

Blood, Cellular Therapy Products, Tissues and Organs: Common Patient Safety Concerns

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D. Michael Strong, PhD,
MT(ASCP), BCLD(ABB)



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AABB's Mission

- To advance the practice and standards of transfusion medicine and cellular and related biological therapies.



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Human-derived products



- Blood components
- Blood derivatives
- Cellular Therapy Products (HPCs)
 - Bone Marrow
 - Cord blood
 - PBPCs
- Tissue
- Organs



Common Goals



- Donor and patient safety
- Availability (itself a safety issue)
- Efficacy



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Common Risks



- Infectious
- Noninfectious



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Prevalence of Infectious Disease Markers

Percent Confirmed Positive

<i>Marker</i>	<i>Tissue Donor*</i>	<i>First Time Blood Donor**</i>
Anti-HIV	.09	.01
HBsAg	.23	.08
Anti-HCV	1.1	.3
Anti-HTLV	.07	.01

* *N=11,391* ** *N=1,630,745*

(Stramer, SL, et. al. Screening of U.S. Blood Donors for HIV-1 and HCV RNA. NEJM, Aug. 2004)

(Zou, S, et., al. Probability of Viremia Among U.S. Tissue Donors. NEJM, Aug. 2004)

Comparison of Residual Risks

<i>Marker</i>	<i>Tissue Donors</i>	<i>Blood Donors*</i> <i>(000)</i>
HIV *	1:55,000	1:1,900 - 2,400
HBV *	1:34,000	1:250 - 1,500
HCV *	1:42,000	1:1,200 - 1,700
HTLV	1:128,000	1:1,212 - 2,993

** Post - MP NAT*

(Stramer, SL, et.. al. Screening of U.S. Blood Donors for HIV-1 and HCV RNA. NEJM, Aug. 2004)

(Zou, S, et., al. Probability of Viremia Among U.S. Tissue Donors. NEJM, Aug. 2004)

Comparison of Prevalence Rates / 10,000 Donations

	Combined Whole Blood	Autologous Whole Blood	Combined HPCs
Anti-HIV	0.30	2.91*	0.36
Anti-HCV	5.10	104.7*	15.40
Anti-HBc	35.61	401.3*	274.4
HBsAg	1.49	14.16	25.44*,**
<i>N =</i>	<i>6.5M</i>	<i>1.1M</i>	<i>139,654</i>

*p<0.05 for one or multiple Comparisons; **Ortho System 3

Transfusion Recipient Fatalities Reported to FDA

CATEGORIES	FY04	FY05	FY06
TRALI	21 30.9%	30 36.6%	35 50.7%
Non-ABO Hemolytic Reactions (K, JKa, FYa, etc.)	20 29.4%	25 30.5%	22 31.9%
Bacterial Contamination	6 8.8%	9 11.0%	5 7.2%
ABO Hemolytic Transfusion Reaction	7 10.3%	5 6.1%	3 4.3%
Transfusion not Ruled Out	14 20.6%	13 15.9%	4 5.8%
TOTAL	68	82	69

Hemovigilance Networks

Partial Listing



Austria
Czech Republic
Denmark
Finland
France
Germany
Greece
Ireland

Italy
Norway
Poland
Slovak Republic
Spain
Switzerland
The Netherlands
United Kingdom

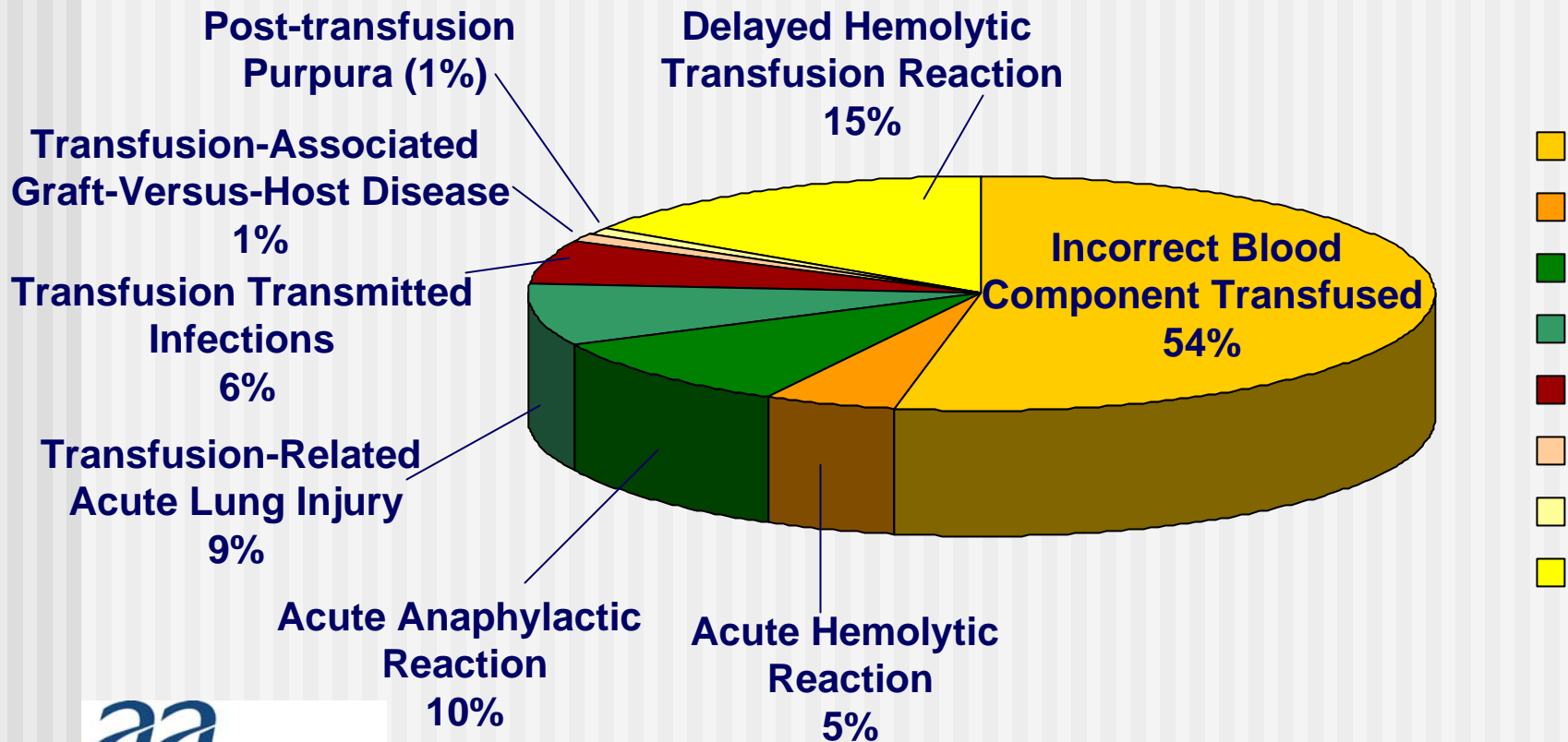
Brazil
Canada/Québec
Japan

Russia
New Zealand
South Africa



What Can Be Learned?

Data from Denmark



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Vox Sanguinis 2006; 90:207-41.

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Learning from the System

Recipient Outcomes (SHOT)

Mortality	1/250,000 transfusions
Major morbidity	1/92,000
Serious hazard	1/11,000
Acute hemolysis	1/102,000



#1 cause: TACO

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Non-infectious Risks: Tissue

- Graft failure
 - Mechanical
 - Non-unions / loosening
 - Incorporation
- Immune rejection
- Technical
 - Mis-measurement
 - Mis-labeling



Non-infectious Risks: Cellular Therapy Products

- Graft failure
- Immune rejection
- GVH
- Technical
 - Counting errors
 - Processing errors
 - Bag breakage
- Mis-labeling
- Administration side effects
(e.g., DMSO toxicity)

Common Layers of Safety

- Donor Screening and Eligibility
- Collection
- Infectious Disease Testing
- Processing
- Labeling
- Traceability
- Transportation
- Storage
- Surveillance of Product Quality
- Outcomes Analysis
- Adverse Event Surveillance



Commonalities: Donor Screening and Eligibility

- FDA regulations and private standards apply
- Similar donor history questionnaires
 - Medical/social history
- Donors screened and tested for infectious agents
- Donor counseling (some variation)



Commonalities: Collection

- Informed consent
- Sterility
- Apheresis (blood and HPCs)
- Allogeneic vs. autologous (blood, PBPCs, bone marrow, tissue)



Commonalities: Infectious Disease Testing

Blood	CT Products	Tissue
HIV-1/2	HIV-1/2	HIV
HBV	HBV	HBV
HCV	HCV	HCV
HTLV-I/II	HTLV-I/II	HTLV-I/II
Syphilis	Syphilis	Syphilis
CMV (sometimes)	CMV	
WNV (not required)	WNV (not required)	WNV (not required)
Chagas' (not required)	Chagas' (not required)	

Commonalities: In-process Tests

Blood	CT Products	Tissue
ABO group	ABO group	Limited ABO group*
Rh type	Rh type	Limited Rh type*
Unexpected antibodies to RBC antigens	Total nucleated cell count	
Limited HLA typing	HLA typing	
Minimal cell doses	CD34 analysis or comparable assay	Residual moisture (freeze-dried)
Bacterial contamination	Microbial contamination	Microbial contamination
	Cell viability	

* *Cardiovascular Tissue*

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Commonalities: Processing

- Cell separation (except tissue)
- Sometimes cryopreservation
- Storage
- Quarantine
- Specialized labeling



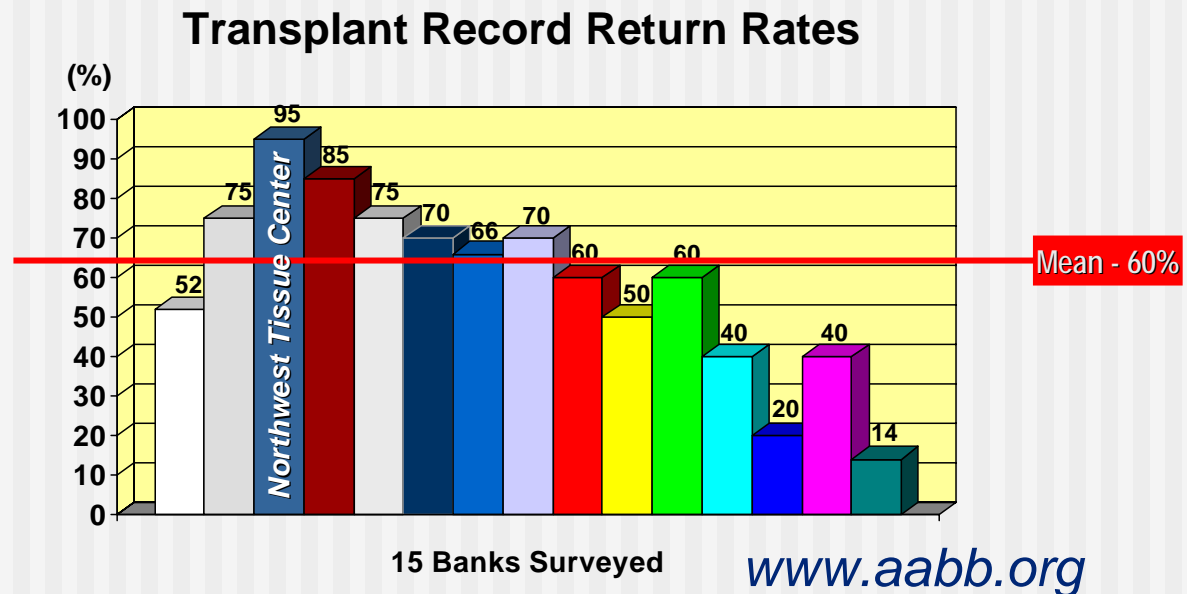
Commonalities: Labeling

- Uniform system needed
- ISBT 128
 - Blood: implement by 2008
 - CT: standard setting organizations expected to require implementation
 - International Cellular Therapy Coding and Labeling Advisory Council
 - Tissue: North American Tissue Technical Advisory Group investigating application of ISBT 128 to finished allografts



Commonalities: Traceability

- Identification and traceability of product and related samples from source to final disposition
 - Critical raw materials and equipment included
 - Records



Commonalities: Transportation

- Limit deterioration, prevent damage and protect quality of products in transport
- Controlled/validated packaging
- Temperature control and monitoring
- Labeled to ensure appropriate handling and allow identification
- Int'l shipping more of an issue for CT products and tissue



Commonalities: Storage

- Temperature control
- Increasingly, more products stored in hospital-based blood banks
 - Tissue: new TJC standard (QC.5.300 and QC.5.310)



Commonalities: Surveillance of Product Quality

- Blood
 - RBCs: increase in hemoglobin
 - Platelets: increase in platelet count
 - Plasma/cryo: correction of bleeding
- CT products/tissue: engraftment
- Tissue: graft function



Commonalities: Adverse Event Surveillance

- Donor and patient
- Report to FDA (through different mechanisms)
- Hemovigilance ➡ Biovigilance
 - Public/private initiative



Adverse Event Surveillance

Blood	CT Products	Tissue
Infectious diseases	Infectious diseases	Infectious diseases
Mis-tx (e.g., wrong ABO)	Mis-transplantation	Mis-transplantation
Bacterial contam.	Bacterial contam.	Bacterial contam.
Febrile Reactions	Febrile Reactions	Febrile Reactions
GVHD	GVHD	Graft failure
Immune reactions	Immune reactions	Immune reactions
TRALI/TACO		

Commonalities: Patient Access

- Ensuring an adequate supply key for all products
- Fair reimbursement is critical



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Conclusion

- Common strategic plan is needed
 - Public-private initiative
- Focus on similarities, taking note of significant differences as well

