EVIDENCE BASED HEMOVIGILANCE: A GOAL WE CAN REACH ?

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TRIP Dutch National Hemovigilance Office

TRIP Office

- **December 2002: start TRIP office in The Hague**
- **May 2003: start national reporting, request for available data on reactions in 2002 (baseline results)**

TRIP foundation

Board
(Medical Societies)
Advisory board
(Hospital associations, Sanquin BB)

national TRIP office

Hospitals
blood Tx comm.

Sanquin
HV
programme

Hospital
laboratory
clinicians

Transfusion reactions

recalls & look-back

Sanquin
blood bank
Tx specialist
QA manager

TRIP objectives

- **Safety and quality improvement of blood transfusion in patients**
- **Development of education in haemovigilance**
- **Research**
- **Publications**

What does each system record?

Event	SHOT	France	Ireland	TRIP	EU
Hemolysis	serious	+	serious	+	serious
Anaphylaxis	serious	+	anaphylactoid	+	serious
TRALI	serious	+	serious	+	serious
Volume overload		+	serious	+	
PTP	serious	+	serious	+	serious
TA-GVHD	serious	+	serious	+	serious
Bacterial contamination	serious	+	serious	+	serious
Viral infection	serious	+	serious	+	serious
Other infection	serious	+	serious	+	serious
Other events	serious	+	serious	+	serious
New antibodies		immunological incompatibility		+	
NHTR		‘unknown’		+	
Other allergic reaction		+		+	
Minor febrile reaction		+		optional	
Near accident	+	?		optional	

TRANSFUSIE REACTIES IN PATIËNTEN

TRIP

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Blood supply

- 4 regional blood bank divisions
- Voluntary unpaid donors
- Self-sufficiency
- 927,000 donations
- 533,000 donors (population 16-17 million)

Labile blood components delivered nationally

900000
800000
700000
600000
500000
400000
300000
200000
100000
0

2003
2004
2005

FFP
Platelets
RBC

Participation

Hospitals

120
100
80
60
40
20
0

2002 baseline
2003*
2004*
2005*

no info
nonparticipant
nil to report
reports

Reports per hospital (2005)

reports/1000 bp

7
6
5
4
3
2
1
0

Gr 0-2 (main categories)

Gr 3-4

Reports per hospital (2005)

variation in number of reports

Mild unavoidable events a measure for quality?

- The higher the better ?
- Inversely correlated to the number of serious potentially avoidable events?

correlation between reporting level and TR category

‘Please number in order of importance’

Factors which can increase the number of reports	**Top 3?**
We encourage the departments to report all events associated with transfusion	
Many seriously ill patients	
Relatively high use of platelet concentrates	
Hemato-oncology and/or cardiothoracic department	
Nurses receive specific teaching on blood transfusion	
the medical staff are interested in transfusion policy	

‘Please number in order of importance’

Factors which can reduce the number of reports	**Top 3**
Nursing staff are too busy (to conduct observations and/or to initiate reports)	
relatively straightforward pathology in our patient population	
Some departments are not aware of procedure for transfusion reactions	
Errors are not often reported	
Hospital under refurbishment/ reorganisation	
Last year we only reported serious AEs to TRIP	

TRIP — TRANSFUSIE REACTIES IN PATIËNTEN

Responses

- 104 hospitals received the questionnaire (3 weeks ago)
- 35 hospitals responded rapidly as requested:
  - 2/9 university, 7/19 teaching, 26/74 other
  - median no. of reports in 2005 per 1000 bp: 1.9 (range 0 – 6.7; national median was 2.08)
  - blood use median 3670 (range 14 – 27902; national median was 3970)

‘Please number in order of importance’

Factors which can increase the number of reports	**Top 3?**
We encourage the departments to report all events associated with transfusion	**1**
Many seriously ill patients	<mentioned
Relatively high use of platelet concentrates	<by university hospitals
Hemato-oncology and/or cardiothoracic department	
Nurses receive specific teaching on blood transfusion	**2**
the medical staff are interested in transfusion policy	**3**

'Please number in order of importance'

Factors which can reduce the number of reports	**Top 3?**
Nursing staff are too busy (to conduct observations and/or to initiate reports)	2
relatively straightforward pathology in our patient population	3
Some departments are not aware of procedure for transfusion reactions	1
Errors are not often reported	
Hospital under refurbishment/ reorganisation	
Last year we only reported serious AEs to TRIP	

A few observations

Factors which can reduce the number of reports	**->More variation**
Nursing staff are too busy (to conduct observations and/or to initiate reports)	**2**
relatively straightforward pathology in our patient population	**3**
Some departments are not aware of procedure for transfusion reactions	**1**
Errors are not often reported	in top 3 for 21 hospitals, large and small
Hospital under refurbishment/ reorganisation	in top 3 for 4 hospitals
Last year we only reported serious AEs to TRIP	A number of large hospitals

AE	Number 2003*	Number 2004*	Number 2005	Number 05 ≥ grade 2
NHTR	318	345	393	6
AHTR	8	14	9	8
DHTR	19	14	12	2
TRALI	6	9	15	9
TACO	7	6	26	2
Anaphylatic reaction	8	21	23	15
Other allergic reactions	132	171	195	6
Hemosiderosis	0	0	3	0
Bacterial contamination	9	5	10	5
Viral infection	5	7	8	0
T 1-2ºC	326	341	356	1
New Antibodies	244	428	523	0
Other reactions	54	64	62	1
Incident				
IBCT	34	36	58	4
Incidents	5	14	53	1
Near misses	31	62	79	Nvt
Pos. bacterial screening	60	10*	10*	0
TOTAL	1267	1547	1840	60

Report types

2000
1600
1200
800
400
0

2002*
2003*
2004*
2005

Near miss
Incident, no clinical consequences
Incident with clinical consequences
IBCT, no consequences
IBCT with clinical cons.
clinical TR

Transfusion Reactions reported to TRIP

600
500
400
300
200
100
0

2002* 2003* 2004* 2005

New Antibodies
NHTR
Allergic reactions

NHTR
AHTR
VHTR
TRALI
anaphylactic
other allergic
TACO
bact contamination
viral infection
hemosiderosis
new allo-antibody
other TR
minor NHTR

grade ≥ 2 reports

reports/1000 bp

0,16
0,14
0,12
0,10
0,08
0,06
0,04
0,02
0,00

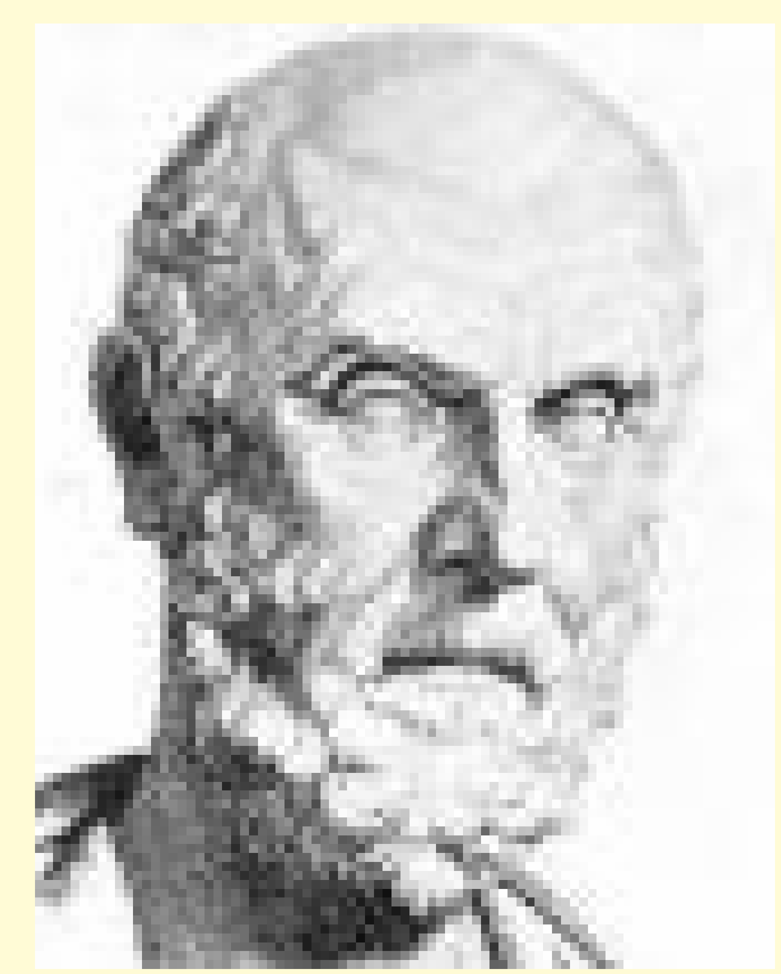
NO
NW
SO
SW

2002
2003*
2004*
2005

Transfusion medicine

Blood Transfusion

- **Primo non Nocere:**
- **First, Do No Harm!**



8 years of SHOT data 1996 -2004
Adverse events and reactions

600
500
400
300
200
100
0

TOTAL IBCT ATR DTR PTP TA-GVHD TRALI TTI Unclassified

- 1996/1997
- 1997/1998
- 1998/1999
- 1999/2000
- 2000/2001
- 2001/2002 (15 months)
- 2003
- 2004

The blood/plasma chain

risks

potential blood donor → donor → donation → product → recipient → adverse event

adverse event

blood centres

hospitals

The transfusion chain within the hospital

Incidents in the transfusion chain, TRIP 2005

Systematic analysis of incidents

- HFMEA (prospective) method: representive forum of mixed professionals
- PRISMA (retrospective) method: 10 pilot hospitals (hemovigilance officers)

TRANSFUSIE REACTIES IN PATIËNTEN
TRIP

Risk Inventarisation Matrix

Severity → / ↓ Frequency of occurrence	**3.**	**2.**	**1.**
4. > 1 : 1000 bp	12	8	4
3. > 1 : 1000.000 but < 1 : 1.000 bp	9	6	3
2. < 1 : 1000.000 bp	6	4	2
1. < 1 : 10.000.000 bp	3	2	1

The blood/plasma chain

risks

potential blood donor → donor → donation → product → recipient → adverse event

adverse event

blood centres

hospitals

Blood Transfusion, Independent of Shock Severity, Is Associated with Worse Outcome in Trauma

Debra L. Malone, MD, James Dunne, MD, J. Kathleen Tracy, MA, A. Tyler Putnam, MD, Thomas M. Scalea, MD, and Lena M. Napolitano, MD

- Blood transfusion is risk factor for:
  - Mortality
  - ICU admission
  - ICU length of stay
  - Hospital length of stay

Backgro... shown that bl... hours is an i... tality, intensi... and increase... acute trauma... Injury Severi... score, and ag... deficit, serum... hemodynami... sure, heart ra... were conside... ables in that... study were t... and blood transfusion within the first 24 hours as independent predictors of mortality, ICU admission, ICU length of stay (LOS), and hospital LOS, with serum lactate level, base deficit, and shock index (heart rate/systolic blood pressure) as covariates.

Methods: Prospective data were col-

interval [CI], 1.82–4.40; $p < 0.001$), ICU admission (OR, 3.27; 95% CI, 2.69–3.99; $p < 0.001$), ICU LOS ($p < 0.001$), and hospital LOS (Coef, 4.37; 95% CI, 2.79–5.94; $p < 0.001$) when stratified by indices of shock (base deficit, serum lactate, shock index, and anemia). Patients who under-

...hree ...han ...d to ...it < ...r of ...p = ... is ...r of ...and ...ling ...base ...mia. ...oxy-gen-carrying resuscitation fluids (such as human or bovine hemoglobin substitutes) in the acute postinjury period warrants further investigation.

Key Words: Blood transfusion, Trauma, Injury, Hemorrhage, Anemia, Shock, Nosocomial infection.

J Trauma. 2003;54:898–907.

Examples of adverse events of blood transfusion

- **Allogeneic blood transfusions explain increased mortality in women after coronary artery bypass graft surgery**
- **Rogers MA, Blumberg N, et al.**
- *American Heart Journal 2006; 152:1028*

Examples of adverse events of blood transfusion

- **Blood Transfusion in Elderly Patients with Acute Myocardial Infarction**
- **Wen-Chih Wu, M.D., Saif S. Rathore, M.P.H., Yongfei Wang, M.S., Martha J. Radford, M.D., and Harlan M. Krumholz, M.D.**
- *NEJM, Volume 345:1230-1236, 2001.*

Blood Transfusion in Elderly Patients with Acute Myocardial Infarction 2

Medicare/Medicaid database for 250,000 patients entering the emergency room with chest pain.

only patients older than 65 years were segmented into different hemoglobin levels. (only 3200 patients)

patients who had a hematocrit level of 33% or below who had a transfusion, had an improved mortality rate if they received a transfusion.

The study was accompanied by an editorial claiming that "now we know that the old standard 10 g/dL transfusion trigger was correct"

- **Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes.**
- **Rao S.V., Jollis J.G., Harringtong R.A., et al**
- *JAMA 292. 1555-1562.2004;*

- This database study involved more than 24,000 patients, and those patients who had transfusions during the time of PCI had almost a four-fold increase in mortality

- **A multicenter, randomised, controlled clinical trial of transfusion requirements in critical care.**
- **Hebert PC, Wells G, Blajchman MA, *et al.***
- *N Engl J Med 1999; 340: 409–17*

- it has been named: “the single most important report in the history of transfusion.”

Results from the TRICC study

Category	Restictive (7 g/dl)	Liberal (10 g/dl)	P value
All patients	18.7	23.3	0.10
APACHE II	8.7	16.1	0.03
<55 yr	5.7	13.0	0.02
Cardiac dx	20.5	22.9	0.69
Death in Hospital	22.2	28.1	0.05
MI	0.7	2.9	0.02
Pulmonary edema	5.3	10.7	<0.01
Angina	1.2	2.1	0.28
ARDS	7.7	11.4	0.06
Infections	10.0	11.4	0.38

Conclusion from TRICC study

- Nowhere in these data did patients who had more transfusions do better.
- There were large differences in the rate of MI and in pulmonary dysfunctions. (TRALI ?).

RCT for effect of leucocyte-depletion

- **Randomised controlled trial comparing transfusion of leucocyte-depleted or buffy-coat-depleted blood in surgery for colorectal cancer.**
- **Houbiers JGA, Brand A, van der Watering LMG, Hermans J, Verwey PJM, Bijnen AB.**
- *Lancet 1996; 344: 573–8*

- **Randomised comparison of leucocyte-depleted versus buffy-coat-poor blood transfusion and complications after colorectal surgery.**
- **Jenson LS, Kissmeyer-Nielsen P, Wolff B, Qvist N.**
- *Lancet 1996; 348: 841–5*

Safety of blood loss reduction

- **Role of hemodilutional anaemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: implications on operative outcome**
- **Habib RH, Zacharias A et al.**
- *Crit Care Med, 2005 Aug, 33(8): 1749*

- "Hemodilation to hematocrit < 24% is associated with a systematically increased likelihood of renal injury "

- **Mortality Associated With Aprotinin During 5 Years Following Coronary Artery Bypass Graft Surgery**
- **Dennis T. Mangano, PhD et al**
- *JAMA. 2007;297:471-479*

Conclusion:

- Adverse events of bloodtransfusion is patient category related.
- Preventive measures can not be generalized
- Case-control or RCT are required in haemovigilance

What really are the risks of homologous transfusion and what should we tell our patients ?

Classical Risks

- Transfusion Effects of Lesions Storage
- Transfusion Related Immunomodulation
- Incorrect blood component transfused
- Immunological incompatibility
- Transfusion transmitted infections

Public confidence in blood

- Blood Transfusion

- Primo non Nocere:
- First, Do No Harm!

First, know what harms !