

How we View & Approach TACO

Annual Blood Transfusion & Hemovigilance
Symposium

Ede, Netherlands

May 22, 3014

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Agenda

- Setting the stage
- What is TACO?
- Why does TACO matter?
- Risk factors
- Prevention

Serious Non-Infectious Consequences of Transfusion

Type	Mortality	Morbidity
Hemolysis	10%	Renal failure Shock DIC
Anaphylaxis	<5%	
Graft vs. host disease	>75%	Profuse diarrhea Hepatocellular damage Pancytopenia
TACO	1-8%	↑Length of stay
TRALI	5-20%	Respiratory failure
Immunomodulation	?	↑Infections ↑Cancer reoccurrence (?)

Differential Diagnosis of Transfusion-Associated Respiratory Distress

- Allergic/Anaphylactic transfusion reaction
- Bacterial contamination
- Acute hemolytic reaction
- TACO
- TRALI
- Not transfusion related

TACO Overview

- Occurs in 1-8% of transfusions
- 1st or 2nd most common cause of transfusion-associated (TA) death
- Averaging 15% of FDA TA deaths since 2007
- Hydrostatic pulmonary edema due to transfusion

FDA-Reported Transfusion Deaths - 2012

TRALI	TACO	HTR	Microbial	Anaphylaxis
17 (45%)	8 (21%)	8 (21%)	3 (8%)	2 (5%)

Ref: FDA-CBER, 2013

TACO

Clinical Features & Diagnosis

- Dyspnea
- Orthopnea
- Cyanosis
- Hypoxemia
- Widened pulse pressure
- Elevated brain natriuretic peptide (BNP)
- Tachycardia
- Elevated systolic and/or diastolic blood pressure
- Pulmonary/pedal edema
- Cardiomegaly/widened cardiac silhouette

A Working Definition – ISBT Working Committee

- Acute respiratory distress
- Increased blood pressure
- Acute or worsening pulmonary edema on CXR
- Enlarged heart on frontal CXR
- Positive fluid balance
- Any 4 of these

Role of BNP in TACO Diagnosis

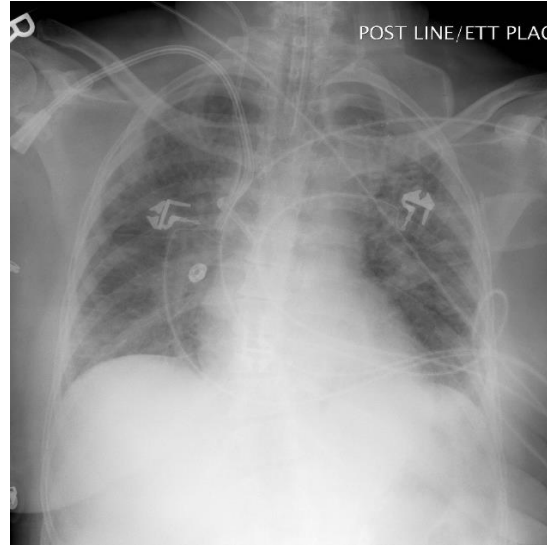
- BNP elevated in both TACO & TRALI
- Post-to-pretransfusion ratio of 1.5 → 81% sensitivity & 89% specificity
- Levels greater in TACO than in TRALI/possible TRALI
- Supports the diagnosis but does not establish it

Li et al. Transfusion 2009;49:13-20

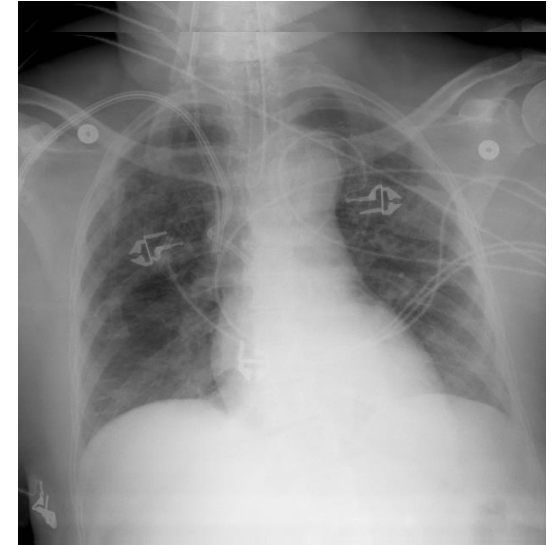
TACO – Case Study



1:50 A.M.



9:15 A.M.



12:05 A.M.

Acknowledgement: M. Looney

Clinical Impact of TACO

- Increases morbidity
 - 21% of cases life-threatening (Robillard)
- Increases ICU stay (Li, 2009)
- Increases hospital length of stay (Popovsky 1996) in orthopedic surgery
- 1 RBC is sufficient to trigger the reaction!
(Popovsky 1985 & 1996, Robillard 2008)
 - >20 – 53% of cases

Transfusion

Transfusion Fatality Rankings - TACO

USA	2 nd
Canada	1 st
U.K.	1 st
Netherlands	3 rd

Mortality

	<u>Case Fatality %</u>
French Hemovigilance	3.7
Quebec Hemovigilance	1.4
UPMC	8.3
Netherlands	2.6 - 4.8
Ireland	2.3

David Vox Sang 2002

Robillard et al. Transfusion 2008;48:204

Narick et al. Transfusion 2011;51:127A

Plasma Transfusion and TACO

University of Pittsburgh Medical Center

- Retrospective: 2003 - 2010
 - Prevalence 1:1566 (1:2564 – 1:1014) patients
- Prospective: 84 patients → 272 units FFP
 - Prevalence: 4.8%
 - None reported to blood bank
 - 14/24 patients in ICU had TACO

Narick et al. Transfusion 2011;51s:127A

Risk Factors for TACO

Case control study (UCSF/Mayo Clinic) (N=328)

FACTOR	ODDS RATIO
Female	2.1
Past history CHF	5.6
History hemodialysis	3.5
Recent surgery	2.3
Mechanical ventil, before TX	2.7
Recent admin. vasoprossors	9.7
Positive fluid balance	1.2

E Murphy. Transfusion 2010;50:127A

TACO Among USA Elderly

- For year 2011
- 2,147,038 inpatient transfusion stays → 1340 TACO diagnosis
- Overall rate: 62.4 per 100,000 stays
- Risk Factors

	<u>O.R.</u>	<u>P</u>
Age	-----	< 0.0001
Units Transfused	-----	< 0.0001
Women vs men	1.40	
White vs non-white	1.38	
CHF	1.61	
Chronic Pulmonary Disease	1.19	

M Menis et al. Vox Sang 2014;106:144-152

Options to prevent TACO

- Promote non-transfusion options
- Mandatory pre-transfusion risk assessment and volume assessment
- Slow the rate of transfusion
- Pre-emptive furosemide: everyone or at-risk?
- 1 RBC at a time
- 'Critical' nursing supervision

J. Callum: Personal communication

Risk assessment

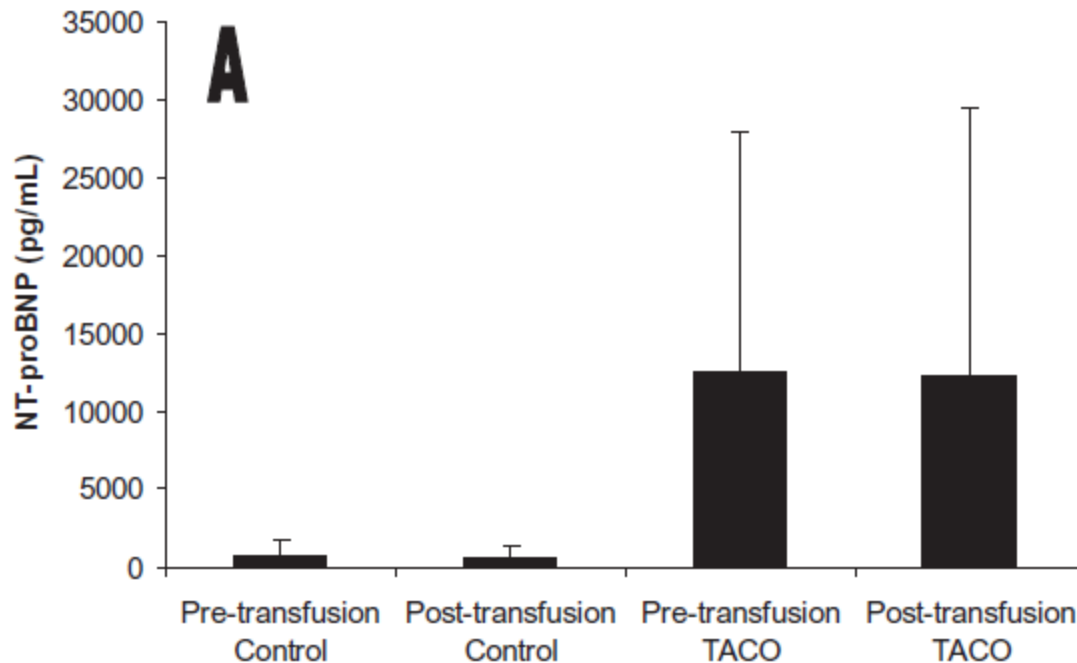
- Fluid balance positive over last 24 hour?
 - Review of unreported TACOs out of 382 joint replacements – mean positive fluid balance of 2480 mL, despite blood loss <500 mL
 - Fluid balance +5.9L in TACO cases vs. +2.0L in controls (p<0.01)

Popovsky MA, et al. *Immunohematology*. 1996;12(2):87-89.

Rana R, et al. *Transfusion* 2006; 46: 1478-83.

Risk assessment

- Fluid balance positive over last 24 hour
 - Patients who develop TACO are overloaded before transfusion as measured by NT-proBNP



Tobian AAR, et al. Transfusion 2008; 48: 1143-50

TACO in the ICU

- Prospective observational study in an ICU
- 6% of 901 transfused patients develop TACO
- Compared with matched controls TACO cases had:
 - more positive fluid balance (1.4 L vs. 0.8 L)
 - larger amount of **plasma** (0.4 L vs. 0.07)
 - faster rate of transfusion (225 mL/hr vs. 168 mL/hr)
- Compared with random controls TACO cases:
 - left ventricular dysfunction increased risk of TACO 8.23x
 - **plasma** ordered for reversal of anticoagulant increased TACO risk 4.31x

Li et al. Transfusion 2011;51:338-43

Slowing the rate of transfusion

- AABB Technical Manual = 2-4 mL/min for RBCs (faster for plasma and platelets!)
 - 120-240 mL/hr = 1 RBC over 1 or 2 hours
- Review of 47 cases of TACO – range 1-48 mL/min
- Rate of infusion faster in TACO vs. control patients (225 vs. 168 mL/hour, $p=0.03$)

Popovsky M. ISBT Science Series 2008; 3: 166-69

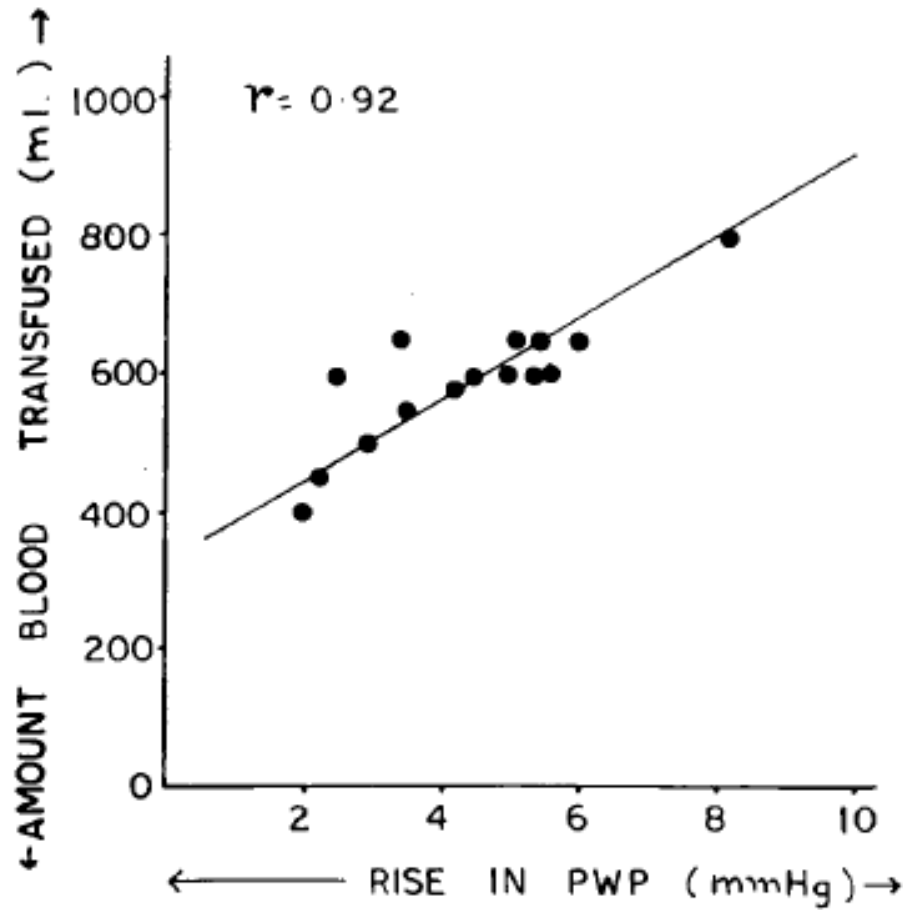
Li G, et al. Transfusion 2011; 51: 338-43

Infusion Rates & Times for Adult Patients – RBC - Prevention Schema

Category	Clinical Setting	Suggested Rates of Infusion	Unit Size
Severe risk for volume overload	CHF, COPD, ARF, Severe anemia history of TACO (multiple episodes)	42 ml/hr to 60 ml/hr	0.5 units
At risk for potential fluid overload	History of TACO (few episodes)	84 ml/hr to 120 ml/hr	Full units
Minimal or no risk	Majority of patients	84 ml/hr – 200 ml/hr	Full units

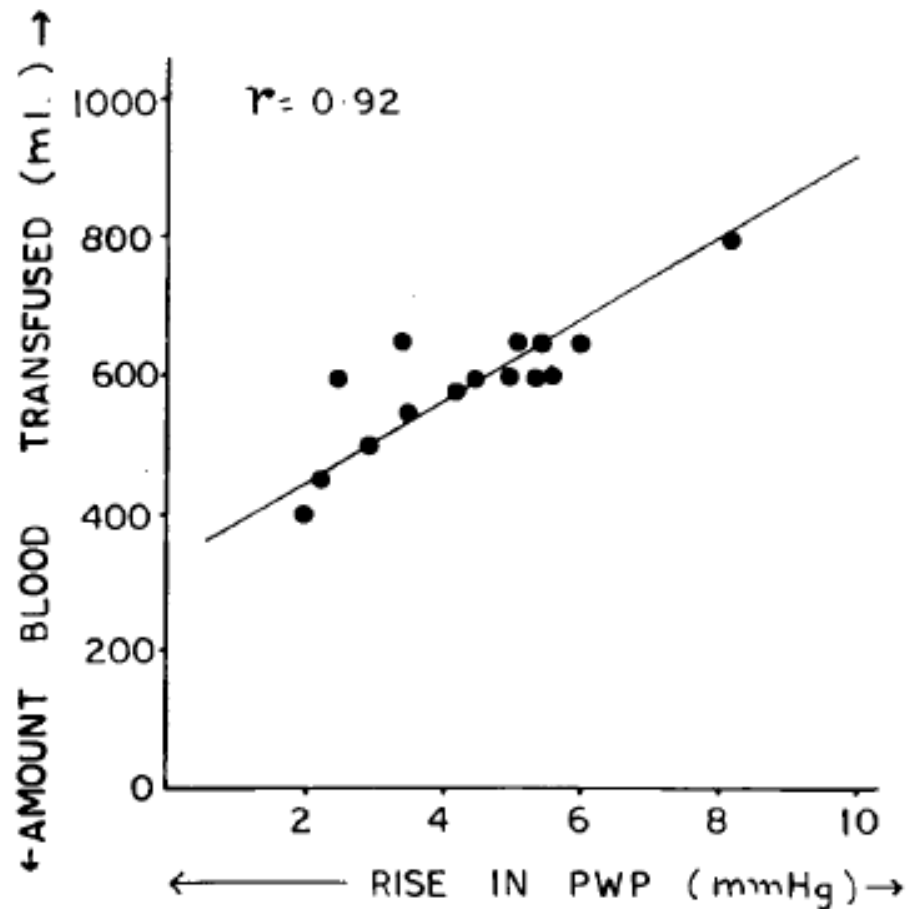
Andrzejewski C. Transfusion Reactions 2012, P574

PCWP and volume infused



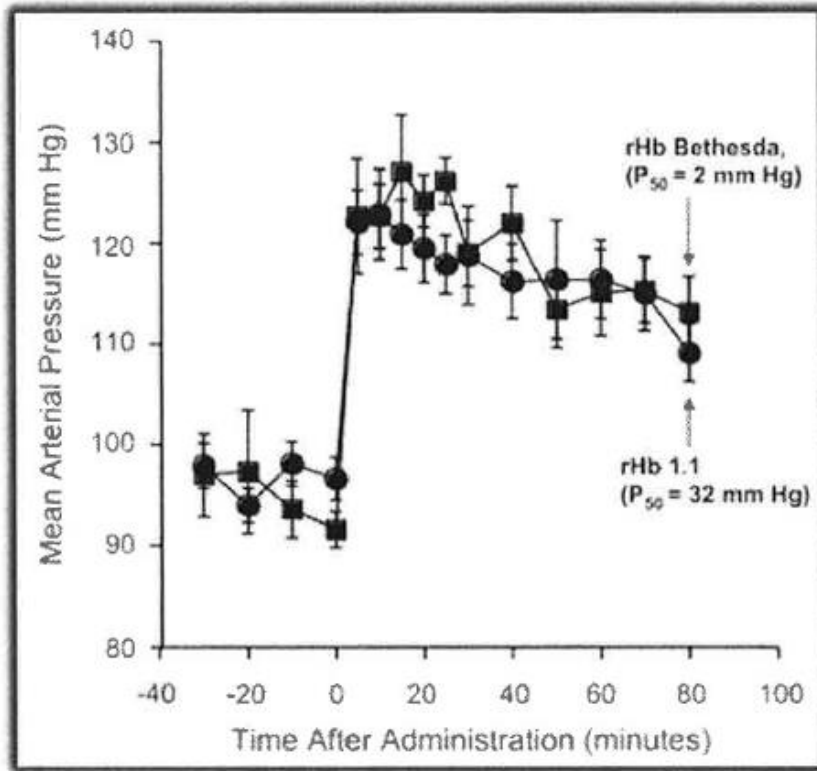
Gupta SP, et al. Angiology 1982; 33: 343-8

Does the transfusion of 1 unit to adults (as opposed to 2 units) reduce the risk of TACO?

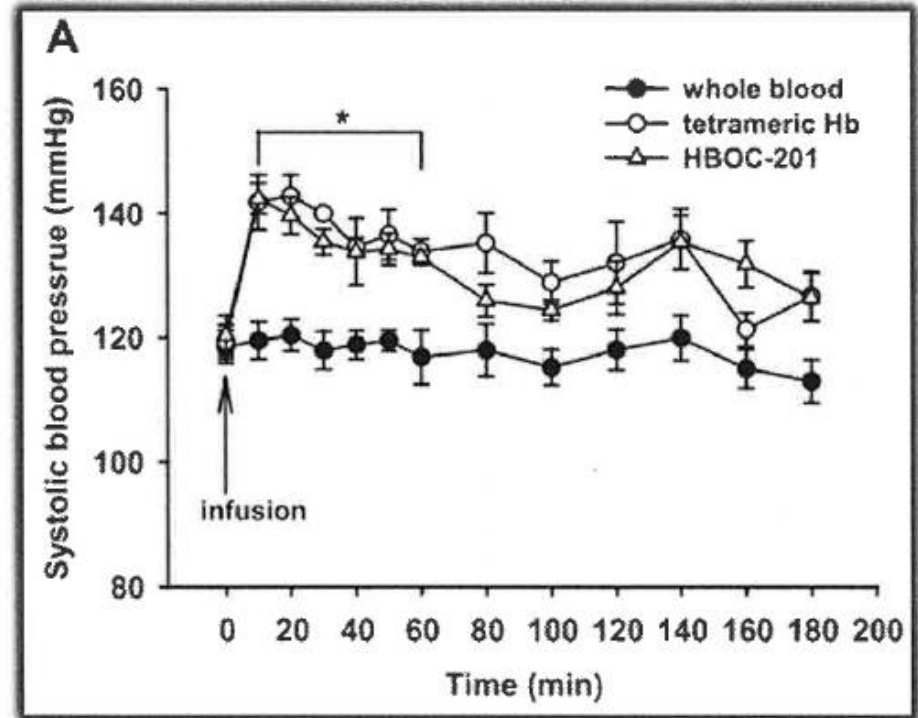


Gupta SP, et al. Angiology 1982; 33: 343-8

Free Hb and Blood Pressure

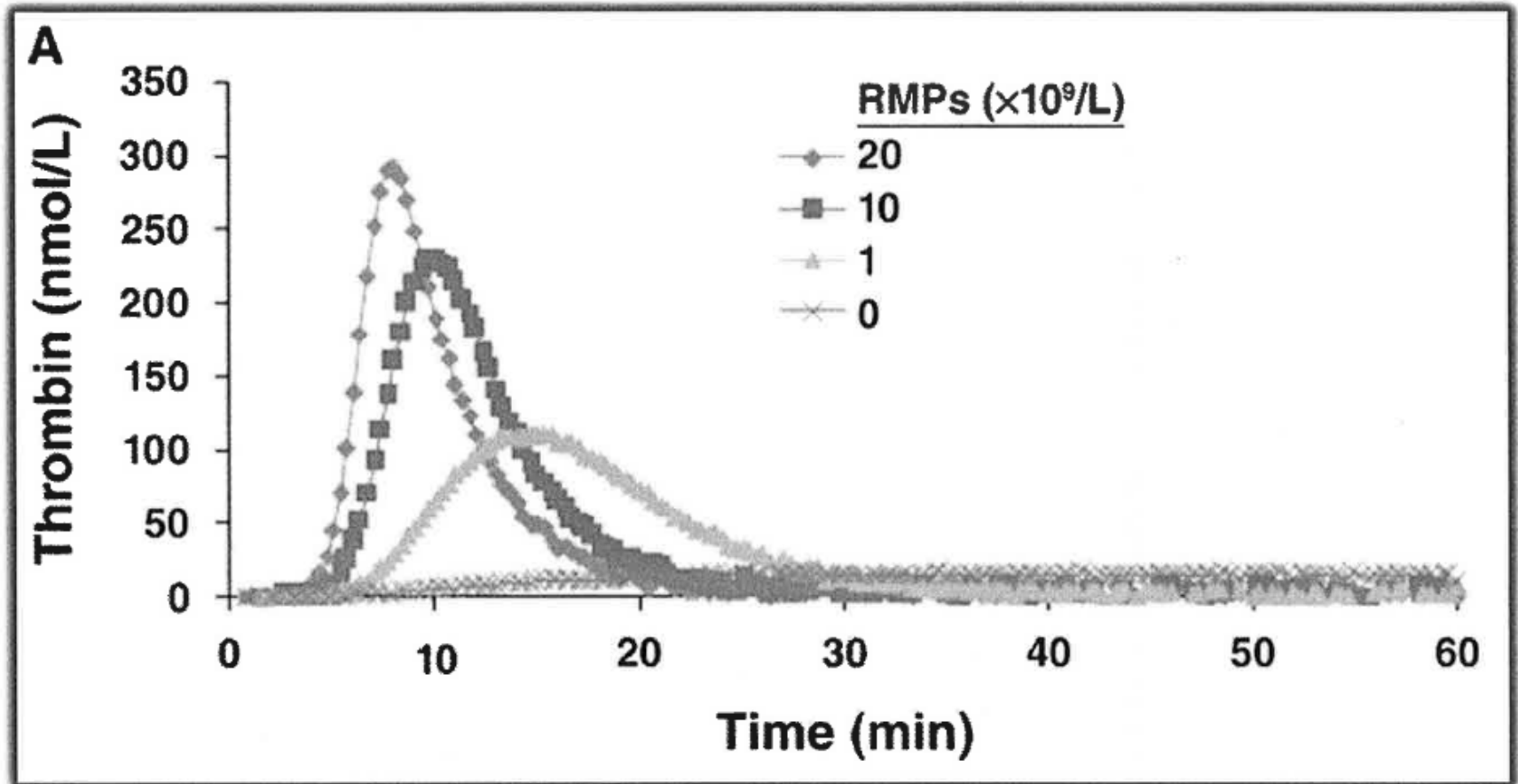


Olsen et al. Free Rad Biol Med 2004; 36:685



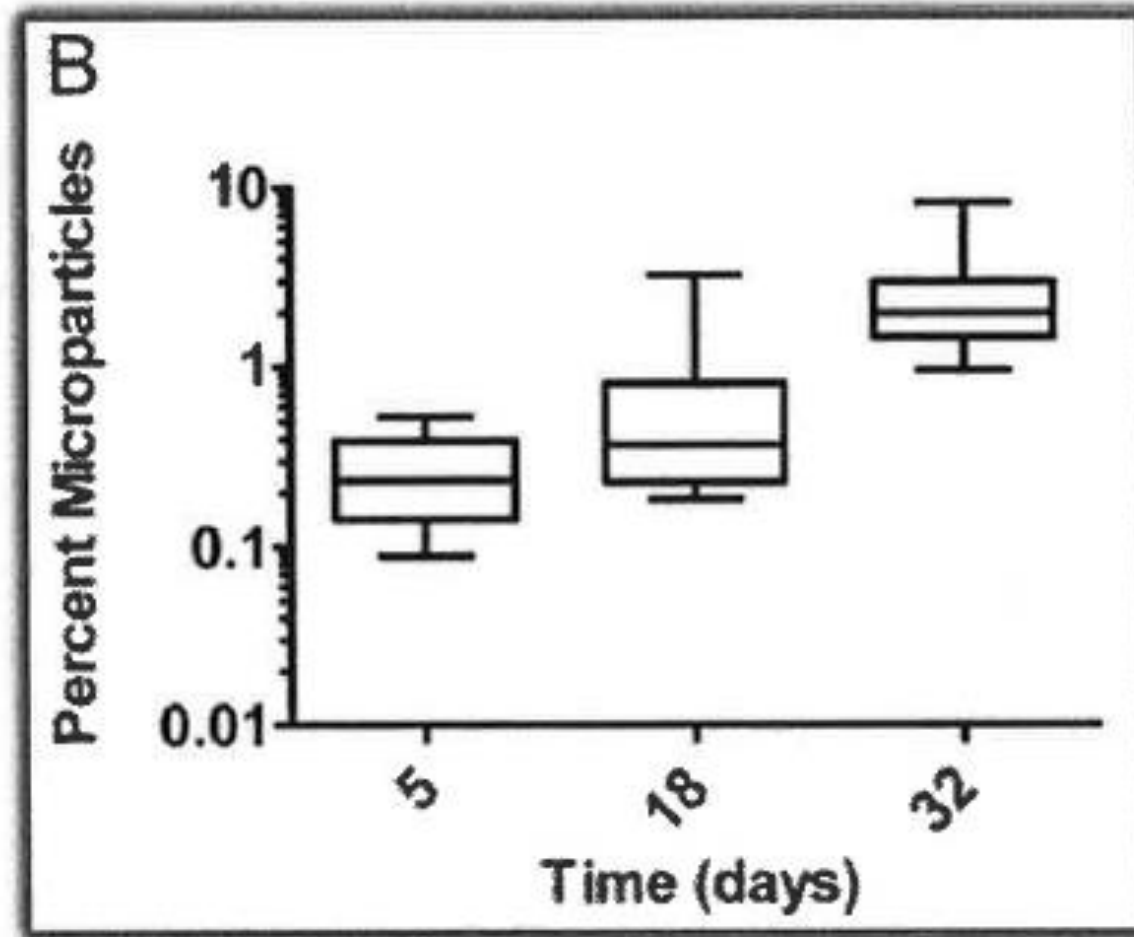
Yu et al. Circulation 2008; 117:1982.

RBC-MPs and Thrombin Generation

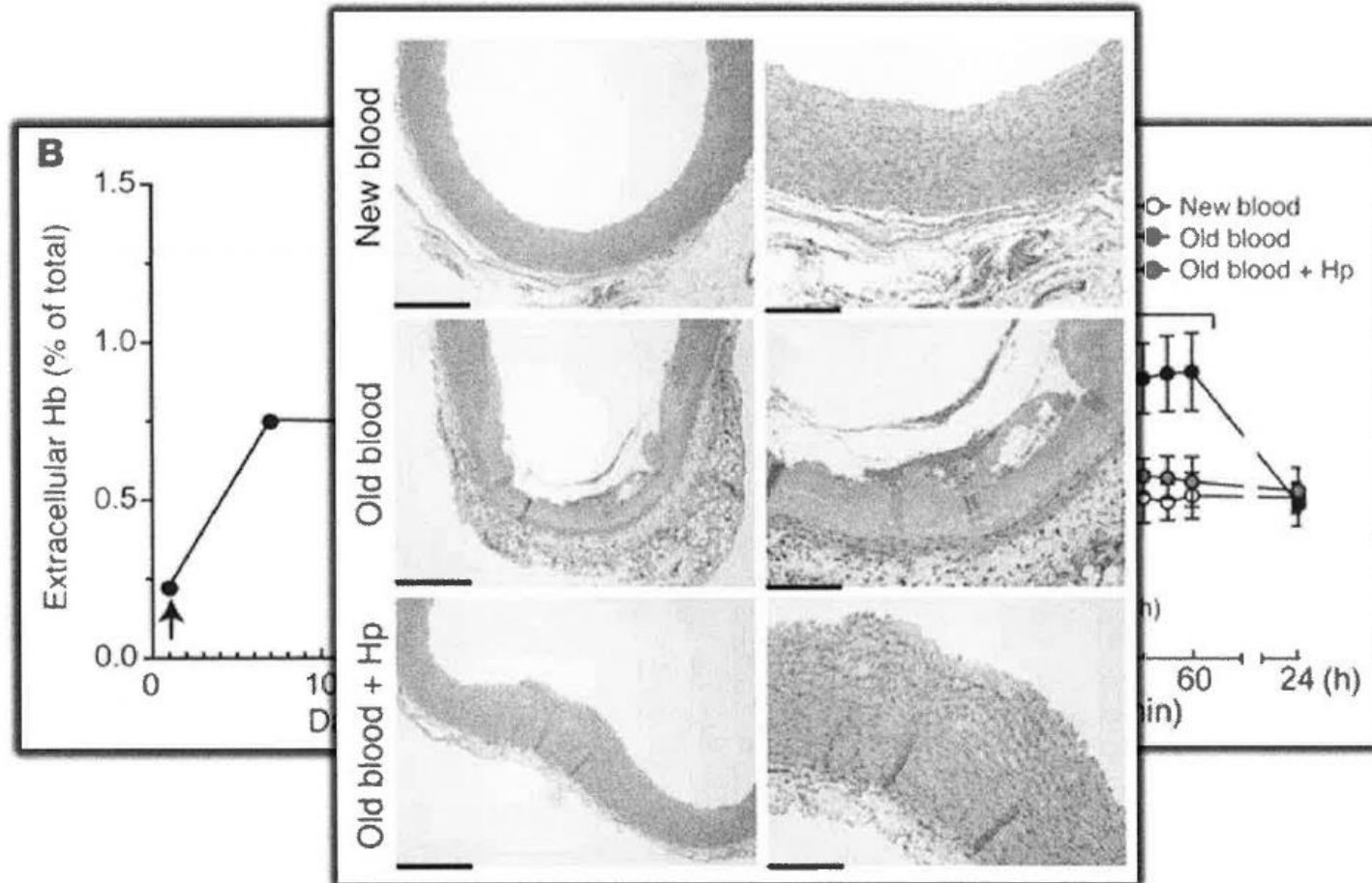


Rubin et al. Transfusion 2013; 53:1744.

RBC – MP & Storage Age



Thrombin Generation and Stored RBCs

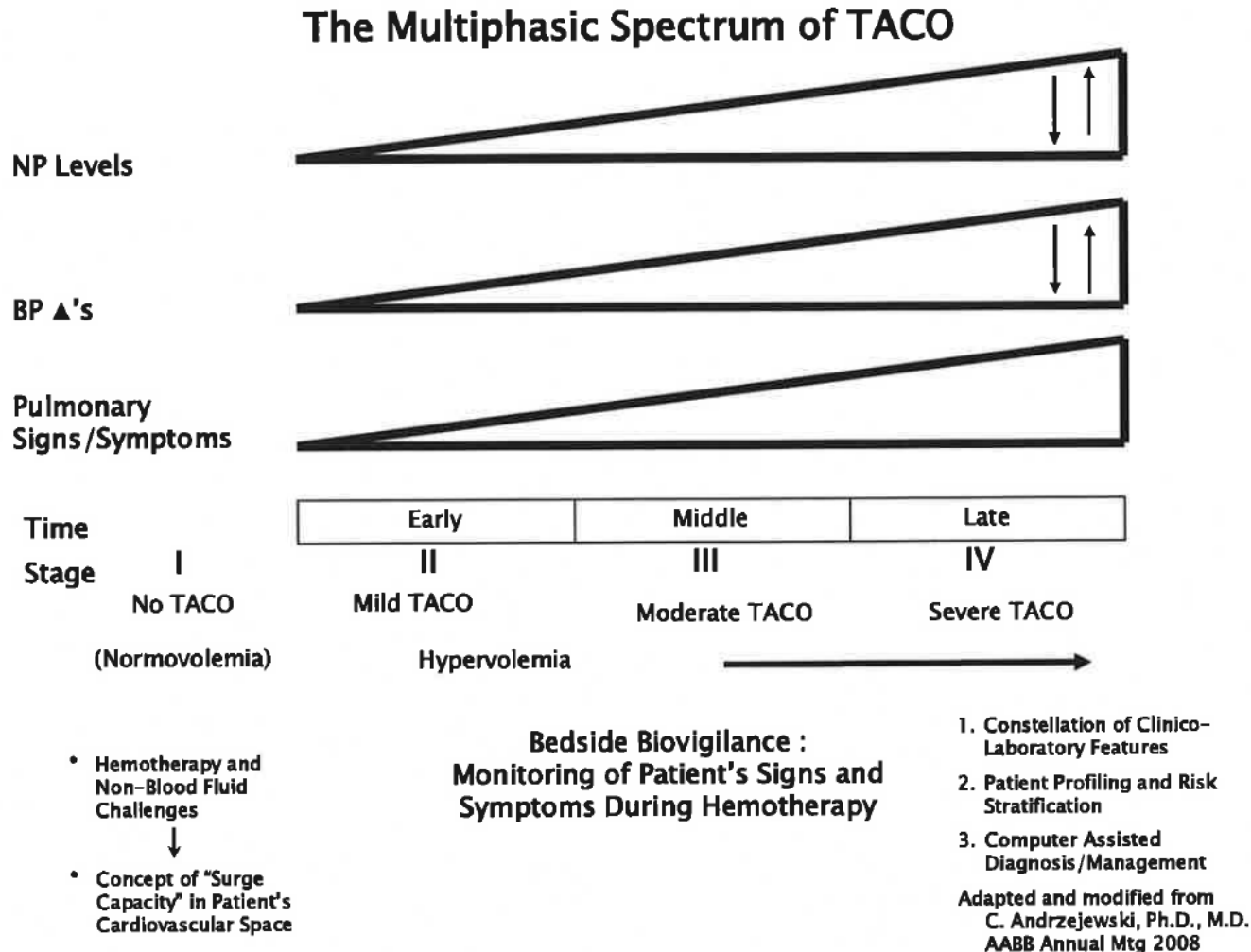


Baek et al. JCI 2012; 122:1444.

Split RBC and TACO



The Multiphasic Spectrum of TACO



Critical nursing supervision

- Pre-transfusion volume assessment
- Question over-zealous physicians
- Refusing verbal orders
- Critical at 15 minute check
 - BP up? O₂sat okay?
- Close monitoring of high risk patients



J. Callum: Personal communication

15 minute vitals

- At the 15 minutes, systolic blood pressure, pulse pressure and mean arterial pressure were higher in overloaded patients compared to controls



Andrzejewski C, et al. Transfusion 2008; 48 suppl: 204A

Vital Signs in Fluid-challenged Patients

TABLE 2. Mean VSVs for PP and temperature (T) observed in various patient transfusion cohorts at select transfusion time points*

Variable	Cohort								
	UCT control (UCT group)			Non-TACO/FC STR (NFC STR group)			TACO/FC STR (TACO/FC STR group)		
	Before	15 min	End	Before	15 min	End	Before	15 min	End
PP (mm Hg)									
Mean	56	57	56	58	59	60	63†‡	69†‡	75†‡§
±SD	±19.1	±19.2	±17.9	±17.0	±18.2	±18.8	±23.5	±21.8	±27
Number	147	119	126	232	139	225	94	60	91
T (°C)									
Mean	36.7	36.8	36.7	37.0	37.6§	38.0§	37.0†	37.2†‡§	37.6†‡§
±SD	±1.3	±1.1	±1.1	±0.6	±0.8	±0.9	±0.7	±0.8	±1.0
Number	139	121	129	232	143	226	95	63	91

* t test ($p \leq 0.050$). Adapted and modified from Andrzejewski et al.,²⁶ Table 3. See reference for details.

† UCT versus TACO/FC STR.

‡ Non-fluid challenge (NFC) STR versus TACO/FC STR.

§ Intragroup.

|| UCT versus NFC STR.

Andrzejewski & Popovsky. Transfusion 2013;53:3037

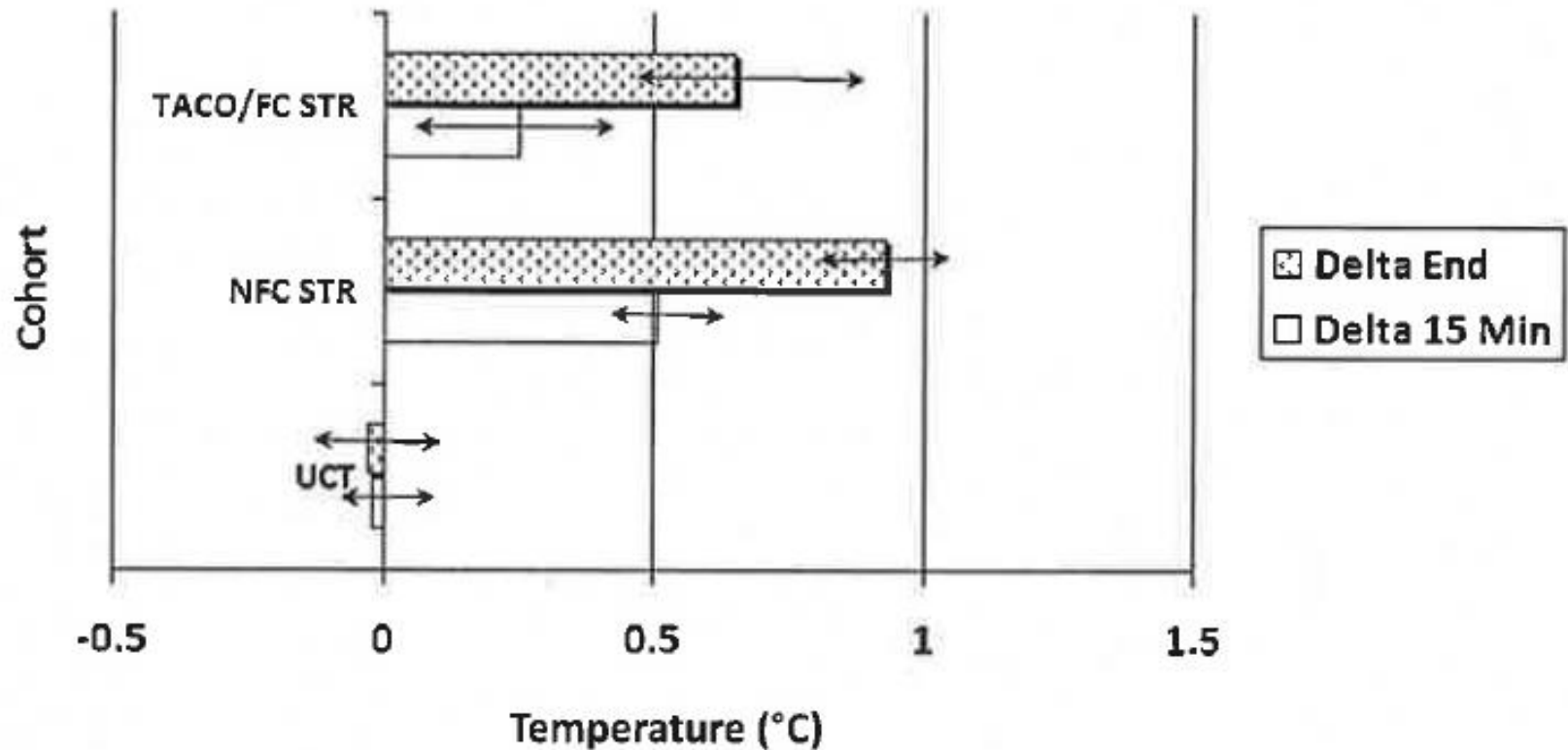
Febrile/Inflammatory Aspect – TACO

- 65% of TACO/FC patients develop a febrile response
- Pulse pressure increase may reflect inflammatory component

Andrzejewski & Popovsky. Transfusion 2013;53:3037

Vital Signs in Fluid-challenged Patients

Mean Temperature Deltas at Various Times



Andrzejewski & Popovsky. Transfusion 2013;53:3037

Summary

- TACO is a serious cause of transfusion morbidity & mortality
- Impacts healthcare costs
- May be due to a number of factors
- Fluid challenge & TACO are preventable

**Dank u
&
Vragen?**