1

Learning Objectives

After participating in this program you should be able to….

- Discuss how this highly regulated industry is dependent on regulatory bodies – constantly changing to meet requirements. (ex. discuss FDA guidance and its impact on platelet transfusion safety).
- Discuss important factors with providing individualized treatment/care.
- Identify challenges with educating ordering providers/clinical staff.

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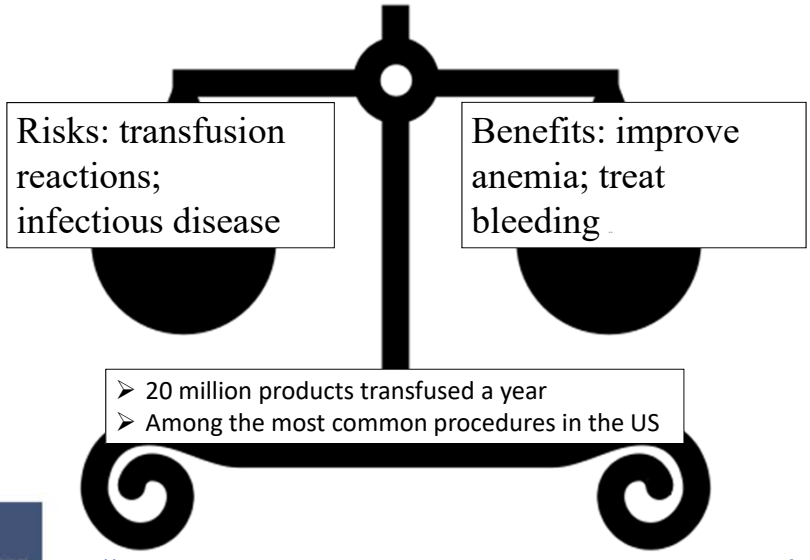
The balance in transfusion therapy



- 20 million products transfused a year
- Among the most common procedures in the US

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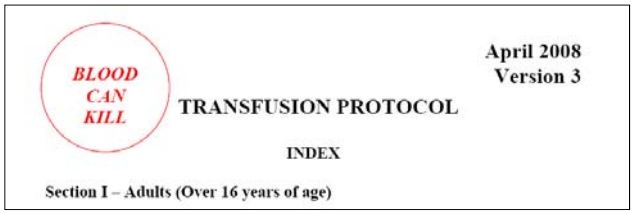
American Red Cross

3

Transfusions can help but can also cause harm



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HTR (ABO)	1	3%	4	13%	2	5%	4	9%	1	3%	**12**	**7%**
HTR (non-ABO)	5	13%	4	13%	4	11						
Hypotensive Reaction	-	0%	1	3%	1	3						
TACO	13	34%	5	17%	11	30						
TRALI*	14	37%	13	43%	12	32						

How can we mitigate risk?
-Regulation
-Evidence-based practice
-Education

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To help prevent harm: accreditation and significant government regulation

- Invited inspections
  - AABB
  - College of American Pathologists (CAP)
  - Foundation for Accreditation of Cellular Therapy (FACT)
  - Joint Commission
- Uninvited inspections
  - FDA
  - State Department of Health

FACT FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY

COLLEGE of AMERICAN PATHOLOGISTS

The Joint Commission

FDA U.S. FOOD & DRUG ADMINISTRATION

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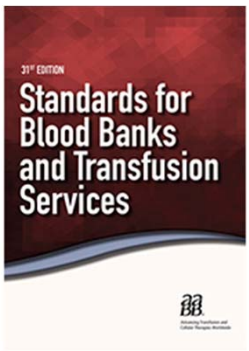
Invited accreditation: Ensuring the best possible care

- AABB: Inspect every 2 years
  - Blood Banking and Transfusion Standards (BBTS)
  - AABB Cell Therapy Standards
  - Others
- CAP : Inspect every 2 years
  - Blood Banking checklist
  - Cell Therapy checklist
  - AABB deemed status
- FACT: Inspect every 3 years
  - Hematopoietic Cell Therapy
  - Immune Effector
  - Cord Blood



AABB
BBTS: 432 individual standards
Cell Therapy: 423 individual standards

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FDA: National rules to ensure safety

- Code of Federal Regulations = Our rule book
  - Covers collection, testing and manufacturing of blood products
- A sampling:
  - Part 493: Laboratory requirements
  - Part 606: Good manufacturing practice (GMP) for blood and blood components
  - Part 610, Subpart E: Testing requirements for relevant transfusion-transmitted infections
  - PART 630: Requirements for blood and blood components intended for transfusion or for further manufacturing use.
  - Part 660, Subpart D: Reagent red blood cells
  - Part 1271: Human cells, tissues, and cellular and tissue-based products
- Need to report
  - Donor or recipient fatalities
  - Effect on product purity, potency, safety

Electronic Code of Federal Regulations e-CFR™

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FDA Guidances: Clarifying the rules

- Potential major changes in practice
- May significantly add to cost of manufacturing
- Allow for comment period
- Some recent
  - Recommendations for Reducing the Risk of Transfusion-Transmitted Babesiosis
  - Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion

FDA U.S. FOOD & DRUG ADMINISTRATION

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Reducing Babesia risk (CFR 630.3)

- Tick-borne illness
  - Not everyone infected has symptoms
- Recently recognized by FDA as transfusion-transmitted infection
- Require
  - Donor history question
  - Test each donation for evidence of Babesia using a licensed nucleic acid test when collected in CT, DE, ME, MD, MA, MN, NH, NJ, NY, PA, RI, VT, VA, WI, DC

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CDC

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Reducing risk of septic reactions (CFR 606.145)

- Platelets stored at room temperature = higher risk of bacterial contamination
- Bacterial contamination has led to fatal septic transfusion reactions
- Most platelets in the US had been cultured at collection
- Now additional steps
  - "The guidance provides recommendations to control the risk of bacterial contamination of platelets…including bacterial testing strategies (using culture-based and rapid bacterial detection devices) and the implementation of pathogen reduction devices."

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utmb.edu

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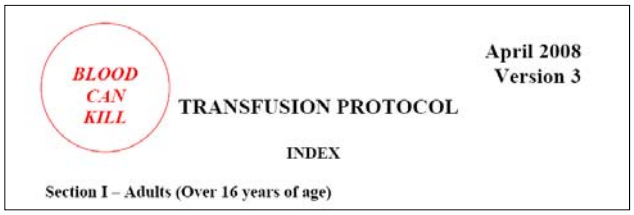
Transfusions can help but can also cause harm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Evidence-based practice: Less may be better for patient care

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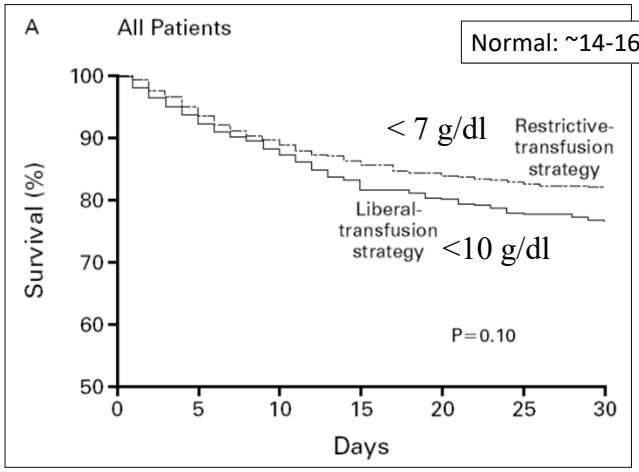
ICU: Restrictive Hgb threshold now standard



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Hebert P et al., NEJM (1999)

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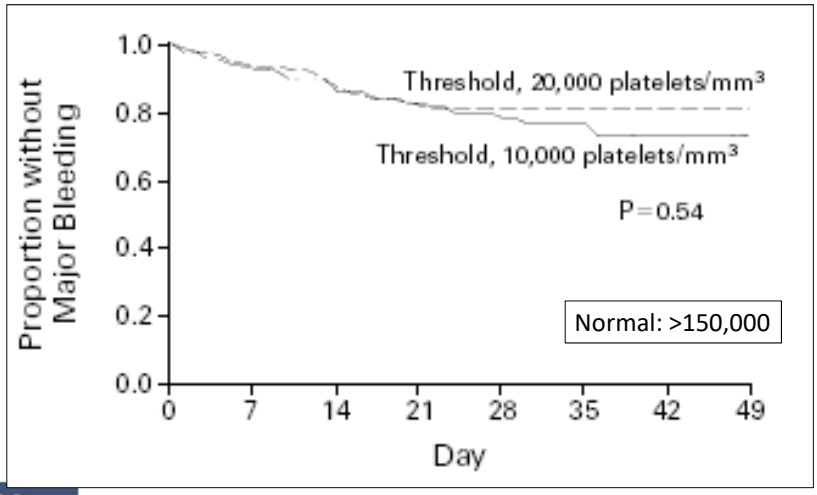
We don't need all our platelets



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Rebulla P, et al. *NEJM* (1997), 337, 1870

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Studies demonstrating efficacy of pre-procedure prophylaxis

0

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Evidence-based practice: Not universal

Details
Order for 2 units of RBCs outside hospital guidelines, transfusion resulted in TRALI
Excessive volume of product transfused ordered (8 L of product over 12 hr) resulting in TACO
Order for 2 units of RBCs outside guidelines at excessive infusion rate (2 units over 1 hr) resulting in TACO
Order for 4 units of plasma when 10 mg of IV vitamin K was indicated resulting in TACO
Order for 1 unit of RBC outside hospital guidelines resulting in an acute transfusion reaction
Order for 1 unit of RBC outside hospital guidelines without informed consent completed resulting in an acute transfusion reaction
Order for 2 units of RBCs outside hospital guidelines resulting in an acute transfusion reaction
Order for 1 unit of RBC outside hospital guidelines resulting in an acute transfusion reaction
Order for 2 units of plasma when 10 mg of IV vitamin K was indicated resulting in an acute transfusion reaction
Order for 2 units of RBCs outside hospital guidelines, transfusion resulted in TACO
Patient overtransfused (posttransfusion Hb > 180 g/L) resulting in TACO
Order for 1 unit of RBCs outside guidelines at excessive infusion rate for elderly patient resulting in TACO
Order for 1 unit of RBCs outside hospital guidelines, transfusion resulted in TRALI, and transfusion continued despite dyspnea due to failure to recognize the transfusion reaction
Order for 9 units of plasma when 10 mg of IV vitamin K was indicated resulting in TACO
Vitamin K order subcutaneously, instead of IV, and subsequently had delayed control of hemostasis and use of plasma
Order for 2 units of RBCs outside hospital guidelines resulting in an acute transfusion reaction
Order for 2 units of RBCs outside hospital guidelines, transfusion resulted in TACO
Order for 2 units of RBCs outside hospital guidelines, transfusion resulted in an acute transfusion reaction
Order for 2 units of RBCs outside hospital guidelines, transfusion resulted in TACO
Order for 2 units of RBCs outside hospital guidelines, transfusion resulted in an acute transfusion reaction
Order for 3 units of plasma outside transfusion guidelines without informed consent resulting in TACO

- 5 years of data from a Transfusion Error Surveillance System at a single hospital
- >15,000 errors reported
- 6,091 “clinical errors”
  - 395 high-severity errors due to inappropriate blood product use (6.5%)
- All 21 errors resulting in harm were due to inappropriate ordering (0.35% of clinical errors)
  - 20 of 21 leading to a transfusion reaction

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Maskens C, et al. *Transfusion* (2014), 54, 66

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Areas of controversy: Examples

- Trauma care
  - Appropriate product ratios
  - Use of whole blood vs. components
  - Cold-stored platelets
- Iron deficiency in blood donors

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Whole Blood: A Debate

- "Whole blood is what patient's are losing so that's what we should transfuse"
  - Liquid plasma not as good as freshly thawed FP24
  - Conflicting data on cold platelets (but clearly don't last as long)
- "There's ample data that whole blood is safe and better than components"
  - Minimal contemporary data
  - Vietnam: WB similar coag and platelet issues as pRBC (dilutional coagulopathy)
- "Even if we're not 100% sure whole blood is better, what's the harm?"
  - Some evidence for increased plasma = increased adverse events
  - Can't always predict MT, even one unnecessary product has risk
  - Incompatible plasma: Many unknowns
  - Many other logistical and supply issues
- My opinion: We need to study if whole blood better before extended implementation

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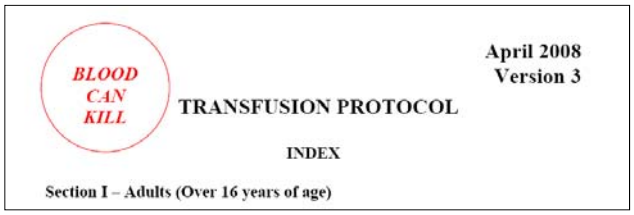
Transfusions can help but can also cause harm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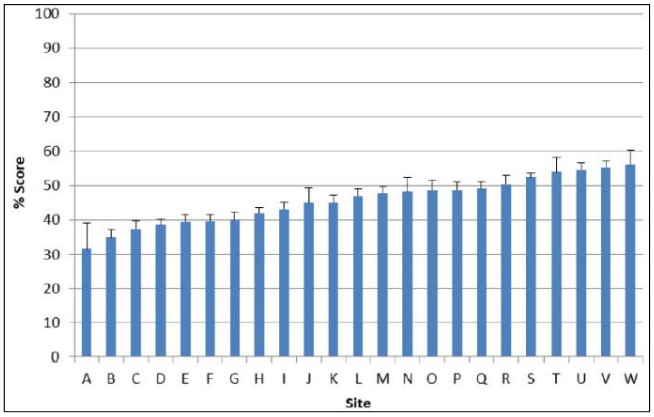
We need to do a better job with education



- 474 medicine residents at 23 programs in 9 countries
- Validated exam; Mean score: 46%
- 89% had obtained transfusion informed consent

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Haspel RL, et al. *Transfusion* (2015), 55, 1355

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More training needed

- Minimal training in medical school/residency
  - >20 million products transfused a year!
  - Potential harm
- Trainees recognize need

Amount of training (%)	Medical school	Residency
None	12.1	27.6
1 hr	28.0	32.9
2 hr	24.8	21.9
3 hr	16.8	10.8
4+ hr	18.3	6.8
Quality of training (%)	Medical school	Residency
Not helpful	14.8	23.9
Slightly helpful	38.1	21.4
Moderately helpful	36.0	37.7
Very helpful	9.6	14.8
Extremely helpful	1.5	2.1

How helpful would you find additional training in transfusion medicine?	
Not helpful	0.8
Slightly helpful	6.3
Moderately helpful	28.1
Very helpful	44.3
Extremely helpful	20.5

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Key Points

- Blood transfusions have benefits and risks
  - One of the most prescribed procedures in the US
- Ways to mitigate risk
  - Regulations and accreditation
  - Evidence-based practice
    - Less transfusion may be better (“Surplus City”)
    - Evidence-based practice is not universal
    - Still areas of controversy
    - Need more research
  - Education
    - Evidence for poor physician transfusion knowledge
    - Need more time and more effective teaching methods

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Questions?

Contact
AABB eLearning Team
eLearning@aabb.org

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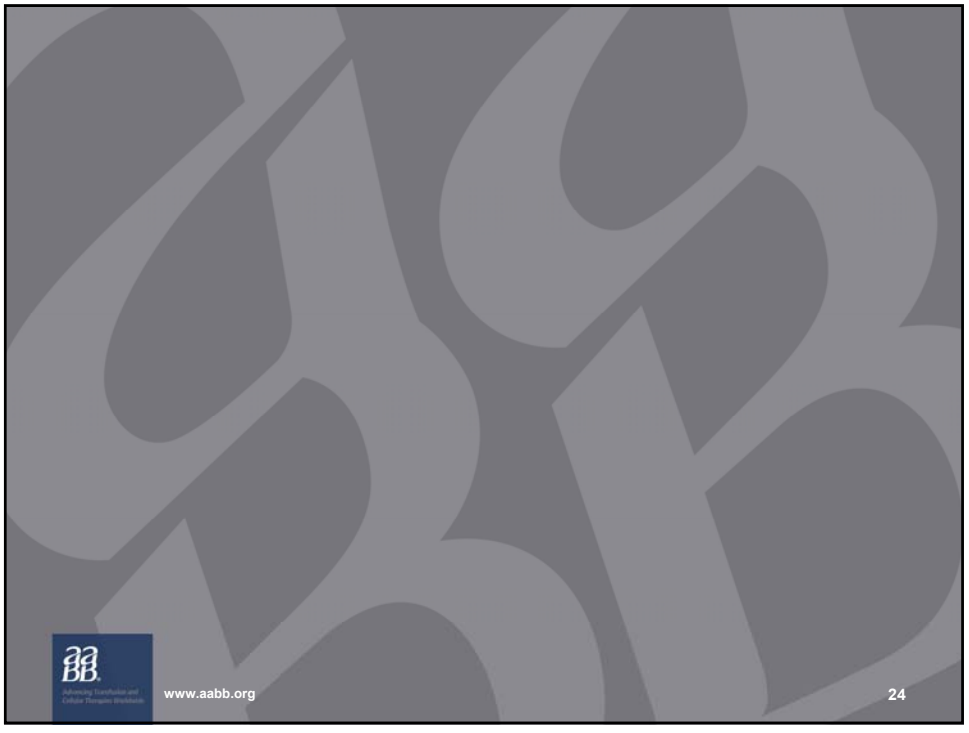

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