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Blood Supply Issues

Impacting whole blood access in the pre-hospital setting

National Whole Blood Summit

June 20, 2024

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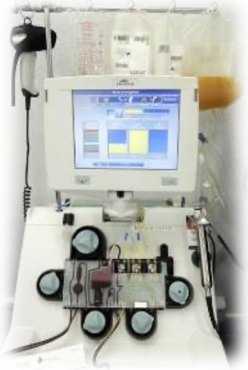
In U.S. 16M components transfused annually, one about every 2 seconds.

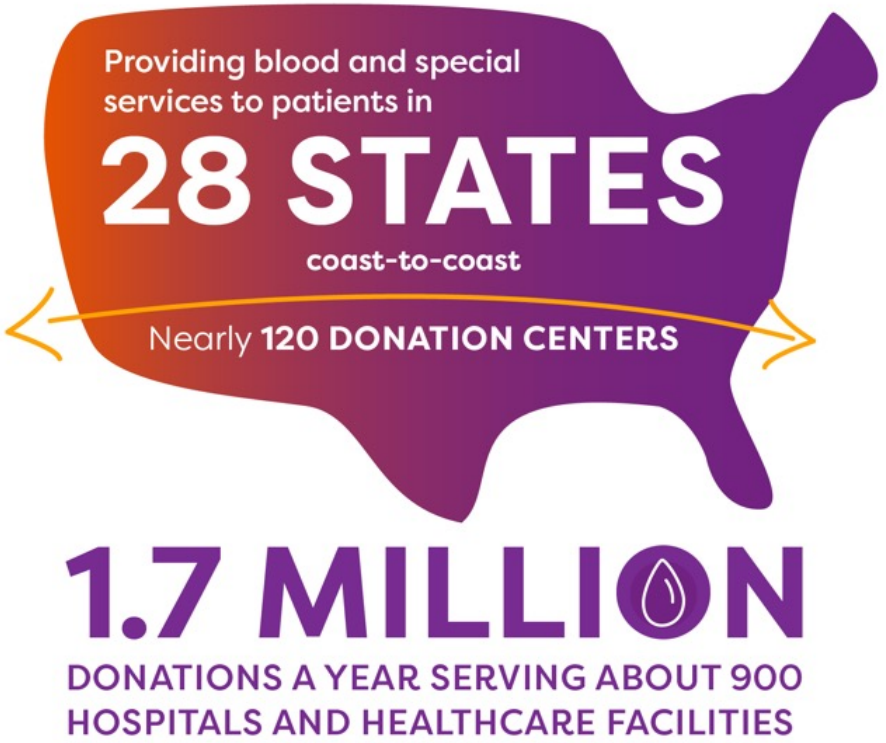
Collected from
53 community centers
90 hospital-based centers.

When blood is needed in a hospital,
3 units used on average.



<u>Daily Estimates</u>
29,000 red cells
5,000 platelet
6,500 plasma

One of the nation's largest nonprofit blood services providers.



FDA

Center for Biologics Evaluation and Research

21 CFR 1271 Parts

210 (cGMP in manufacturing, processing, packing, or hold of drugs): Status, Applicability
211 (cGMP for Finished Pharmaceuticals): Subparts B-K
600 (Biologics: Products: General): Subpart D – Establishment Standards
606 (cGMP Blood & Blood Components): Subparts B-I
820 (Quality Systems Regulations): Subparts B-O

21 CFR Chapter I (DHHS), Subchapter F (Biologics); 600s.

600 General: Subparts A-D
601 Licensing
606 cGMP for Blood and Components
607 Establishment Registration & Product Listing: Subparts A-E
610 General Biologic Products Standards
630 Requirements for Blood Intended for Transfusion or further manufacturing: Subparts A-C
640 Additional Standards for Human Blood & Blood Products
660 Additional Standards for Diagnostic Substances for Lab Tests
680 Additional Standards for Miscellaneous Products

Blood Guidances

https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/blood-guidances
n=80 dating back to 1984

510(k) Clearance

Required by devices used by the blood banking industry including blood establishment computer software, transfer devices, collection systems, separators, culture bottles, fluid warmers, etc.

OSHA

EPA

DEPARTMENT OF TRANSPORTATION UNITED STATES OF AMERICA

Blood is a biologic drug regulated by federal and state competent authorities and overseen by credentialing organizations with deemed status from CMS. Donor and patient safety topics covered.

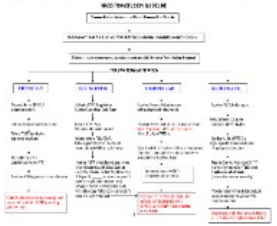
The Joint Commission

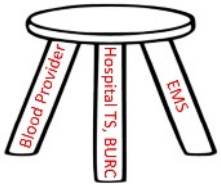
cap
Master
Every patient deserves the GOLD STANDARD
Transfusion Medicine Checklist
CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

aabb STANDARDS
Blood Banks and Transfusion Services
AABB Accredited

DOH
New York State Department of Health

Pre-hospital service providers must understand that transfusion of blood is only one of many parts of a complex supply chain which collectively must be optimized for all patients.

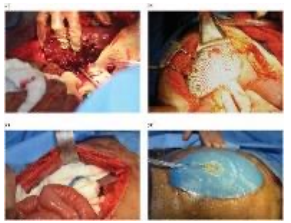




Transfusion Service
Additional testing, audits
SAR, recalls, lookbacks,
Inventory Management
Wastage
designed for all patients

What will blood stewardship look like in the new paradigm?

"Early recognition + aggressive management + vigilant monitoring"



How will we get there?

*Even if large-scale use of LTOWB in the pre-hospital setting results in a net reduction of overall red cell usage, the **10s of 1000s** of additional O (only) red cells that will need to be collected and broadly distributed for a nationwide implementation, is NOT currently feasible.*

How will we handle the haves versus the have nots?

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Donor agency, loss of classical altruism, & fatigue

What does agency mean?

Copilot

Agency refers to an individual's independent capability or ability to act on their own will [1]. It encompasses both mindset and learnable actions that help us attain what we want in life. Here are the key aspects of agency:

If you build it, who will come?

Robbing Peter to pay Paul?
LTOWB, which is manually collected, comes from a donor pool that is pushed to automation to most effectively meet all patient need.

Type	POP	Demand
A	40%	32%
B	11%	08%
O	45%	57%

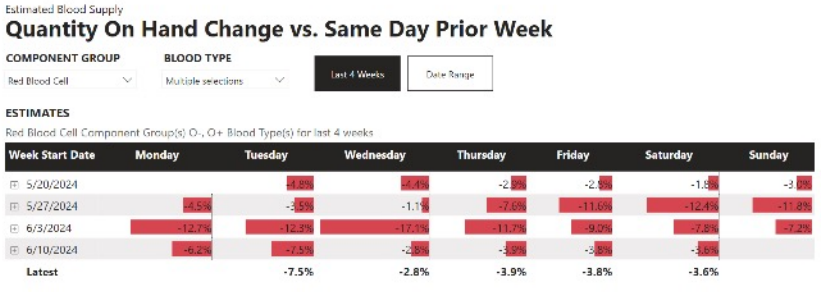
≥25% of all collections must come from automation to meet **current** RBC demand.

How will we make sure the right blood types get to the right patients?

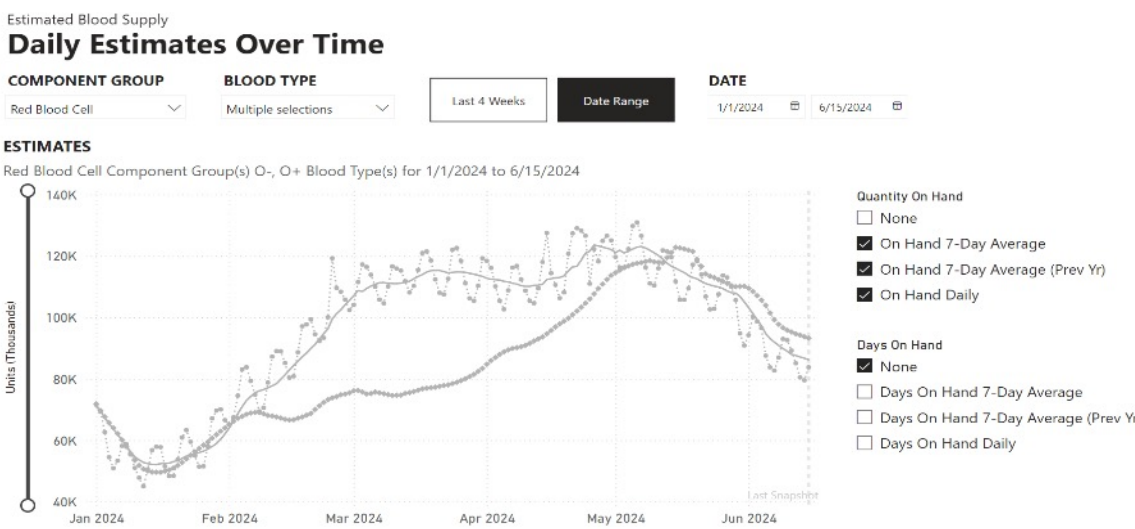
Circulate

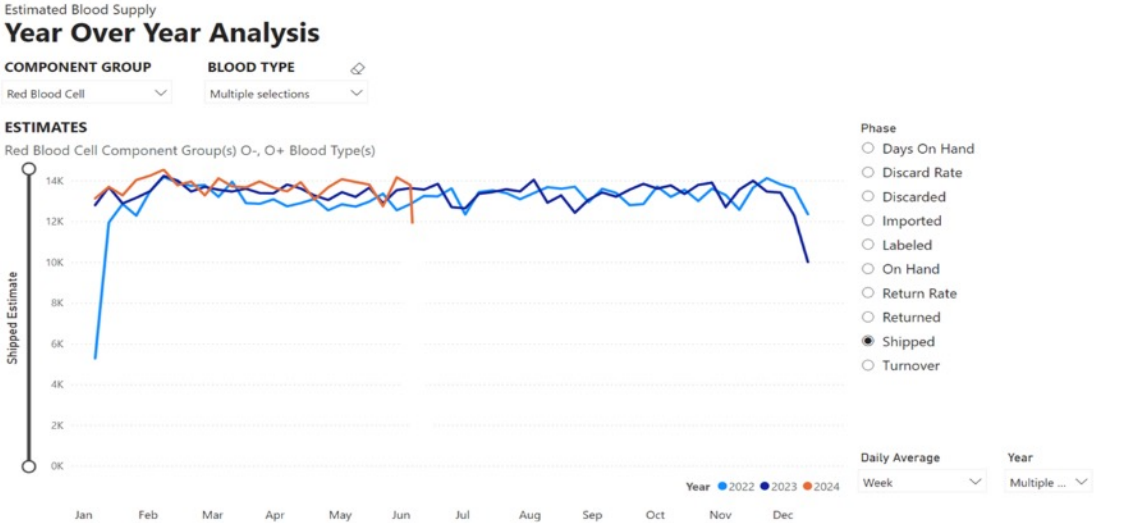
an independent data warehouse organization

estimates national inventory using data from 4 blood operators (~2/3) plus a proprietary estimator model



Mission: Empower and educate blood operators, community partners and government stakeholders through the collection, reporting, and analysis of timely and accurate blood inventory data.





The current blood supply is fragile

We frequently collect below hospital stated need, especially summer.

- Ideal inventory holds >7 days of blood on hand.

LATEST DAYS ON HAND ESTIMATES

Cryoprecipitate, Plasma, Platelet, Red Blood Cell Component Group(s) All Blood Type(s) on 6/16/2024

Component Group	O-	O+	A-	A+	B-	B+	AB-	AB+	Overall
Red Blood Cell	3.6	5.6	6.2	8.4	4.3	9.0	15.7	17.8	**6.9**
Platelet	1.5	1.5	1.6	1.6	1.5	1.6	1.9	1.5	**1.5**

Large-scale access to pre-hospital LTOWB at least short term will result in net decrease in utilizable blood supply for **ALL**

- Product competes with already taxed O donor base.
- Splits O RBC into separate inventories not readily accessible by all patients.
- Will mean many refrigerators will contain fewer units than desired.

When LTOWB is not available, will your group accept substitutes (pRBC, A liquid plasma, CPD, etc.)?

Desired 2º Attributes
CMV seronegative
Leukoreduced
Irradiated
Antigen matched
Low plasma volume
Minimal antibody content
Unit age
Anticoagulant
Dose (aliquot)
Emergency released
Stored close to patient need

The fragility includes limited bag vendor options & bag penetration in market

- Fresenius Kabi – announced they are sunsetting their CPDA-1 bag 2026, citing the bag represents 0.1% of their entire portfolio and is not sustainable/profitable to continue.

- Terumo – currently has CPDA-1 bag. Assuming they capture the entire US CPDA-1 market, the bag still represents <<1% of their entire bag portfolio.

NON-LR 35-DAY (CPDA-1) O WHOLE BLOOD IS AND WILL CONTINUE TO BE A NICHE PRODUCT COMPETING WITH PRIMARY O LR-PRBC COMPONENT WHICH SUPPORTS **VAST MAJORITY** OF PATIENTS.

NOTE: CPD VARIANT OF WB CAN BE PICKED OUT OF REGULAR MANUFACTURING LINE AND CREATED ON DEMAND

What is currently hindering broad adoption of Whole Blood in pre-hospital setting?

Current economics unsustainable

EMS pre-hospital reimbursement
Hospital (re)usability & wastage
Blood Centers model pushes for minimal unique products

Blood Supply in existential crisis

LTOWB = Exclusive use of O donors
Declining, fragmented donor base
Products compete for same donors
WB reduces collection efficiency
O donor fatigue

Competing priorities don't always align

Ideal product variably defined
Policies optimized for single pt type across clinical domains
single BC can't make all varieties
Preference >> Science/Evidence/Practice

Resistant to Scalability

No national standards
Regional variation not accepted elsewhere
New supply chain solutions needed
Changes to products expensive

The blood supply is (and must continue to be) optimized for the needs of all patients served, including pre-hospital patients.

Thank you!

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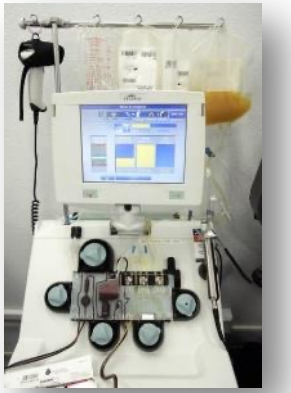
We will need to be creative to get what **all patients** need when they need it.

EXTRA SLIDES IN CASE OF QUESTIONS

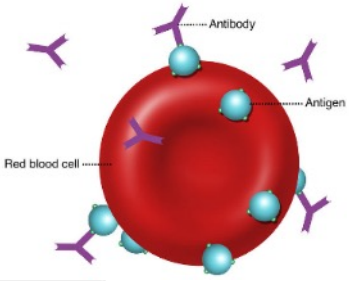
Whole Blood donation removes around 500mLs (~2 cups) containing all blood components including Red Blood Cells, Platelets, White Blood Cells and Plasma and primarily undergoes further manufacturing.

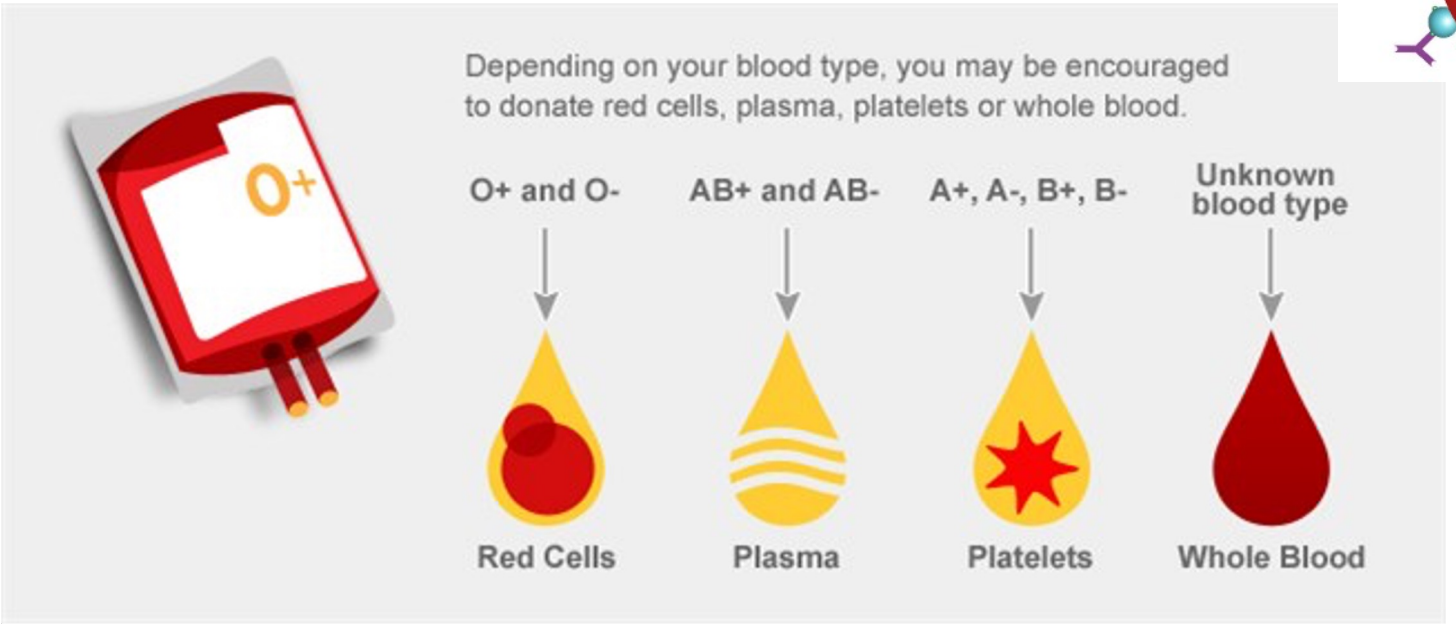
Both collections come from pre-screened, volunteer donor using a sterile set containing anticoagulant (citrate) that then must pass IDM and QC testing.

During an apheresis donation, whole blood is drawn into a sterile kit, the **desired** components are kept, while the remaining components are returned to the donor. ***Allows maximal collection of desired component***

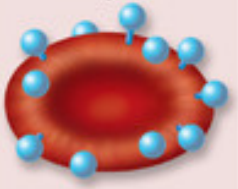
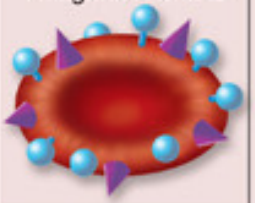


It seems simple enough…





ABO Blood Types

	Antigen A	Antigen B	Antigens A and B	Neither antigen A nor B
Erythrocytes				
Plasma	Anti-B antibodies 	Anti-A antibodies 	Neither anti-A nor anti-B antibodies	Both anti-A and anti-B antibodies 
Blood type	**Type A** Erythrocytes with type A surface antigens and plasma with anti-B antibodies	**Type B** Erythrocytes with type B surface antigens and plasma with anti-A antibodies	**Type AB** Erythrocytes with both type A and type B surface antigens, and plasma with neither anti-A nor anti-B antibodies	**Type O** Erythrocytes with neither type A nor type B surface antigens, but plasma with both anti-A and anti-B antibodies

(a)

Blood Component Compatibility Table.
Or why componentization works for most pts.

Patients with blood type	May safely receive these red blood cells	May safely receive this type of plasma	May safely receive these platelets[3,4]	May safely receive this type of cryoprecipitate
O Rh Positive (O POS)	O POS, O NEG	O, A, B, AB[5]	O, A, B, AB	Any group is safe to transfuse; however some care is taken to give ABO identical or compatible plasma type when available.
O Rh Negative (O NEG)	O NEG (sometimes O POS)[2]			
A Rh Positive (A POS)	A POS, A NEG, O POS, O NEG	A, AB[5]	A, AB, B, O	
A Rh Negative (A NEG)	A NEG, O NEG (sometimes A or O POS)[2]			
B Rh Positive (B POS)	B POS, B NEG, O POS, O NEG	B, AB[5]	B, AB, A, O	
B Rh Negative (B NEG)	B NEG, O NEG (sometimes B or O POS)[2]			
AB Rh Positive (AB POS)	AB POS, AB NEG, A POS, A NEG, B POS, B NEG, O POS, O NEG	AB	AB, B, A, O	
AB Rh Negative (AB NEG)	AB NEG, B NEG, A NEG, O NEG, (sometimes O A, B, or AB POS)[2]			
Unknown[1]	O NEG for females of reproductive potential and neonates; O POS for all others	AB (sometimes A)[5]	O, A, B, AB	

Componentization of Blood reduces adverse events & supply issues and increases component flexibility and dosing

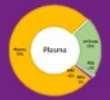
- Fractionation of blood into components
  - More of what you need, less of what you don't

- Selected Innovations
  - Blood type and beyond (Immunohematology)
  - Sterile, flexible bags
  - Optimal storage conditions for each component type
  - Anticoagulants and additive solutions
  - Apheresis collection allows donor collection optimization
  - Universal Leukoreduction

Allowed researchers to explore which combination of innovations were the best for each patient type

Whole Blood: Potential Benefits

- More concentrated than components (higher Hct)
  - ↓ risk of dilutional coagulopathy due to less anticoagulant/ additive solutions

	Product	V_{CPD} (mL)	V_{AS} (mL)	V_{CPD+AS} (mL)	V_T (mL) Product	$V_{(CPD+AS)}/V_T$
	Plasma	48	0	48	225+/-25	21%
	pRBC	8	110	118	350+/-50	34%
	aPLT	35	0	35	300+/-50	12%
	WB	70	0	70	570	12%

70 mL anticoagulant

110 mL additive

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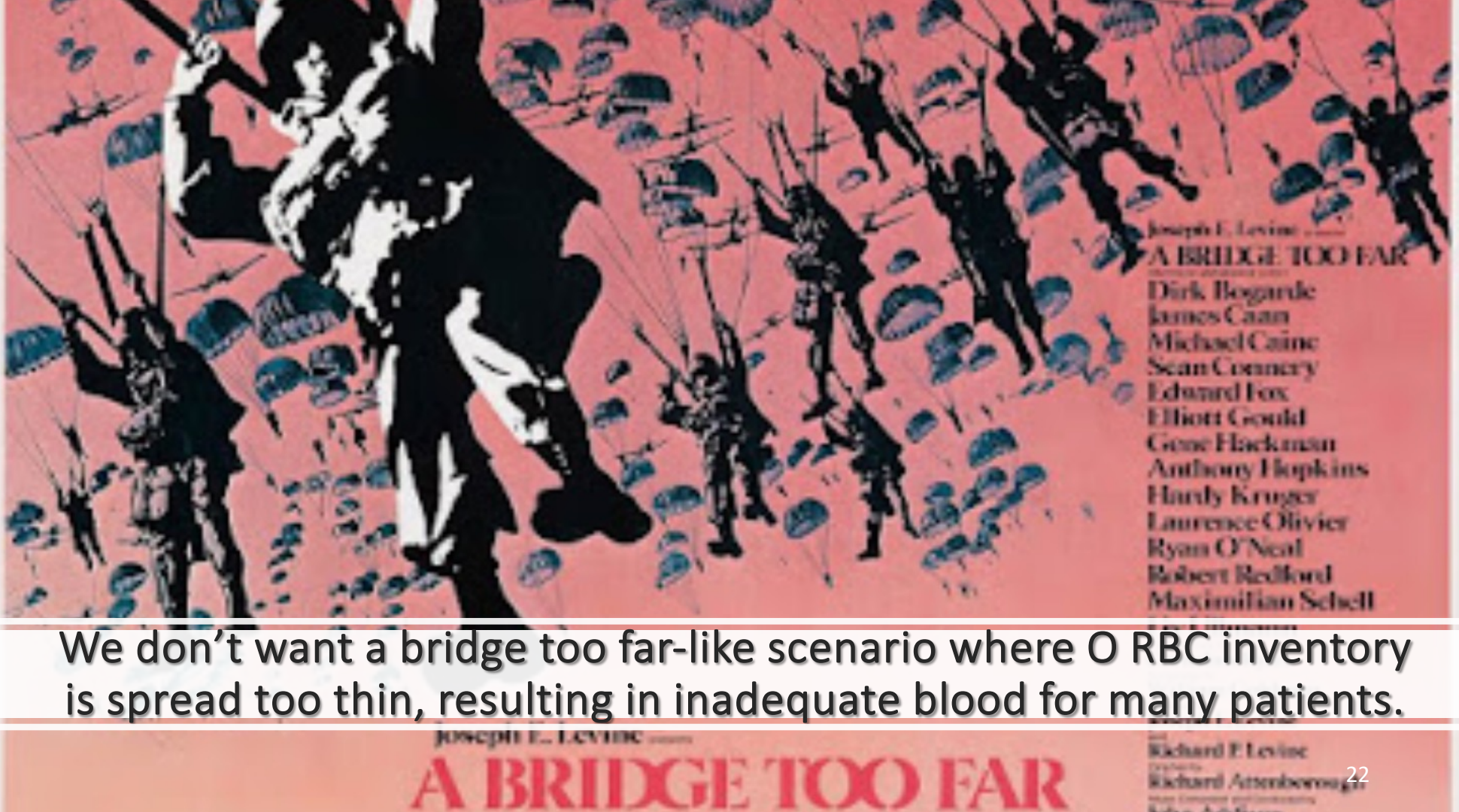
Management Issues

- Special donors
  - Group O ♂ (non-TT) / never-pregnant ♀ donors, aspirin-free, anti-A/-B titers" (IS saline A_1/B titers <100 / 128 / 200 / 256 ?) represents 10-40% of potential donors.
- Special bags
  - 35d CPDA-1 is a special bag request necessitating targeted drives & targeted donors – complex for staff and wasteful w/ high-titer donors
  - LR requires Terumo Imuflex WB kits
  - Non-LR CPD units can be picked out of usual collections as needed!
- Special handling
  - 2nd O-pos inventory substituted for O-pos RBCs → req. careful stewardship, predictable needs, proactive crossover management (MTPs in LR-, irradiation-, & Rh(D)-appropriate OB, med-surg pts.)
  - ED refrigerator management & reluctance to resume type-specific transfusion after some # of O plasmas



We don't want a bridge too far-like scenario where O RBC inventory is spread too thin, resulting in inadequate blood for many patients.