Mercoledì 18 dicembre ore 14.30
Aula didattica 2 CR
-Journal Club-

Nessuno versa il sangue di un altro per il gusto di uccidere, o almeno pochi ...

Seneca

Dott.ssa P. Bera, Dott. F. Setti,
Dott.ssa S. Capuccini, Dott.ssa F. Caminiti

Anemia

defined by the World Health Organization as a

hemoglobin level less than 13 g/dL in men and less than 12 g/dL in women,

is an epidemic afflicting one-quarter of the world's population, approximately 50% of hospitalized patients, and up to 75% of elderly hospitalized patients.

Anemia, Bleeding, and Blood Transfusion in the Intensive Care Unit:
Causes, Risks, Costs, and New Strategies.
Michael T. McEvoy and Aryeh Shander. Am J Crit Care 2013;22:eS1-eS13 doi: 10.4037/ajcc2013729

A high percentage of patients become anemic during a stay

in an intensive care unit (ICU),

from 60% to 66% at admission,

up to 90% by day 3,

and 97% by day 8.

Vincent JL, Baron JF, Reinhart K, et al. Anemia and blood transfusion in critically ill patients. JAMA. 2002;288(12) 1499-1507.

Corwin HL, Gettinger A, Pearl RG, et al. The CRIT Study: anemia and blood transfusion in the critically ill—current clinical practice in the United States. Crit Care Med. 2004;32(1):39-52.

Gattinoni L, Chiumello D. Anemia in the intensive care unit: how big is the problem? Transfus Altern Transfus Med. 2002; 4(4):118-120.

Thomas J, Jensen L, Nahirniak S, Gibney RT. Anemia and blood transfusion practices in the critically ill: a prospective cohort review. Heart Lung. 2010;39(3):217-225.

Type	Causes
Nutritional deficiencies	Low iron levels Low folate levels Low vitamin B levels
Erythropoietin deficiencies	Anemia of chronic disease Renal insufficiency Infection Endocrine disorders
Hemolysis	Drug reactions Toxins
Coagulation abnormalities	Thrombocytopenia Sepsis syndrome Liver disease Viral infection Splenomegaly
Blood loss	Phlebotomy Trauma Surgery Gastrointestinal bleeding

Drugs commonly linked to hemolytic anemia[a]

Mechanism of hemolysis	Common medications
Immune	Cephalosporins/cephamycins Cefotetan Ceftriaxone
	β-lactams Penicillin derivatives Piperacillin
	Nonsteroidal anti-inflammatories Diclofenac Ibuprofen
	Antineoplastics Fludarabine
	Others Methyldopa Quinine/quinidine
Nonimmune	Nitrofurantoin
	Phenazopyridine
	Primaquine
	Sulfa drugs

[a] Based on information from Shander et al.[26]

- Blood is an indispensable product in modern medical practice.

- Red blood cells are used to improve oxygen delivery to tissues in situations of haemorrage and anaemia.

- Red blood cell transfusion constitutes one of the mainstays of therapy in the management of anaemic patients and is one of the few treatments that adequately restores tissue oxygenation when oxygen demand exceeds supply.

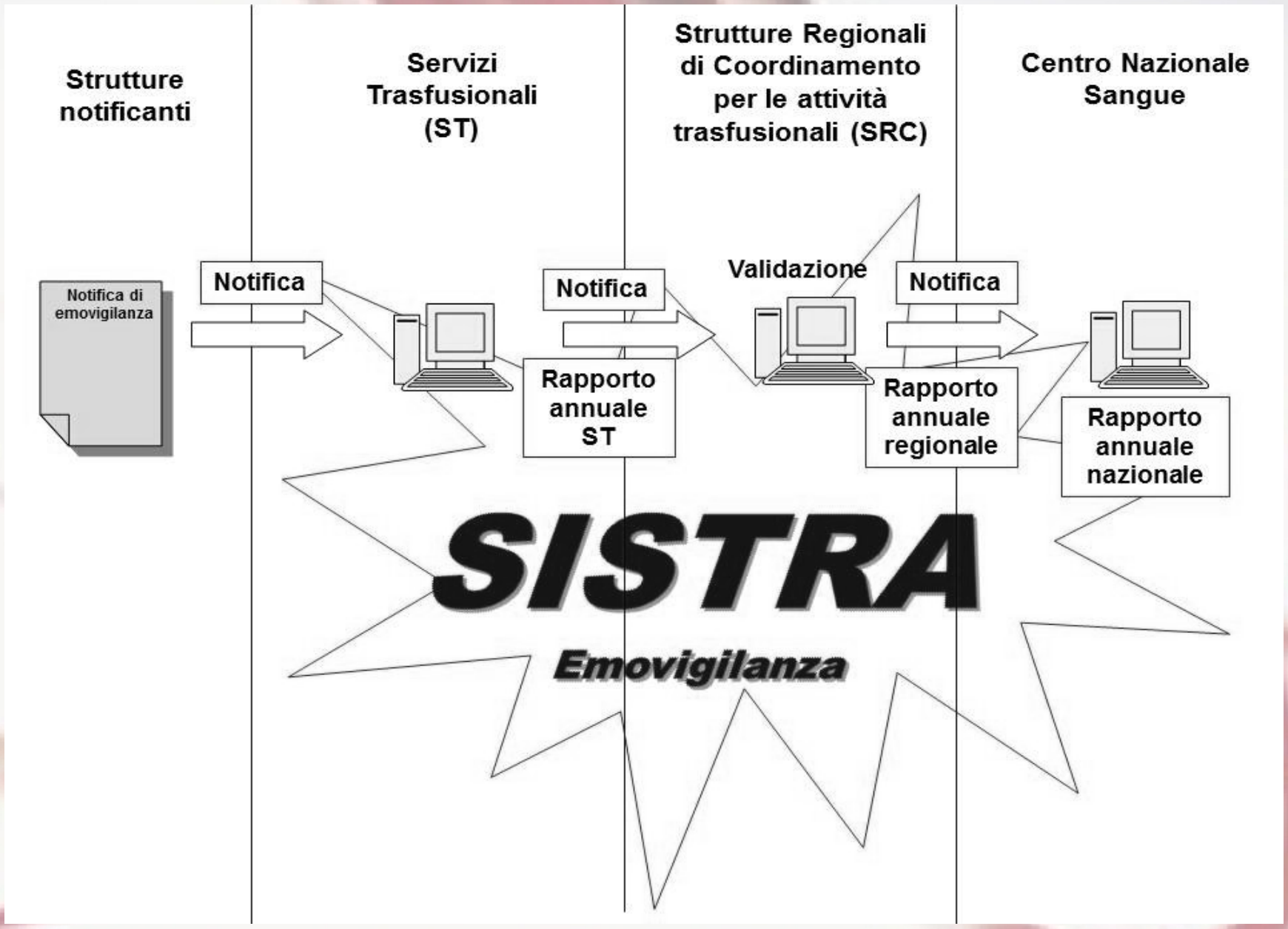
Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion (Review); Carson JL, Carless PA, Hebert PC; The Cochrane Collaboration 2012, Issue 4

- The *risk* and *availability* of red blood cell transfusion varies throughout the world.
- In most developed countries with well-regulated blood supplies, the safety of allogeneic red cell transfusion has improved significantly over the past 30 years.
- This has been primarily due to improvements in donor blood screening procedures and the implementation of more stringent quality control measures.

SISTEMA DI EMOVIGILANZA ITALIANO

La segnalazione di reazioni indesiderate gravi, intese come le risposte inattese che possono provocare la morte, mettere in pericolo di vita o produrre invalidità o incapacità nel donatore, connesse con la donazione di sangue e emocomponenti, sono soggette ad obbligo di notifica per disposizione del DL.vo del 20 dicembre 2007 n. 261 (4), che recepisce la Direttiva 2002/98/CE.

FLUSSO INFORMATIVO DELL'EMOVIGILANZA



Rapporti
ISTISAN

13/21

Attività di emovigilanza in Italia. Rapporto 2009-2011

ISSN 1123-3117

G. Facco, V. Piccinini, L. Catalano,
S. Pupella, G. Grazzini

Tabella 6. Effetti indesiderati nei riceventi di ogni livello di imputabilità e gravità (anni 2009-2011)

Reazione	2009		2010		2011	
	n.	%	n.	%	n.	%
Manifestazioni allergiche	343	34,6	489	37,1	657	39,0
Reazione febbrile non emolitica	324	32,7	382	29,0	600	35,6
Altro	133	13,4	205	15,6	147	8,7
Dispnea associata alla trasfusione	54	5,5	69	5,2	85	5,0
Ipotensione	28	2,8	36	2,7	37	2,2
Sovraccarico circolatorio (TACO)	23	2,3	22	1,7	43	2,6
Ipertensione	18	1,8	22	1,7	21	1,2
Anafilassi	16	1,6	18	1,4	25	1,5
Alloimmunizzazione	6	0,6	17	1,3	28	1,7
Edema polmonare non cardiogeno (TRALI)	6	0,6	12	0,9	4	0,2
Reazione emolitica acuta da AB0	13	1,3	5	0,4	3	0,2
Ipotermia	4	0,4	6	0,5	6	0,4
Reazione emolitica ritardata	3	0,3	5	0,4	2	0,1
Reazione emolitica ritardata da altri sistemi gruppo ematici	3	0,3	4	0,3	3	0,2
Porpora post trasfusionale	1	0,1	5	0,4	3	0,2
Altre infezioni batteriche	1	0,1	6	0,5	0	0,0
Emolisi non immunologica - Causa fisica	2	0,2	3	0,2	2	0,1
Shock anafilattico	1	0,1	3	0,2	3	0,2
Emolisi non immunologica - Causa chimica	0	0,0	1	0,1	5	0,3
Emolisi non immunologica - Causa meccanica	1	0,1	3	0,2	2	0,1
Ipocalcemia	0	0,0	1	0,1	4	0,2
Anemia emolitica autoimmune	2	0,2	1	0,1	1	0,1
Reazione emolitica immediata	1	0,1	1	0,1	2	0,1
Iperkaliemia	1	0,1	0	0,0	1	0,1
Reazione emolitica acuta da altri sistemi gruppo ematici	1	0,1	1	0,1	0	0,0
Reazione emolitica ritardata da Rh	2	0,2	0	0,0	0	0,0
Graft versus Host Disease (GvHD)	1	0,1	0	0,0	0	0,0
Inefficacia trasfusionale	1	0,1	0	0,0	0	0,0
Reazione emolitica acuta da Rh	1	0,1	0	0,0	0	0,0
Reazione emolitica ritardata da AB0	0	0,0	0	0,0	1	0,1
Totale	990	100,0	1.317	100,0	1.685	100,0

Tabella 8. Imputabilità dell'emocomponente (anni 2009-2011)

Livello di imputabilità		2009		2010		2011	
		n.	%	n.	%	n.	%
Non valutabile	N.V.	52	5,3	96	7,3	125	7,4
Esclusa/Improbabile	0	158	16,0	228	17,3	214	12,7
Possibile	1	237	23,9	309	23,5	512	30,4
Probabile	2	416	42,0	508	38,6	668	39,6
Certa	3	127	12,8	176	13,4	166	9,9
Totale		990	100,0	1.317	100,0	1.685	100,0

Tabella 9. Luogo della trasfusione (anni 2009-2011).

Luogo della trasfusione	2009		2010		2011	
	n.	%	n.	%	n.	%
Reparto	797	80,5	1.090	82,8	1.342	79,6
Emergenza/Terapia intensiva	66	6,7	76	5,8	93	5,5
Day hospital	37	3,7	66	5,0	114	6,8
Servizio Trasfusionale	20	2,0	41	3,1	73	4,3
Sala operatoria	36	3,6	27	2,1	20	1,2
Ambulatorio	26	2,6	12	0,9	30	1,8
Domicilio	8	0,8	5	0,4	13	0,8
Totale	990	100,0	1.317	100,0	1.685	100,0

Tabella 7. Gravità degli effetti indesiderati alla trasfusione (anni 2009-2011)

	Livello di gravità	2009		2010		2011	
		n.	%	n.	%	n.	%
0	Nessun sintomo	6	0,6	19	1,4	21	1,2
1	Sintomatologia lieve (nessun intervento terapeutico)	280	28,3	453	34,4	568	33,7
2	Sintomatologia con necessità di intervento terapeutico	685	69,2	825	62,6	1.070	63,5
3	Sintomatologia grave che richiede procedure rianimatorie	15	1,5	17	1,3	25	1,5
4	Morte	4	0,4	3	0,2	1	0,1
	Totale	990	100,0	1.317	100,0	1.685	100,0

Emocomponenti trasfusi

Gli emocomponenti trasfusi sono stati:

- 3.391.626 nel 2009
- 3.383.241 nel 2010
- 3.407.448 nel 2011

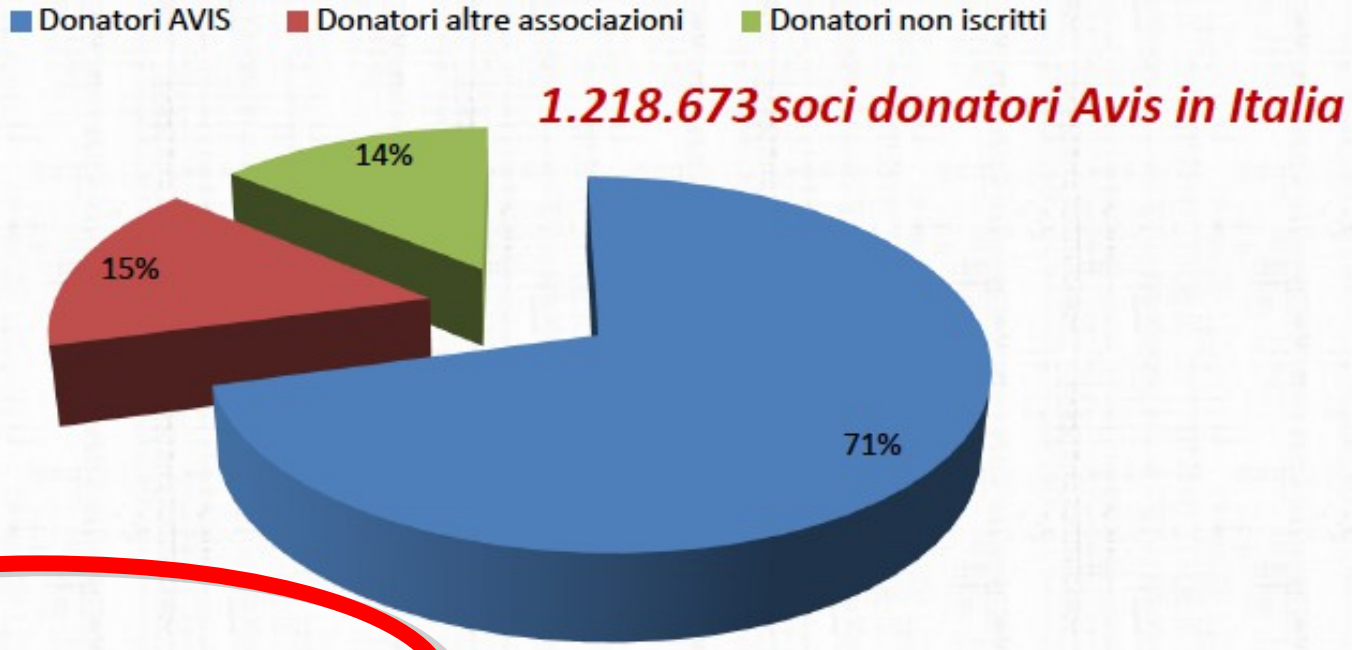
Tabella 24. Numero di donazioni omologhe effettuate divise per tipologia di donazione (anni 2009-2011).

Donazioni	2009	2010	2011
Sangue intero	2.554.597	2.609.191	2.679.581
Plasmaferesi	369.330	388.008	400.144
Plasma-Piastrino aferesi	48.571	50.381	52.923
Eritro-Plasma aferesi	22.448	19.473	22.749
Plasmapiastrinoaferesi in unica sacca	12.314	6.711	8.892
Eritro-Piastrino aferesi	8.449	8.664	8.718
Piastrinoaferesi	8.236	7.628	8.808
Piastrino aferesi doppia unità	3.461	5.117	2.184
Multicomponent	1.642	6.152	0
Cellule staminali da aferesi	2.317	2.303	1.537
Eritroaferesi doppia unità	833	817	694
Leucoaferesi	1.090	882	92
Linfocitoaferesi	642	288	219
Granulocitoaferesi	361	128	163
Eritro-Plasma-Piastrino aferesi	120	95	270
Totale	3.034.411	3.105.838	3.186.974

CERGAS
Centro di Ricerche sulla Gestione dell'Assistenza Sanitaria e Sociale

I numeri di AVIS

I donatori e le associazioni/federazioni



1.218.673 soci donatori Avis in Italia

1.722.503 donatori in Italia

POTENTIAL RISKS OF BLOOD TRANSFUSION

1- TRANSFUSION-ASSOCIATED ACUTE LUNG INJURY

2- TRANSFUSION-ASSOCIATED CIRCULATORY OVERLOAD

3- INFECTIOUS AGENTS

4- TRANSFUSION REACTIONS (ANAPHYLAXIS)

5- ALLOIMMUNISATION

6- OTHERS (MEDICAL ERRORS -wrong blood to patient because of mislabelled specimen or patient misidentification-, IRON OVERLOAD, IMMUNOMODULATION, STORAGE LESIONS -age of blood-)

TRANSFUSION-RELATED ACUTE LUNG INJURY

TRALI is a rare but potentially fatal complication of blood product transfusion.

TRALI has been defined by both a National Heart, Lung, and Blood Institute (NHLBI) working group as well as a Canadian Consensus Conference (2004) , as new acute lung injury (ALI) occurring during or within six hours after blood product administration.

Table I. Criteria for the clinical diagnosis of transfusion-related acute lung injury (TRALI).

TRALI Consensus Conference Committee 2004 and European Haemovigilance Network

- Acute respiratory distress
- Bilateral lung infiltrations in the chest radiograph
- Occurrence during or within 6-h after completion of transfusion
- No evidence of transfusion-associated circulatory overload/cardiogenic lung oedema
- Hypoxaemia (PaO_2/FiO_2 <300 mmHg or O_2 saturation <90% or other clinical evidence)
- New acute lung injury (ALI) and no other ALI risk factors present (aspiration, multiple trauma, pneumonia, cardiopulmonary bypass, burn injury, toxic inhalation, lung contusion, pancreatitis, drug overdose, near drowning, shock, severe sepsis)

If one or more ALI risk factors are present, possible TRALI should be diagnosed.

EPIDEMIOLOGY:

TRALI occurs at a rate of approximately

0,08 to 8 percent of transfused patients

or in approximately

0,002 to 1,12 percent transfused blood components

However, the true incidence of TRALI is not known, largely due to poor syndrome recognition, the reliance on passive reporting rather than active surveillance strategies, and the inclusion of cases that did not meet the NHLBI or Canadian Consensus Conference definitions of TRALI in some reports.

EPIDEMIOLOGY:

MORTALITY:

Historical estimates for TRALI–associated mortality have ranged from 5 to 8 percent. Not surprisingly, the mortality rate for TRALI/possible TRALI in critically ill populations appears substantially higher, in the range of 35 to 58 percent.

Fatalities Reported to U.S.FDA Following Blood Collection and Transfusion: Annual Summary for Fiscal Year 2012

During FY2012 (October 1, 2011, through September 30, 2012), we received a total of 88 fatality reports. Of these reports, 74 were transfusion recipient fatalities and 14 were post-donation fatalities.

Of the 74 transfusion recipient fatality reports, we concluded:

- 38 (51%) of the fatalities were transfusion-related,
- 27 (36%) of the fatalities were cases in which transfusion could not be ruled out as the cause of the fatality,
- 9 (12%) of the fatalities were unrelated to the transfusion.

Of the 14 post-donation fatality reports, we concluded:

- 11 (79%) of the fatalities were cases in which donation could not be ruled out as the cause of the fatality,
- 3 (21%) of the fatalities were unrelated to the donation.

Table 1: Transfusion-Related Fatalities by Complication, FY2008 through FY2012

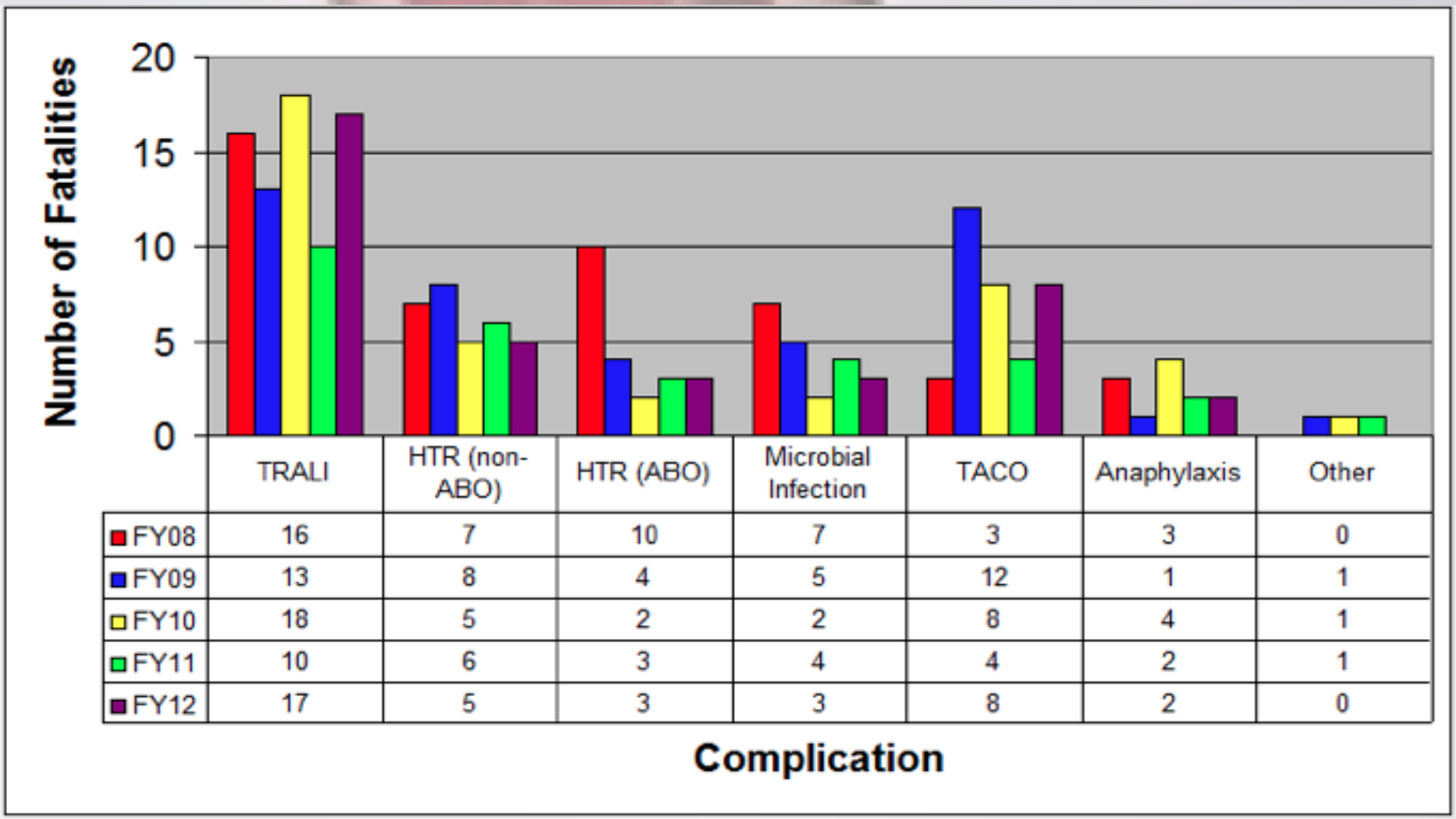
Complication	FY08	FY08	FY09	FY09	FY10	FY10	FY11	FY11	FY12	FY12	Total	Total
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
TRALI*	16	35%	13	30%	18	45%	10	33%	17	45%	74	37%
HTR (non-ABO)	7	15%	8	18%	5	13%	6	20%	5	13%	31	16%
HTR (ABO)	10	22%	4	9%	2	5%	3	10%	3	8%	22	11%
Microbial Infection	7	15%	5	11%	2	5%	4	12%	3	8%	21	11%
TACO	3	7%	12	27%	8	20%	4	13%	8	21%	35	18%
Anaphylaxis	3	7%	1	2%	4	10%	2	7%	2	5%	12	6%
Other	0	0%	1**	2%	1**	3%	1**	3%	0	0%	3	1%
Totals	46	100%	44	100%	40	100%	30	100%	38	100%	198	100%

*These numbers include both "TRALI" and "possible TRALI" cases[10,11]

**Other:
FY2009: Hypotensive Reaction
FY2010: Graft vs. Host Disease (GVHD)
FY2011: GVHD[12]

Figure 1: Transfusion-Related Fatalities by Complication, FY2008 through FY2012

In combined Fiscal Years 2008 through 2012, Transfusion Related Acute Lung Injury (TRALI) caused the highest number of reported fatalities (37%), followed by hemolytic transfusion reactions (total of 27%) due to non-ABO (16%) and ABO (11%) incompatibilities. Complications of Transfusion Associated Circulatory Overload (TACO) (18%), microbial infection (11%), and anaphylactic reactions (6%) each accounted for a smaller number of reported fatalities.



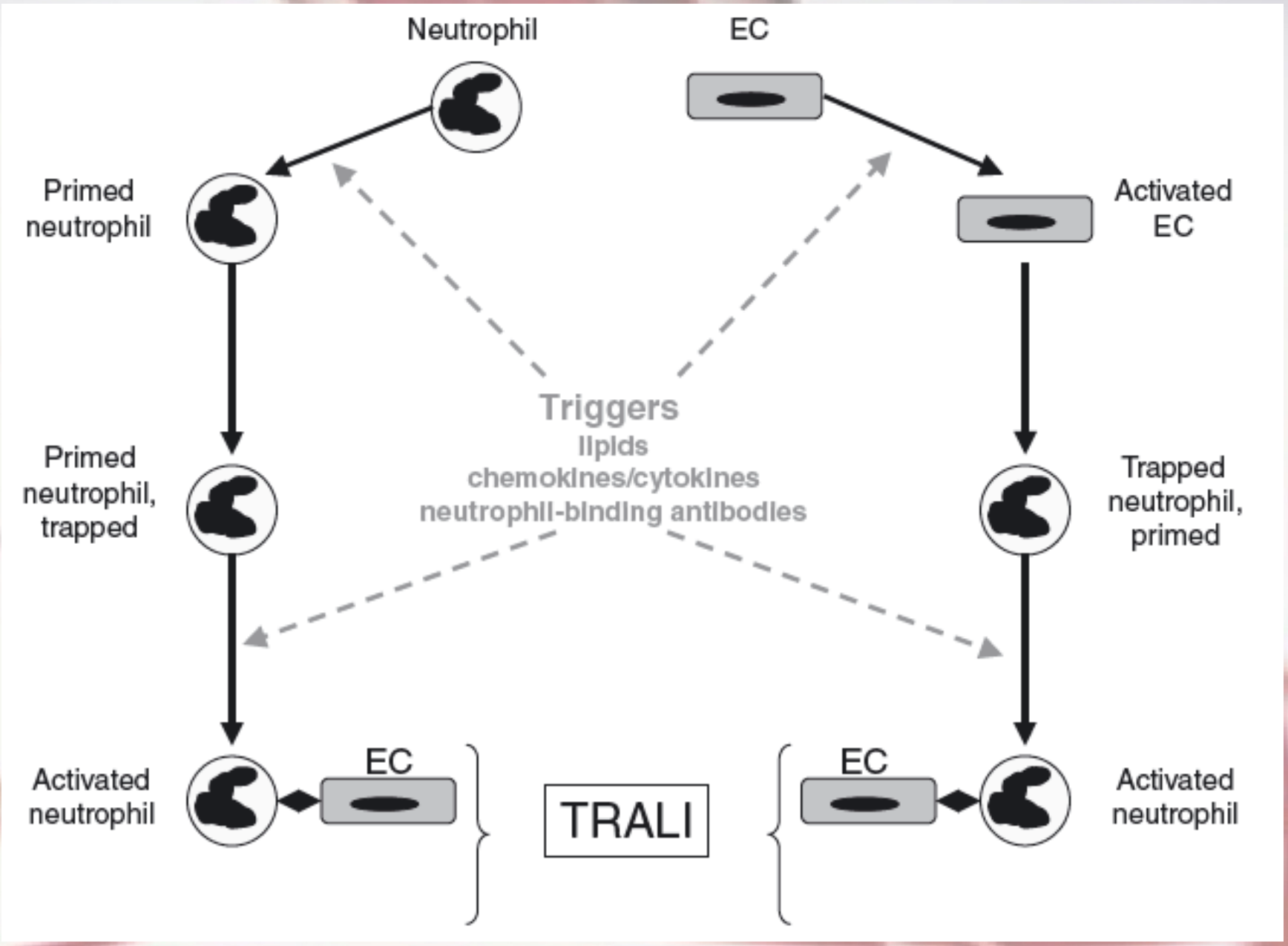
	TRALI	HTR (non-ABO)	HTR (ABO)	Microbial Infection	TACO	Anaphylaxis	Other
FY08	16	7	10	7	3	3	0
FY09	13	8	4	5	12	1	1
FY10	18	5	2	2	8	4	1
FY11	10	6	3	4	4	2	1
FY12	17	5	3	3	8	2	0

Figure 1:
FY08:TRALI:16;HTR(non-ABO):7;HTR:(ABO):10;Microbial Infection:7;TACO:3;Anaphylaxis:3;Other:0
FY09:TRALI:13;HTR(non-ABO):8;HTR(ABO):4;Microbial Infection:5;TACO:12;Anaphylaxis:1;Other:1
FY10:TRALI:18;HTR(non-ABO):5;HTR(ABO):2;Microbial Infection:2;TACO:8;Anaphylaxis:4;Other:1
FY11:TRALI:10;HTR(non-ABO):6;HTR(ABO):3;Microbial Infection:4;TACO:4;Anaphylaxis:2;Other:1
FY12:TRALI:17;HTR(non-ABO):5;HTR(ABO):3;Microbial Infection:3;TACO:8;Anaphylaxis:2;Other:0

PATHOGENESIS:

Leukocyte antibodies and biologically active substances such as lipids and cytokines that have neutrophil priming activity.

Leukocyte antibody in donors, often multiparous women, activates recipient neutrophils in pulmonary capillaries and causes pulmonary damage and capillary leak.


Neutrophil
EC
Primed neutrophil
Activated EC
Triggers
lipids
chemokines/cytokines
neutrophil-binding antibodies
Primed neutrophil, trapped
Trapped neutrophil, primed
Activated neutrophil
EC
TRALI
EC
Activated neutrophil

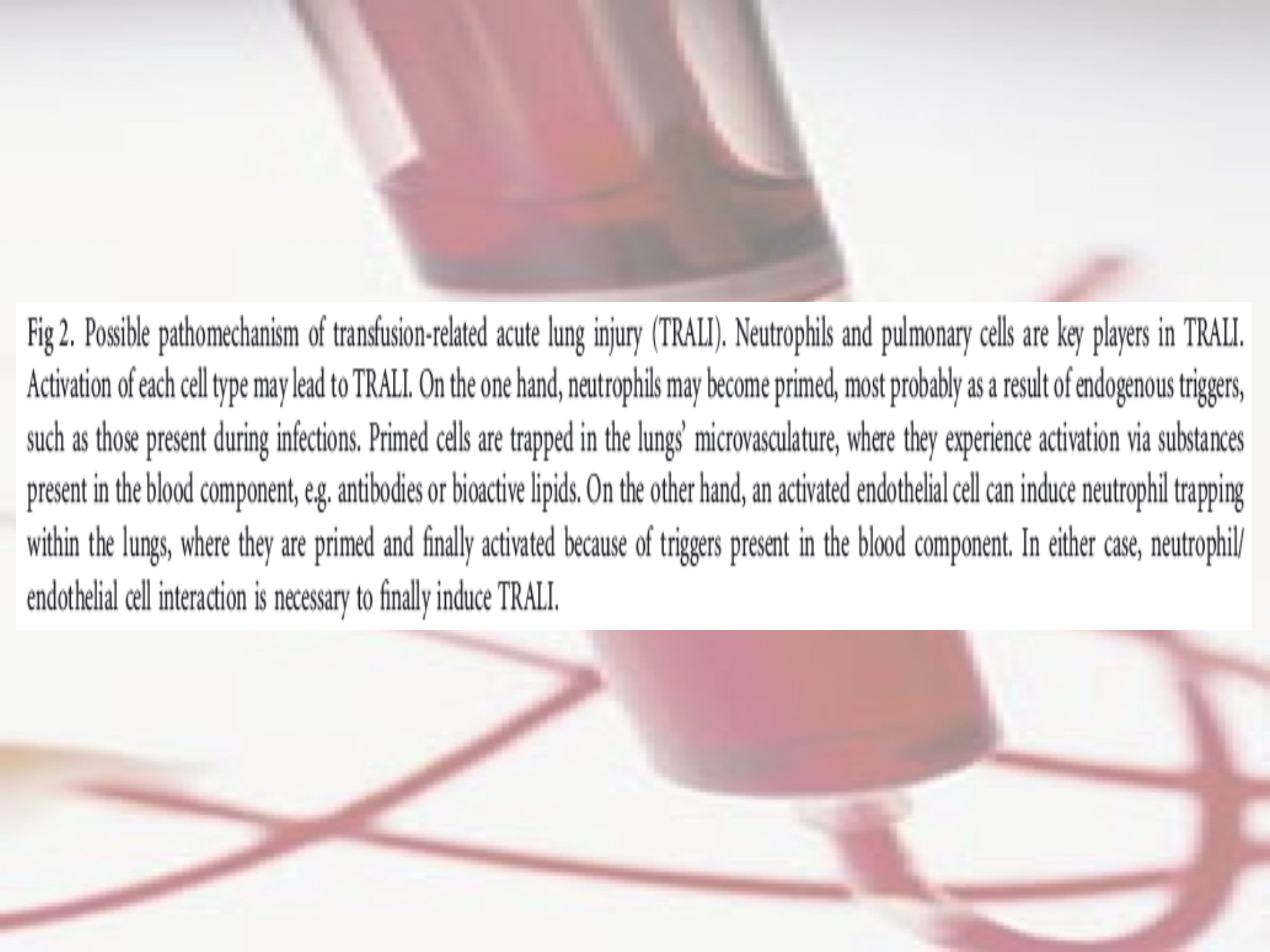


Fig 2. Possible pathomechanism of transfusion-related acute lung injury (TRALI). Neutrophils and pulmonary cells are key players in TRALI. Activation of each cell type may lead to TRALI. On the one hand, neutrophils may become primed, most probably as a result of endogenous triggers, such as those present 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.

TRALI è stata descritta a seguito della trasfusione della maggior parte dei prodotti del sangue, compresi emazie concentrate, PFC (plasma fresco congelato), piastrine (da sangue intero e da aferesi); sono stati riportati anche alcuni casi associati alla somministrazione endovenosa di immunoglobuline (IVIG), crioprecipitati, cellule staminali midollari allogeniche e trasfusione di granulociti.

TREATMENT:

If TRALI/possible TRALI is suspected,

the transfusion should be discontinued immediately.

Physicians should alert the blood bank and initiate an evaluation for a transfusion reaction.

This is important for the protection of future recipients as well as for TRALI laboratory testing and work-up.

- Oxygen supplementation for the correction of hypoxemia

-

- Non-invasive respiratory support with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) may be sufficient in less severe cases, but endotracheal intubation with invasive mechanical ventilation is often required.

- **Hemodynamic support** — Patients with TRALI often present with hypovolemia and associated hypotension.

- **Steroids**

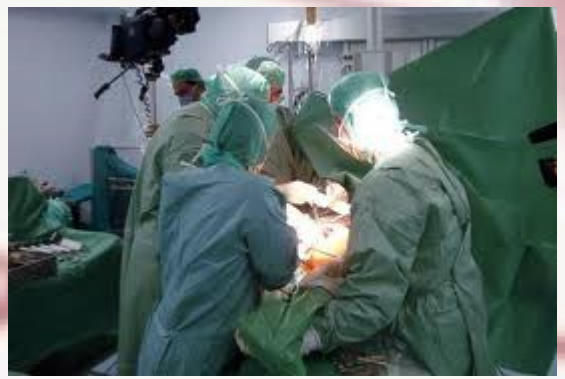
- **Investigational strategies** — In addition to the therapies described above, a number of additional ALI/ARDS and, by association, TRALI treatment and prevention strategies have been proposed and are under various stages of investigation.
  However, at present, none of these therapies has sufficient evidence to justify its use as a routine TRALI prevention or treatment measure.

- **Additional transfusions** — Patients who recover from TRALI do not appear to be at increased risk for recurrent episodes following transfusions from other donors; however, published experience is limited. Survivors of TRALI can receive additional blood products in the future, and transfusion of needed blood products should not be withheld.

Importantly, however, individuals should **not** receive plasma-containing blood products from the implicated donor.

TACO: TRANSFUSIONAL VOLUME OVERLOAD

- Pulmonary edema secondary to congestive failure.



Taco

- dyspnea
- orthopnea
- tachycardia
- wide pulse pressure
- often with hypertension and hypoxemia
- Haedache is common.

- may begin near the end of the transfusion, or within six hours.

Helpful features in distinguishing TRALI and TACO

Feature	TRALI	TACO
Body temperature	Fever may be present	Unchanged
Blood pressure	Hypotension may be present	Hypertension may be present
Respiratory symptoms	Acute dyspnea	Acute dyspnea
Neck veins	Unchanged	May be distended
Auscultation	Rales	Rales and S3 may be present
Chest radiograph	Diffuse bilateral infiltrates	Diffuse bilateral infiltrates
Ejection fraction	Normal	Decreased
PAOP	Most often 18 mmHg or less	Greater than 18 mmHg
Pulmonary edema fluid	Exudate	Transudate
Fluid balance	Neutral or negative	Positive
Response to diuretics	Inconsistent	Significant improvement
White cell count	Transient leukopenia may be present	Unchanged
BNP	<250 pg/mL	>1200 pg/mL

TRALI: transfusion-related acute lung injury; TACO: transfusion-associated circulatory overload; PAOP: pulmonary artery occlusion pressure; BNP: brain natriuretic peptide.

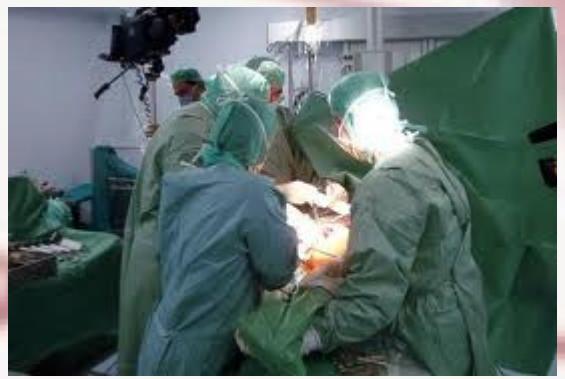
Modified with permission from: Skeate RC, Eastlund T. Distinguishing between transfusion related acute lung injury and transfusion associated circulatory overload. Curr Opin Hematol 2007; 14:682.

Prevention of Taco

- A transfusion rate of approximately 2.0 to 2.5 mL/kg per hour is acceptable for routine transfusions of blood components
- For an average sized adult, we use the following transfusion times:

- One unit of packed red cells with a volume of 350 mL should be transfused over a 1.5 to 2-hour period.
- Six units of pooled platelets or one apheresis unit of platelets with a volume of 200 to 300 mL should be transfused over a 30- to 60-minute period. There are no definitive data, though some argue that, after a slow initial rate to monitor for an immediate reaction, the 30-minute timeframe is preferable if the patient can tolerate it.
- One unit of fresh frozen plasma with a volume of 200 to 250 mL should be transfused over a 30- to 60-minute period depending upon the clinical situation and the patient's ability to handle the volume load

1 ml / kg / h



- Limiting transfusion of red cells to two units per day in patients who are not actively bleeding.
- Evaluating the patient's symptoms and physical signs (eg, estimated or measured venous pressure, examination of the lung bases for detection of rales) prior to infusion of each additional unit to be transfused within the same 24-hour period.
- The blood bank can centrifuge red blood cells immediately prior to their administration to remove the anticoagulant/preservative solution and reduce the volume.
- Administration of small doses of a diuretic between transfusions

Management

- fluid mobilization (diuretics)
- supplementary oxygen and consider NIV

- Phlebotomy in 250 mL increments, with or without reinfusion of the removed red cells, may be necessary if symptoms persist or diuresis cannot be promoted.

INFECTIOUS AGENTS

Transfusion-trasmitted disease for which donors are tested:

Hepatitis B virus

HIV

Hepatitis C virus

Human T-cell lymphotropic virus

West Nile virus

Bacteria

Trypanosoma cruzi

Cytomegalovirus

Syphilis

Transfusion-trasmitted disease for which donors are not routinely tested:

Hepatitis A virus Parvovirus B19 Dengue fever virus Malaria Babesia spp Plasmodium spp Leishmania spp Brucella spp New variant Creutzfeldt-Jakob disease prions Unknown pathogens

Data from developed countries show the residual risk of transfusion-transmitted viral infections range from

0.22 to 2.48 per 1 million donations for HIV,

0.05 to 3.94 per 1 million donations for HCV

and 1.51 to 9.78 per 1 million donations for HBV.

In developing countries, the supply of blood is inadequate and may not be safe because it often is not tested for viral pathogens. Blood donations are not routinely tested in 39 countries for transfusion transmissible infections including HIV, hepatitis B, hepatitis C and syphilis (WHO 2011). In 40 countries, less than 25% of the blood supply is collected from voluntary unpaid blood donors, with most coming from family or paid blood donors (WHO 2011). The prevalence of HIV in low-income countries is 2.3% of blood donations compared to 0.001% in high-income countries (WHO 2011).

L' ENTITA' DEL PROBLEMA IN ICU

Table 3
Anemia and blood transfusion in the intensive care unit (ICU)

Feature	Anemia	Blood transfusion
Frequency	>60% of ICU patients upon admission[4] 90% of ICU patients by day 3 in ICU[5] 97% of ICU patients by day 8[6]	20% to 62% of ICU patients receive 1 or more units of blood[4,55,56]
Increased morbidity and mortality	Associated with increased 90-day mortality in patients with chronic obstructive pulmonary disease[57] Associated with adverse outcomes in patients with congestive heart failure, acute myocardial infarction, and chronic kidney disease[58-60]	Associated with as much as a 40% increase in 30-day morbidity[61] Associated with as much as a 38% increase in 30-day mortality[56,61]
Increased costs	Associated with >twice inpatient costs in patients with chronic conditions[7] Associated with increased length of stay in patients with heart failure[62]	Activity costs are $522 to $1183 per unit of blood[63] Associated with ≥2 day increase in length of stay per transfusion[64]

PREVENIRE LE TRASFUSIONI NON NECESSARIE

-Trasfondere quando vi sono i sintomi e non basarsi solo sulla concentrazione di Emoglobina;

- Adottare un atteggiamento “restrittivo”.

COSA SIGNIFICA "ATTEGGIAMENTO RESTRITTIVO"?

	Recommendations
NIH Consensus Conference,[42] 1988	<70 g/L (acute)
American College of Physicians,[43] 1992	No number
American Society of Anesthesiologists,[44] 1996	<60 g/L (acute)
American Society of Anesthesiologists,[45] 2006	No number
Canadian Medical Association,[26] 1997	No number
Canadian Medical Association,[46] 1998	No number
College of American Pathologists,[47] 1998	60 g/L (acute)
British Committee for Standards in Haematology,[48] 2001	No number
British Committee for Standards in Haematology,[49] 2012	70 g/L*
Australasian Society of Blood Transfusion,[50] 2001	70 g/L
Society for Thoracic Surgeons, Society of Cardiovascular Anesthesiology,[51] 2007	70 g/L
Society for Thoracic Surgeons, Society of Cardiovascular Anesthesiology,[52] 2011	80 g/L*
American College of Critical Care Medicine, Society of Critical Care Medicine,[53] 2009	70 g/L
American College of Critical Care Medicine, Society of Critical Care Medicine,[54] 2009	70 g/L
Society for the Advancement of Blood Management,[55] 2011	80 g/L
National Blood Authority, Australia,[33] 2012	No number
AABB,[56] 2012	70–80 g/L or 80 g/L†
Kidney Disease: Improving Global Outcomes,[57] 2012	No number
National Cancer Center Network,[58] 2012	70 g/L

*For patients with acute blood loss. †For patients with symptoms of end-organ ischaemia.

Table 3: **Medical society clinical practice guidelines for red blood cell transfusion**

PLASMA …

	Main indications
Consensus Conference, National Institutes of Health,[65] 1984	Replacement of isolated factor deficiencies, reversal of warfarin effect, massive blood transfusion, treatment of TTP, antithrombin III deficiency, and immunodeficiencies
British Committee for Standards in Haematology,[66] 1992	Replacement of isolated factor deficiencies in which a specific or combined factor concentrate is unavailable, immediate reversal of warfarin effect, acute DIC, and TTP
College of American Pathologists,[60] 1994	History or clinical course of a coagulopathy (inherited or acquired) with active bleeding or before an invasive procedure, massive transfusion, reversal of warfarin effect, antithrombin III deficiency, immunodeficiencies (in rare instances), and TTP
Canadian Medical Association Expert Working Group,[26] 1997	Several acquired coagulation factor deficiencies—eg, vitamin K deficiency, warfarin, liver disease in which active bleeding is present or before an invasive procedure, acute DIC, massive blood transfusion, TTP, replacement of single coagulation factor deficiencies in which desmopressin or appropriate factor concentrates are unavailable
British Committee for Standards in Haematology,[67] 2004	Replacement of one inherited coagulation factor deficiency in which a virus-safe fractionated product is unavailable, several coagulation factor deficiencies (eg, DIC), TTP, reversal of warfarin effect, vitamin K deficiency in the ICU, and massive transfusion
Italian Society of Transfusion Medicine and Imunohaematology,[64] 2009	Correction of congenital or acquired deficiencies of clotting factors (for which there is not a specific concentrate) when the prothrombin time or a partial thromboplastin time is >1·5 (eg, liver disease), warfarin reversal, acute DIC, or massive transfusion, TTP, reconstitution of whole blood for exchange transfusions, and hereditary angioedema in which C1-esterase inhibitor is not available
AABB,[68] 2010*	Massive transfusion in patients with trauma and warfarin-related intracranial haemorrhage

TTP=thrombotic thrombocytopenic purpura. DIC=disseminated intravascular coagulation. ICU=intensive care unit. *Only six questions relating to plasma use in specific scenarios were considered.

Table 5: **Medical society clinical practice guidelines for plasma transfusion**

… E PIASTRINE …

	Recommendations
British Committee for Standards in Haematology,[59] 1992	10×10⁹/L*
College of American Pathologists,[60] 1994	5×10⁹/L*
Consensus Conference, Royal College of Physicians, Edinburgh,[61] 1998	10×10⁹/L*
American Society of Clinical Oncology,[62] 2001	10×10⁹/L*
British Committee for Standards in Haematology,[63] 2001	10×10⁹/L*
Italian Society of Transfusion Medicine and Imunohaematology,[64] 2009	10×10⁹/L*

*Consider raised threshold for patients with additional risk factors for bleeding.

Table 4: **Medical society clinical practice guidelines for trigger for prophylactic platelet transfusions**

Annals of Internal Medicine | CLINICAL GUIDELINE

Red Blood Cell Transfusion: A Clinical Practice Guideline From the AABB*

Jeffrey L. Carson, MD; Brenda J. Grossman, MD, MPH; Steven Kleinman, MD; Alan T. Tinmouth, MD; Marisa B. Marques, MD; Mark K. Fung, MD, PhD; John B. Holcomb, MD; Orieji Illoh, MD; Lewis J. Kaplan, MD; Louis M. Katz, MD; Sunil V. Rao, MD; John D. Roback, MD, PhD; Aryeh Shander, MD; Aaron A.R. Tobian, MD, PhD; Robert Weinstein, MD; Lisa Grace Swinton McLaughlin, MD; and Benjamin Djulbegovic, MD, PhD, for the Clinical Transfusion Medicine Committee of the AABB

Description: Although approximately 85 million units of red blood cells (RBCs) are transfused annually worldwide, transfusion practices vary widely. The AABB (formerly, the American Association of Blood Banks) developed this guideline to provide clinical recommendations about hemoglobin concentration thresholds and other clinical variables that trigger RBC transfusions in hemodynamically stable adults and children.

Methods: These guidelines are based on a systematic review of randomized clinical trials evaluating transfusion thresholds. We performed a literature search from 1950 to February 2011 with no language restrictions. We examined the proportion of patients who received any RBC transfusion and the number of RBC units transfused to describe the effect of restrictive transfusion strategies on RBC use. To determine the clinical consequences of restrictive transfusion strategies, we examined overall mortality, nonfatal myocardial infarction, cardiac events, pulmonary edema, stroke, thromboembolism, renal failure, infection, hemorrhage, mental confusion, functional recovery, and length of hospital stay.

Recommendation 1: The AABB recommends adhering to a restrictive transfusion strategy (7 to 8 g/dL) in hospitalized, stable patients (Grade: strong recommendation; high-quality evidence).

Recommendation 2: The AABB suggests adhering to a restrictive strategy in hospitalized patients with preexisting cardiovascular disease and considering transfusion for patients with symptoms or a hemoglobin level of 8 g/dL or less (Grade: weak recommendation; moderate-quality evidence).

Recommendation 3: The AABB cannot recommend for or against a liberal or restrictive transfusion threshold for hospitalized, hemodynamically stable patients with the acute coronary syndrome (Grade: uncertain recommendation; very low-quality evidence).

Recommendation 4: The AABB suggests that transfusion decisions be influenced by symptoms as well as hemoglobin concentration (Grade: weak recommendation; low-quality evidence).

Ann Intern Med. 2012;157:49-58. www.annals.org
For author affiliations, see end of text.
This article was published at www.annals.org on 27 March 2012.

Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion (Review)

Carson JL, Carless PA, Hebert PC

THE COCHRANE COLLABORATION®

Main results

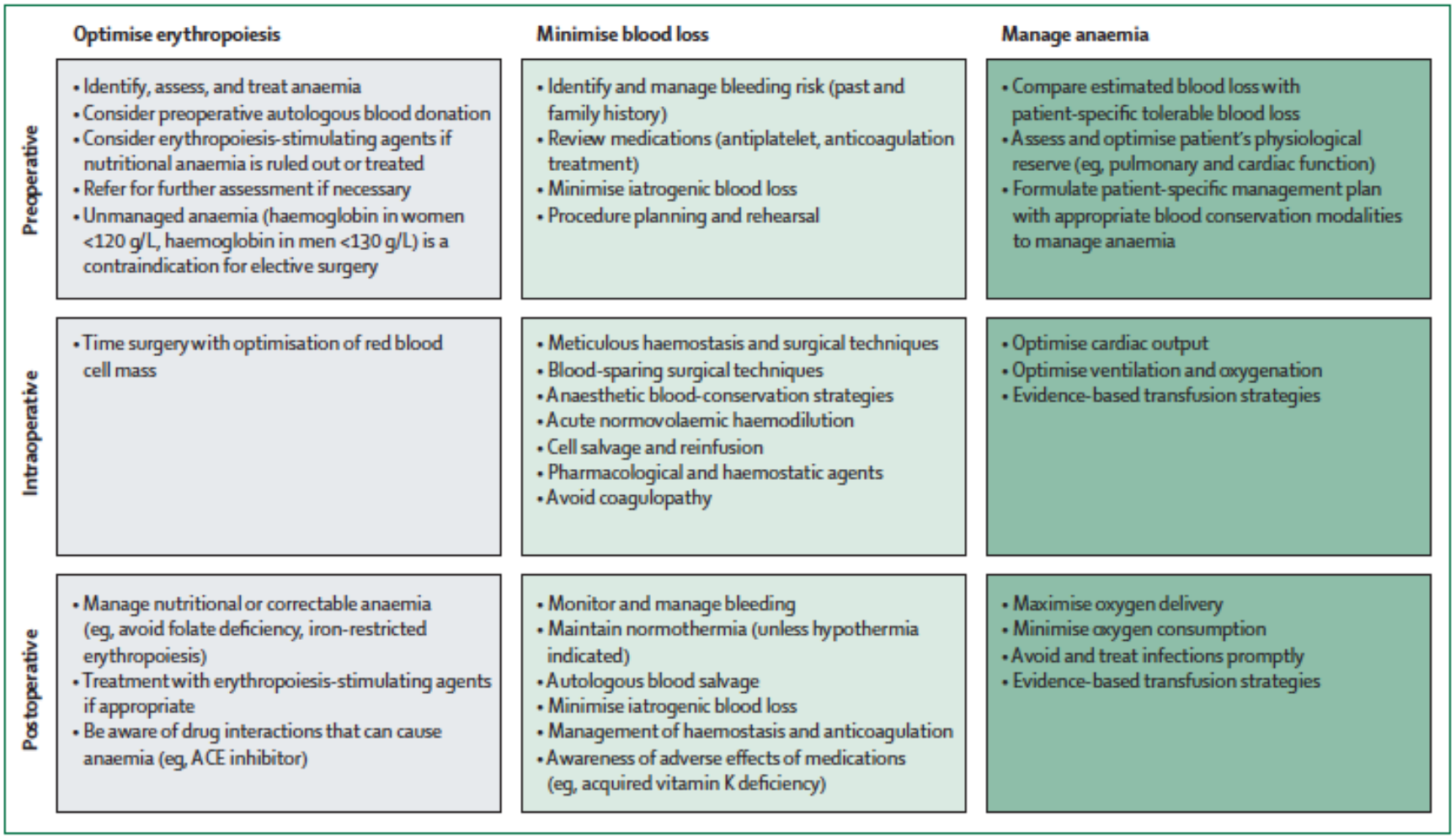
We included 19 trials involving a total of 6264 patients and they were similar enough that results could be combined. Restrictive transfusion strategies reduced the risk of receiving a RBC transfusion by 39% (risk ratio (RR) 0.61, 95% confidence interval (CI) 0.52 to 0.72). This equates to an average absolute risk reduction (ARR) of 34% (95% CI 24% to 45%). The volume of RBCs transfused was reduced on average by 1.19 units (95% CI 0.53 to 1.85 units). However, heterogeneity between trials was statistically significant ($P < 0.00001$; $I^2 \geq 93\%$) for these outcomes. Restrictive transfusion strategies did not appear to impact the rate of adverse events compared to liberal transfusion strategies (i.e. mortality, cardiac events, myocardial infarction, stroke, pneumonia and thromboembolism). Restrictive transfusion strategies were associated with a statistically significant reduction in hospital mortality (RR 0.77, 95% CI 0.62 to 0.95) but not 30-day mortality (RR 0.85, 95% CI 0.70 to 1.03). The use of restrictive transfusion strategies did not reduce functional recovery, hospital or intensive care length of stay. The majority of patients randomised were included in good-quality trials, but some items of methodological quality were unclear. There are no trials in patients with acute coronary syndrome.

PREVENIRE L'OVERUSE: PATIENT BLOOD MANAGEMENT (PBM)

- Ridurre gli esami del sangue "inutili" (evitare salassi);
- Implementare "restrictive transfusion practices";
- Documentare i livelli di Hb dopo ogni singola trasfusione di E.C.;
- Utilizzo di monitoraggio non invasivo e continuo dei livelli di Hb;
- Sorveglianza dei sanguinamenti occulti.

Figure 1 Options to reduce blood from phlebotomy: A, pediatric phlebotomy tubes; B, eliminate discarding blood from arterial catheter; C, read through motion and low-perfusion pulse oximetry instead of blood gas analysis; D, multiwavelength pulse co-oximetry for noninvasive and continuous monitoring of hemoglobin level.

PATIENT BLOOD MANAGEMENT



	Optimise erythropoiesis	Minimise blood loss	Manage anaemia
Preoperative	• Identify, assess, and treat anaemia • Consider preoperative autologous blood donation • Consider erythropoiesis-stimulating agents if nutritional anaemia is ruled out or treated • Refer for further assessment if necessary • Unmanaged anaemia (haemoglobin in women <120 g/L, haemoglobin in men <130 g/L) is a contraindication for elective surgery	• Identify and manage bleeding risk (past and family history) • Review medications (antiplatelet, anticoagulation treatment) • Minimise iatrogenic blood loss • Procedure planning and rehearsal	• Compare estimated blood loss with patient-specific tolerable blood loss • Assess and optimise patient's physiological reserve (eg, pulmonary and cardiac function) • Formulate patient-specific management plan with appropriate blood conservation modalities to manage anaemia
Intraoperative	• Time surgery with optimisation of red blood cell mass	• Meticulous haemostasis and surgical techniques • Blood-sparing surgical techniques • Anaesthetic blood-conservation strategies • Acute normovolaemic haemodilution • Cell salvage and reinfusion • Pharmacological and haemostatic agents • Avoid coagulopathy	• Optimise cardiac output • Optimise ventilation and oxygenation • Evidence-based transfusion strategies
Postoperative	• Manage nutritional or correctable anaemia (eg, avoid folate deficiency, iron-restricted erythropoiesis) • Treatment with erythropoiesis-stimulating agents if appropriate • Be aware of drug interactions that can cause anaemia (eg, ACE inhibitor)	• Monitor and manage bleeding • Maintain normothermia (unless hypothermia indicated) • Autologous blood salvage • Minimise iatrogenic blood loss • Management of haemostasis and anticoagulation • Awareness of adverse effects of medications (eg, acquired vitamin K deficiency)	• Maximise oxygen delivery • Minimise oxygen consumption • Avoid and treat infections promptly • Evidence-based transfusion strategies

Figure 1: **Patient blood management**
These recommendations apply in the perisurgical period enable treating physicians to have the time and methods to provide patient-centred and evidence-based patient blood management to minimise allogeneic blood transfusions. Modified from Goodnough and Shander,[19] by permission of the American Society of Anesthesiologists.

CHIRURGIA IN ELEZIONE E GESTIONE PREOPERATORIA DELL' ANEMIA

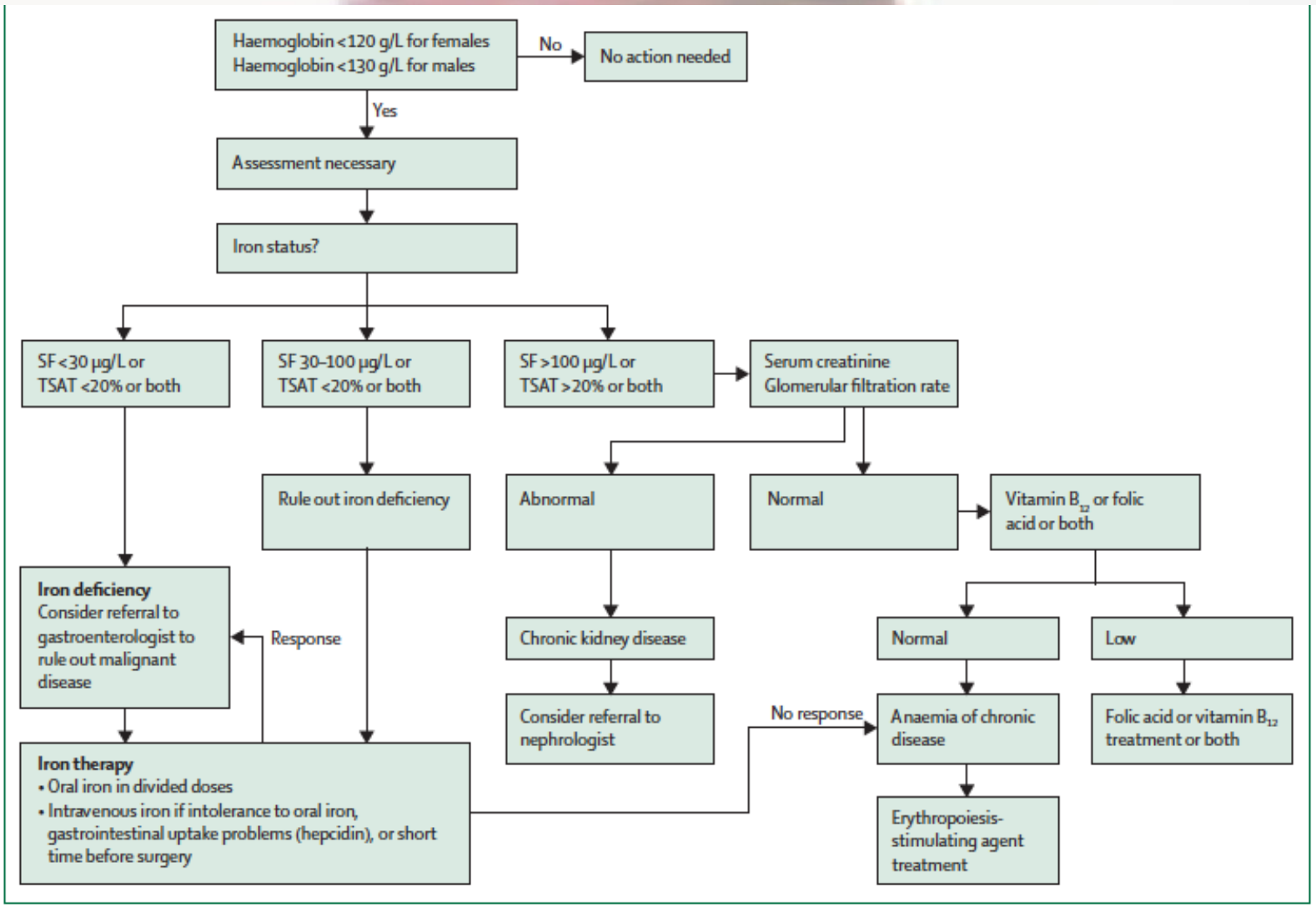


Figure 2: **Algorithm for the detection, assessment, and management of preoperative anaemia**
SF=serum ferritin. TSAT=transferrin saturation. Modified from Goodnough and colleagues,[10] by permission of Oxford Journals.

IL PAZIENTE EMORRAGICO: NON SOLO SANGUE…

- Acido tranexamico (CRASH 2);
- Fibrinogeno;
- Protocollo Trasfusioni Massive (MTP) nel trauma penetrante e nell' emorragia massiva;

- Complesso pro-trombinico e vitamina K in alternativa al plasma in pazienti con coagulopatia da Warfarin; *
- Fattore VII ricombinante (Novoseven) per Emofilia A o B;
- Fattore VIII dopo gli interventi cardiochirurgici;
- Eritropoietina se Insufficienza renale concomitante.

*COME RICOAGULARE PAZIENTE IN TAO

1) Konakion 10 mg ev (sua azione inizia dopo 8-12 ore dalla somministrazione)
2) HUMAN COMPLEX

- Se non hai INR: 20 UI/kg
- Se hai INR: INR <2 = 20 UI/kg
  INR 2-4 = 30 UI/kg
  INR >4 = 50 UI/kg

Appena hai INR termina la correzione prokg.

Dopo 15-20 min ripetere INR e puoi rifare HC secondo i dosaggi sopra.