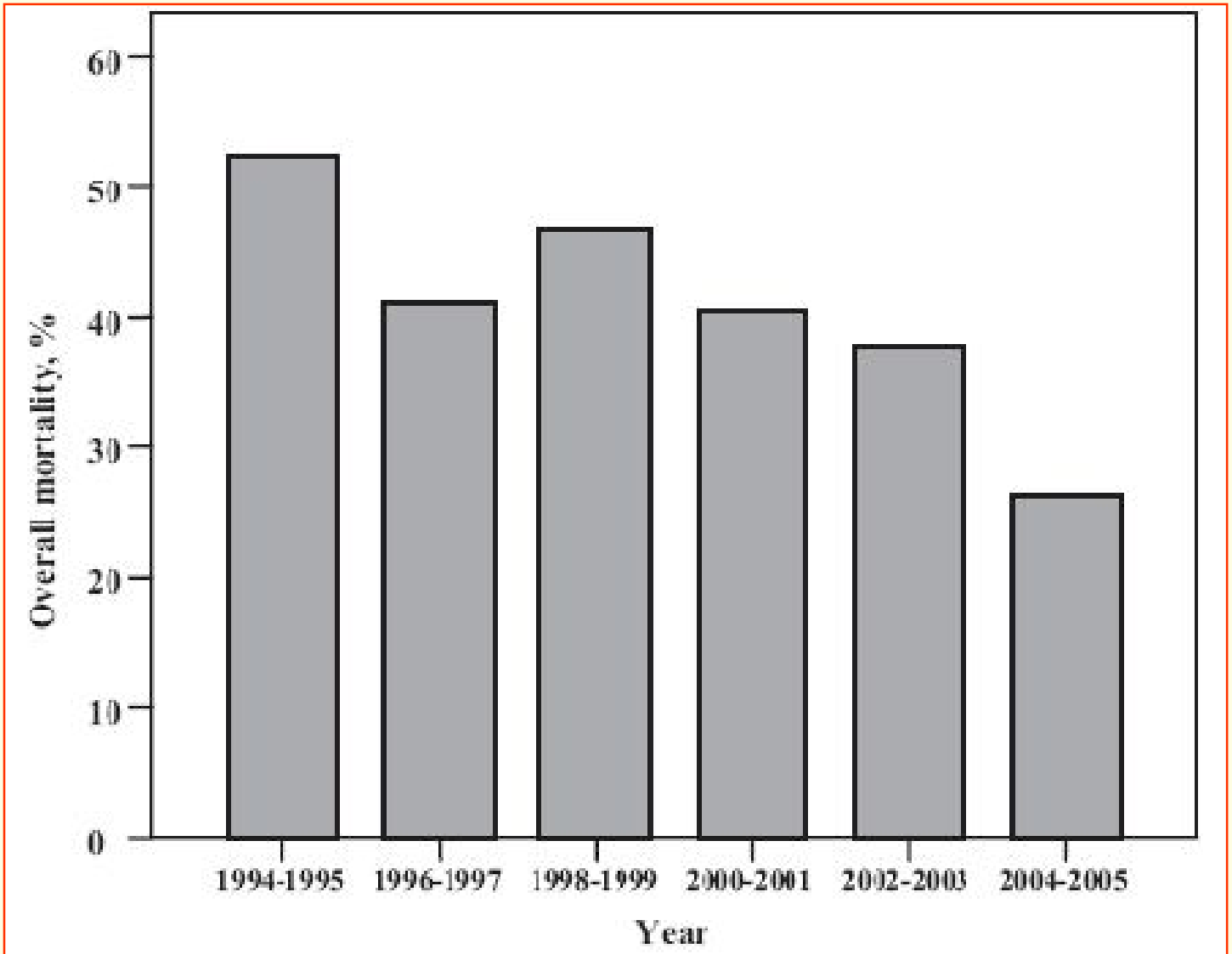


FIGURE 1. Variation in overall pooled mortality rates over time in the 72 ALI/ARDS studies.

Zambon & Vincent, Chest 2008

Ten TRALI issues

8. Treatment

- Aggressive respiratory support, including supplemental oxygen (in mild cases) and mechanical ventilation (in situations of respiratory distress)

Ten TRALI issues

9. Differential diagnosis

Transfusion Associated Cardiac Overload (TACO)

- Dyspnea, cyanosis, tachycardia, increased BP
- Pulmonary edema AND CARDIOMEGALY
- Incidence 1-8% (orthopedics)
- Fatality 1.3%
- 1 case : 708-4,075 RBC transfusions
- Brain Natriuretic Peptide (BNP) post/pre > 1.5
- BNP test 81% sensitive, 89% specific

MA Popowsky. Vox Sanguinis 2008;95(suppl 1) abs 4C-S26-03

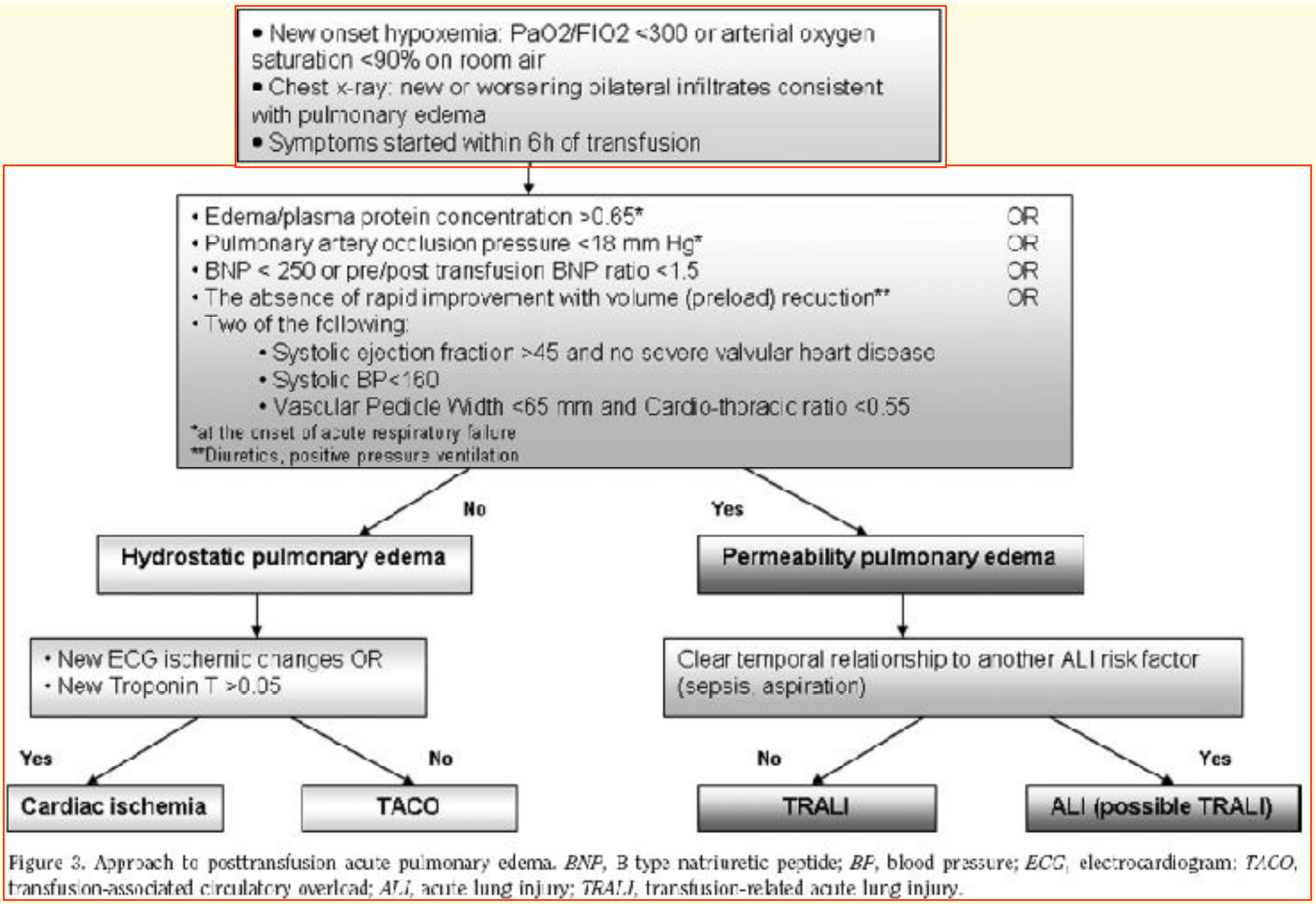


Figure 3. Approach to posttransfusion acute pulmonary edema. *BNP*, B type natriuretic peptide; *BP*, blood pressure; *ECG*, electrocardiogram; *TACO*, transfusion-associated circulatory overload; *ALI*, acute lung injury; *TRALI*, transfusion-related acute lung injury.

O. Gajic Crit Care Med 2006 Vol. 34, No. 5 (Suppl.)

Differential diagnosis other than TACO

- Anaphylactic transfusion reactions
  - may occur after infusion of minimal volumes; hypotension, shock, cutaneous and gastrointestinal symptoms
- Acute hemolytic transfusion reactions
  - fever, oliguria or anuria, diffuse oozing, positive work-up for hemolysis
- Septic shock
  - fever, diffuse oozing, positive cultures

Pulmonary pathology of rapidly fatal transfusion-related acute lung injury reveals minimal evidence of diffuse alveolar damage or alveolar granulocyte infiltration

Constance Danielson, Richard J. Benjamin, Mark M. Mangano, Charles J. Mills, and Dan A. Waxman

doi: 10.1111/j.1537-2995.2008.01879.x
TRANSFUSION **;**:**–**.

TABLE 2. Criteria for the diagnosis of ALI, ARDS, and/or TRALI[21,23]

• Acute onset • Frontal chest radiograph shows bilateral infiltrates • No evidence of left atrial hypertension; if measured, the pulmonary artery occlusion pressure is ≤18 mmHg	ALI ARDS TRALI
• PaO_2/FiO_2 <300 mmHg	ALI TRALI
• PaO_2/FiO_2 <200 mmHg	ARDS TRALI
• Symptoms ≤6 hr of transfusion*	TRALI

* TRALI—The diagnosis is dependent on assessment of clinical course if other risk factors for ALI are also present.

Ten TRALI issues

10. Prevention

- Use of ‘male only’ plasma
  - Spain

Implementation of a strategy to prevent TRALI in a regional blood centre

Transfusion Medicine, 2004, 14, 157–164

A. Insunza,* I. Romon,* M. L. Gonzalez-Ponte,* A. Hoyos,* J. M. Pastor,† A. Iriondo† and V. Hermosa* *Blood and Tissues Bank of Cantabria, and †Department of Haematology of the 'Marqués de Valdecilla' University Hospital, Santander, Spain

We found HLA antibodies in 18·1% of previously pregnant apheresis donors, and our strategy caused a 6·0% loss of apheresis platelets, a 4·8% increase of apheresis fresh frozen plasma (FFP) and a 7·8% loss of transfusable apheresis FFP. The effect on FFP from whole blood donors could be compensated. The platelet preparation method reduced the mean volume of plasma from each donor to 24·4 mL. Fifteen months after the start of our strategy, no cases of TRALI have been reported. Our experience shows that a practical strategy to prevent TRALI is feasible.

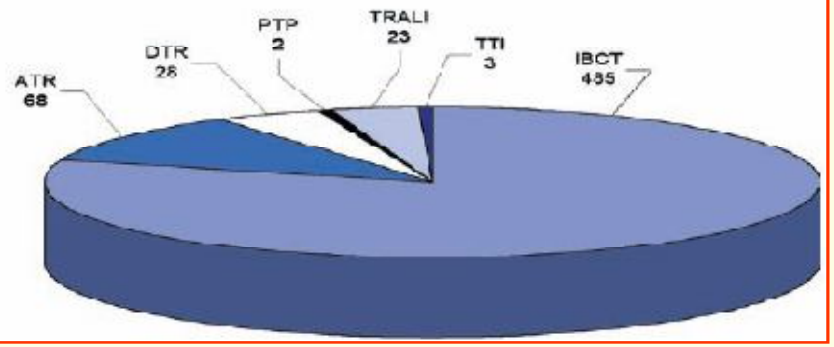
- Use of ‘male only’ plasma
  - UK (SHOT Reports)

2001-2004

Reporting year	2004	2003	2001-2 (15 months)
TRALI cases analysed	23	36	33
Highly likely	10	20	13
Probable	3	2	5
Possible	4	6	14
Unlikely	6	8	1

2005

Fig 1 – Breakdown of reports received in 2005 (n=609)



… ‘male only’ from 2003-2004

2006

IBCT	ATR	HTR	PTP	TA-GvHD	TRALI	TTI	Totals
400	85	34	0	0	10	2	531

2007

IBCT	Anti-D	ATR	HTR	TRALI	PTP	TA-GVHD	TTI	Totals
332	63	114	23	24	2	0	3	561

SHOT Report 2007

Yearly summary of issues by the four UK Blood Services 1999 - 2007

Year	Red blood cells	Platelets	FFP	Cryoprecipitate
1999/2000	2,737,572	249,622	365,547	94,114
2000/2001	2,706,307	250,259	374,760	95,456
2001/2002	2,679,925	251,151	385,236	88,253
2002/2003	2,678,098	251,741	377,381	92,768
2003/2004	2,607,410	264,539	372,855	95,417
2004/2005	2,428,934	258,528	313,019	102,719
2005/2006	2,316,152	259,654	320,852	106,139
2006/2007	2,235,638	255,474	306,444	116,672

- Use of ‘male only’ plasma
  - American Red Cross

TRANSFUSION COMPLICATIONS

TRANSFUSION 2007;47:599-607.

Transfusion-related acute lung injury surveillance (2003-2005) and the potential impact of the selective use of plasma from male donors in the American Red Cross

Anne F. Eder, Ross Herron, Annie Strupp, Beth Dy, Edward P. Notari, Linda A. Chambers, Roger Y. Dodd, and Richard J. Benjamin

CONCLUSION: Plasma components linked to female donors with WBC antibodies were responsible for the majority of probable TRALI fatalities. Prudent measures to limit transfusion of WBC antibody–containing plasma components may prevent as many as six fatalities per year in the Red Cross system.

*… prevention of **6** fatalities/yr…*

The role of donor antibodies in the pathogenesis of transfusion-related acute lung injury: a systematic review

Rutger A. Middelburg, Daniëlle van Stein, Ernest Briët, and Johanna G. van der Bom

doi: 10.1111/j.1537-2995.2008.01810.x
TRANSFUSION **;**:**-**.

TABLE 1. Number of TRALI cases and control patients with and without leukocyte antibodies present in at least one donor

	Leukocyte antibodies				
TRALI	+	–	Total	OR*	95% CI
+	24	4	28		
–	70†	178†	248†	15	5-48
Total	94	182	276		

* The OR has been calculated by the cross-product: $(24 \times 178)/(4 \times 70) = 15$.

† Number of control patients that would have been transfused (in each group) with the 452 products from the randomly drawn donors, if each of them would have received 1.8 transfusions, the same number as received by the 28 TRALI cases.

Testing only donors with a prior history of pregnancy or transfusion is a logical and cost-effective transfusion-related acute lung injury prevention strategy

doi: 10.1111/j.1537-2995.2008.01902.x
TRANSFUSION **;**:**-**.

Amy Powers, Christopher P. Stowell, Walter H. Dzik, Susan L. Saidman, Hang Lee, and Robert S. Makar

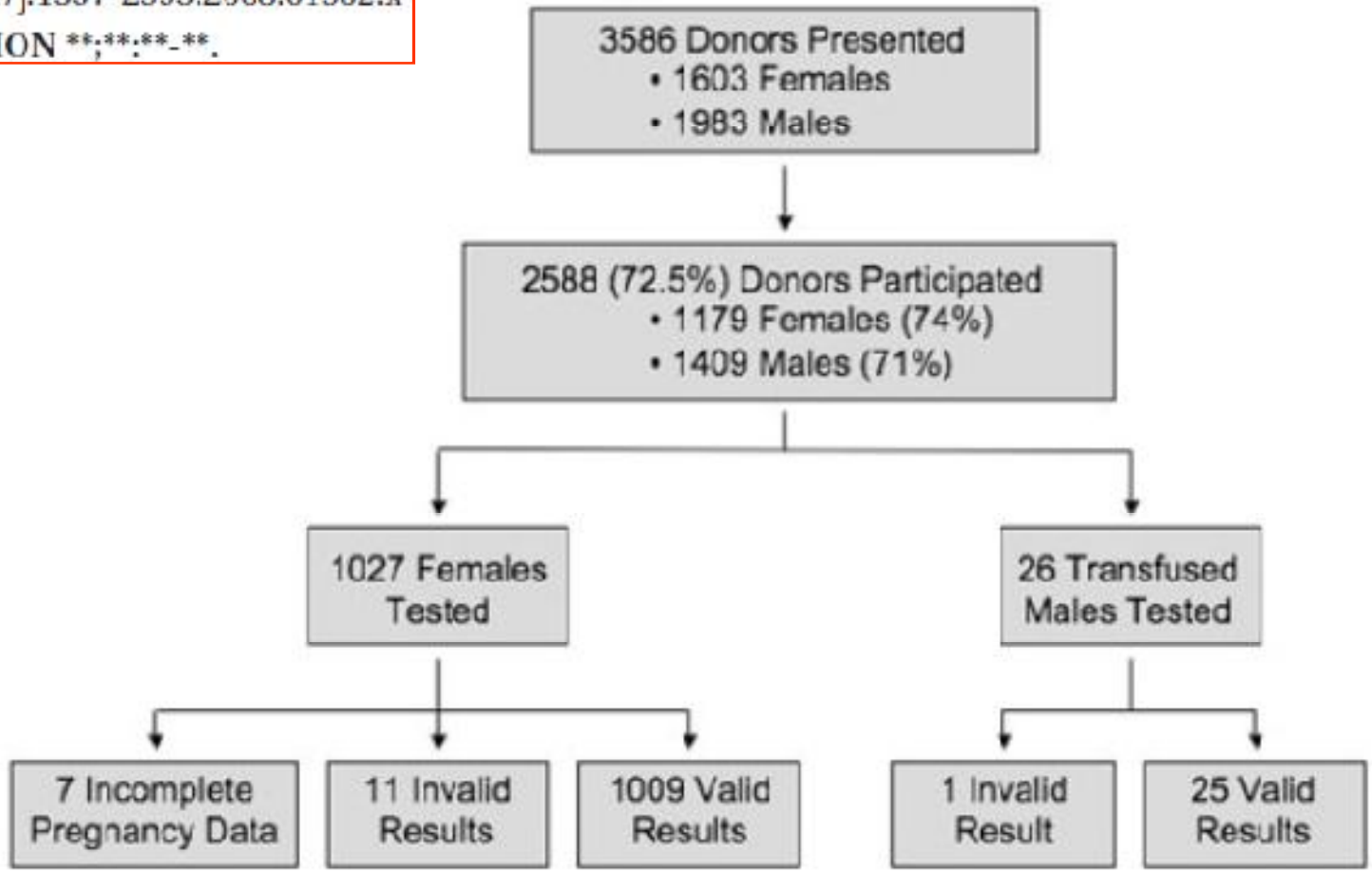


Fig. 1. Study population. Of 3586 potential donors who presented during the study period, 72.5 percent agreed to participate and answer the pregnancy and transfusion questions. After elimination of repeat donors during the study period, 1027 eligible females had samples available for testing; 1009 remained after elimination of those who did not answer the pregnancy questions or had invalid results. Samples from 26 eligible males with a history of transfusion were available for testing after removal of repeat donors. One sample gave a repeatedly invalid result and was eliminated.

Testing only donors with a prior history of pregnancy or transfusion is a logical and cost-effective transfusion-related acute lung injury prevention strategy

Amy Powers, Christopher P. Stowell, Walter H. Dzik, Susan L. Saidman, Hang Lee, and Robert S. Makar

	Strategy	Donor loss (%)
1	No intervention	0
2	Defer all females	43
3	Defer all parous or transfused donors	24.4
4	Universal testing, defer positive donors	11.1
5	Test females only, defer positive donors	10.9
6	Test all parous or transfused donors, defer positive donors	9.8

	Estimated cost per 1000 donors ($)		
	Luminex cost*	FFP cost	Total cost
1	0	0	0
2	0	22,442	22,442
3	0	12,734	12,734
4	13,455.00	5,793	19,248
5	5,761	5,689	11,450
6	3,294	5,115	8,409

	Estimated number of alloimmunized donors remaining/1000†	Cost per alloimmunized unit removed ($)
1	111 males and females	
2	2 males	206
3	12 female donors	129
4	None	173
5	2 males	105
6	12 female donors	85

doi: 10.1111/j.1537-2995.2008.01902.x
TRANSFUSION **;**:** **.

Computer-generated automatic alerts of respiratory distress after blood transfusion.

Finlay-Morreale HE, Louie C, Toy P.

J Am Med Inform Assoc. 2008;15:383-5

- Computer generates alert when blood gas result indicates a **PaO2:FiO2 ratio <300**, within 12 hr of blood issued from the blood bank
- Comparison of detection by ICU rounds vs computer alert
- Results:
  - ICU rounds: 9 of 14 patients **(64%)**
  - Computer alert: 13 of 14 patients **(93%)**
- Conclusions: computer as effective (p=0.125), more efficient (less operator time)

Porpora posttrasfusionale (PTP)

Eziologia:

alloanticorpi piastrinospecifici (anti-HPA-1a (PI^{A1}) nel 70% circa dei casi).

L'anticorpo distrugge le piastrine trasfuse e quelle autologhe (antigene solubile, distruzione da immunocomplessi, anticorpi cross-reagenti)

Sintomatologia:

rapido calo conteggio plt ($<10x10^9/L$) 5-10 giorni dopo la trasfusione (paziente sensibilizzato)

Donatella Riccardi
2000-2003

PTP

Indagini di laboratorio:

- ricerca e identificazione di anticorpi piastrinospecifici
- tipizzazione del paziente per antigeni piastrinospecifici

Trattamento:

Immunoglobuline (IGIV) ad alte dosi, IGIV associate a trasfusione di piastrine negative per antigene implicato, plasma exchange.

Risoluzione spontanea a 2-3 settimane, rischio di emorragia cerebrale; sconsigliata la trasfusione di piastrine random.

Transfusion Associated Graft Versus Host Disease (TA-GVHD)

Eziologia:

attecchimento ed espansione di un clone linfocitario del donatore in un paziente incapace di rigettarlo.

Aggressione immunologica dei tessuti del ricevente.

Soggetti a rischio:

- pazienti con immunodeficienze primarie o secondarie,
- pazienti immunocompetenti che ricevono sangue da donatori con i quali condividono un aplotipo del sistema HLA.

Sintomatologia:

4-30 gg posttrasf., pancitopenia, ipoplasia midollare, febbre, diarrea, lesioni cutanee, ↑ enzimi epatici, ecc.

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2000-2003

TA-GVHD

Indagini di laboratorio:

indagini istologiche (biopsia cutanea), dimostrazione di chimerismo nel paziente, linfociti del donatore circolanti nel sangue del ricevente (tecniche di biologia molecolare e citogenetiche)

Trattamento:

nessuno (mortalità 90%)

Prevenzione:

Irraggiamento di emocomponenti contenenti cellule, almeno 25 Gy al centro dell'unità e 15 Gy ai bordi.

Clinical and Pathological Comparison of GVHD Associated with Bone Marrow Transplantation (BMTA-GVHD) and Transfusions (TA-GVHD)

Manifestation	BMTA-GVHD	TA-GVHD
Time sequence	35–70 days	2–30 days
Rash	+	+
Constitutional symptoms	Profound	Mild to moderate
Liver enzyme elevation	+	+
Pancytopenia	Rare to minimal	Almost always
Bone marrow hypoplasia or aplasia	+/−	++
Occurrence of GVHD	70%	?0.1–1%
Response to therapy	80–90%	None
Mortality	10–15%	80–100%

Modified from Brubaker DB. Transfusion associated graft versus host disease. Hum Pathol 1986;17:1085–1088.

TA-GVHD

Indicazioni all'irraggiamento degli emocomponenti

Pazienti immunodeficienti:

- trasfusione intrauterina
- exanguino-trasfusione dopo tras. intrauterine
- neonati immaturi
- SCID
- sindrome di Wiscott-Aldrich
- auto e allo trapianto di midollo e PBSC
- linfomi di Hodgkin
- pazienti trattati con fludarabina

Pazienti immunocompetenti:

- trasfusioni tra consanguinei di 1° e 2° grado
- emocomponenti HLA compatibili.

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2000-2003

Reazioni da contaminazione batterica dell'unità trasfusa (complicanze infettive)

Eziologia:

- asepsi inadeguata della cute del donatore nel sito di prelievo
- donatore portatore di infezione batterica subclinica (cronica o transitoria)

Microrganismi implicati:

Globuli rossi: Gram negativi - reazioni più gravi - psicrofili, in grado di crescere a basse temperature (0°C) o che utilizzano come substrato il citrato (Yersinia enterocolitica, Citrobacter freundii).
Altri implicati: Pseudomonas species, Escherichia coli, ecc.

Concentrati piastrinici: Gram positivi - (Staphylococcus aureus, S. epidermidis, Streptococci) e Gram negativi (Enterobacter cloacae, Salmonella, ecc.)

Contaminazione batterica dell'unità trasfusa

Sintomatologia:

rigor, febbre, tachicardia, nausea e vomito, dolore lombare, dispnea, ipotensione, ipertensione, DIC
reazioni febbrili, anche di modesta entità.
Gram negativi e tossine prodotte: reazioni più gravi
Gram positivi: reazioni febbrili di modesta entità fino a reazioni fatali

Trattamento:

Interrompere la trasfusione, somministrare antibiotici ad ampio spettro, terapia intensiva (dello shock, della DIC, dell'insufficienza renale)

Indagini di laboratorio:

emocoltura sull'unità trasfusa e sul sangue del paziente

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Contaminazione batterica

Strategie di prevenzione

- Prevenzione della sepsi
- Identificazione delle unità infette
- Inattivazione degli agenti patogeni

La scelta della strategia migliore è difficile per problemi di:
- costi elevati
- difficoltà logistiche e organizzative
- problemi tecnici (sensibilità/specificità/sicurezza)

Prevenzione della sepsi

- scrupolosa disinfezione della cute del donatore
- selezione del donatore
- cura nella manipolazione del sangue (frazionamento, ecc.)
- sistemi di eliminazione della quota iniziale della donazione

Inattivazione degli agenti patogeni

Plasma:

- trattamento con solventi-detergenti (plasma)
- fotoinattivazione fotodinamica (Blu di Metilene + sorgente di luce visibile)

Piastrine, plasma:

- fotoinattivazione fotochimica (derivati sintetici dello Psoralene + UVA [S-59], Riboflavina + luce visibile)

RBC:

- inactina
- derivato dello psoralene (S-303)

In summary …

Risks per RBC unit
Klein et al
Lancet 2007

	Estimated risk
Febrile reaction	1 in 300
Urticaria or other cutaneous reaction	1 in 50–100
RBC alloimmunisation	1 in 100
Mistransfusion	1 in 14 000–19 000
Haemolytic reaction	1 in 6000
Fatal haemolysis	1 in 1 000 000
TRALI	1 in 5000
HIV 1 and HIV2	1 in 2 000 000–3 000 000
Hepatitis B	1 in 100 000–200 000
Hepatitis C	1 in 1 000 000–1 in 2 000 000
HTLV I and II	1 in 641 000
Bacterial contamination	1 in 5 000 000
Malaria	1 in 4 000 000
Anaphylaxis	1 in 20 000–50 000
GvHD	Uncommon
Immunomodulation	Unknown

Table 3: Estimated risks in transfusion per unit transfused in the USA