CareForum 2022

The WellSky® Conference

A National Registry of Red Blood Cell Antibodies

CareForum 2022

The WellSky® Conference

Today’s speakers

Gagan Mathur, MD, MBA, CPE
Medical Director Transfusion Medicine
Children's Hospital Los Angeles

Jay Menitove
CEO
JEM Consulting

Conflict of interest

GM Member, Alloantibody Exchange, a nonprofit organization

JM Independent contractor, CSL Plasma

Independent contractor, Accumen Clinical Optimization

Agenda

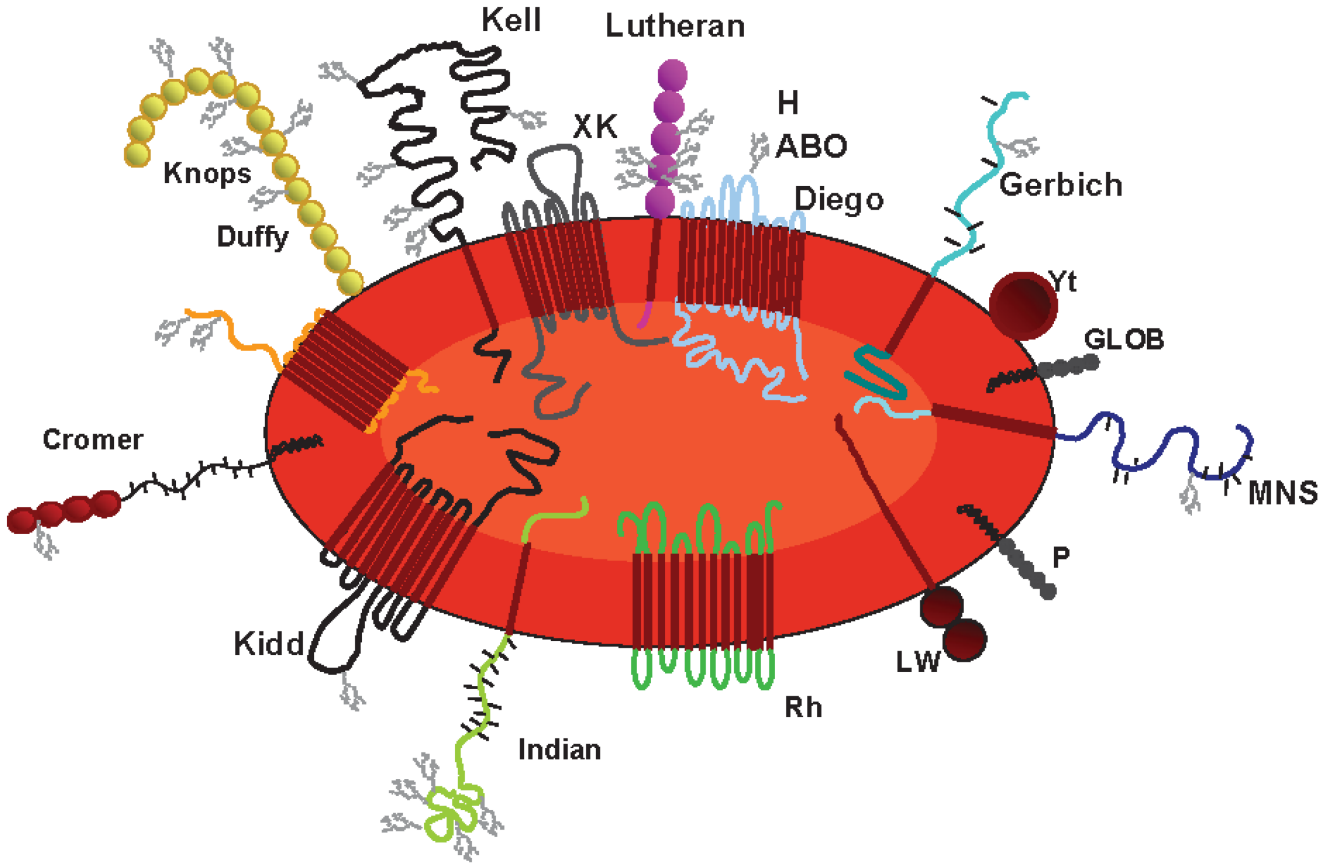
- Alloantibody evanescence
- Regional alloantibody registry (Kansas City)
- Recent regional registry experience
- Regional registries as prototype for national registry
- Proposed National Registry

Alloantibody Evanescence

What are Alloantibodies?

- Antibodies produced in response to exposure to non-self blood group antigens.

- RBC transfusions, pregnancy, transplantation, needle sharing or injections of immunogenic material.

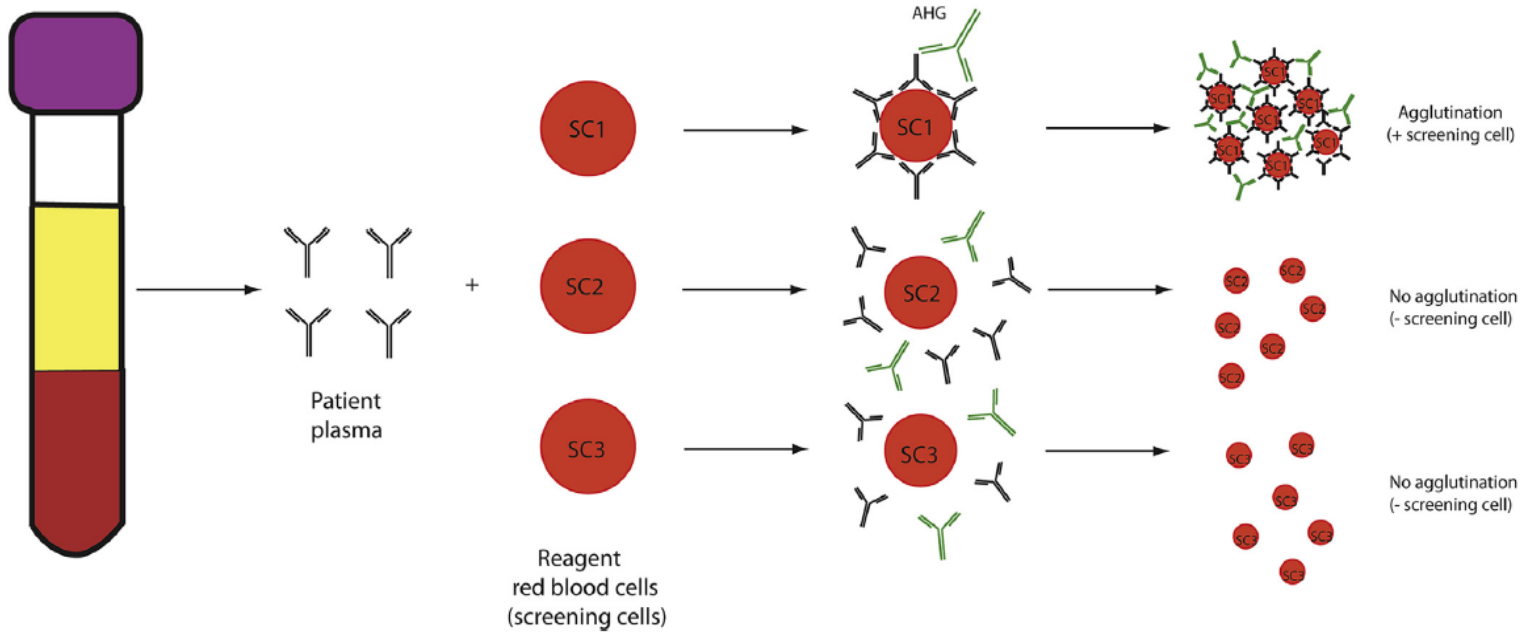


Adapted from E. Sjöberg Wester, reproduced in Blood 2019

Identification

- Antibody screens identify RBC alloantibodies.

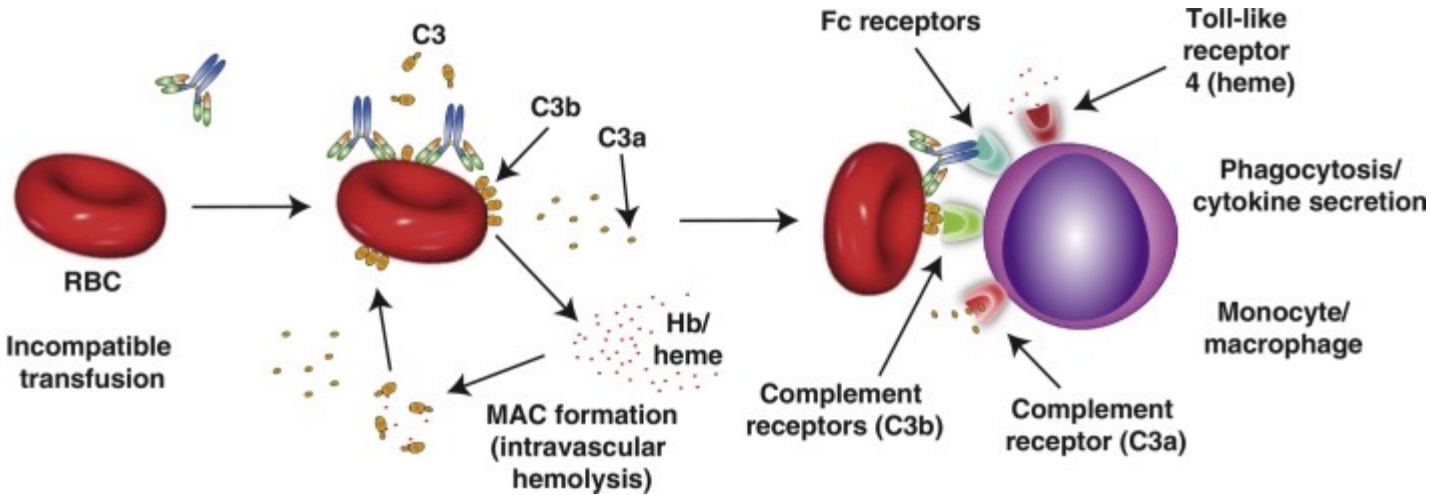
- Units lacking those antigens are selected for transfusion in addition to being ABO/Rh compatible.



Hendrickson and Tormey, Hem Onc Clinics, 2016

Clinical Significance

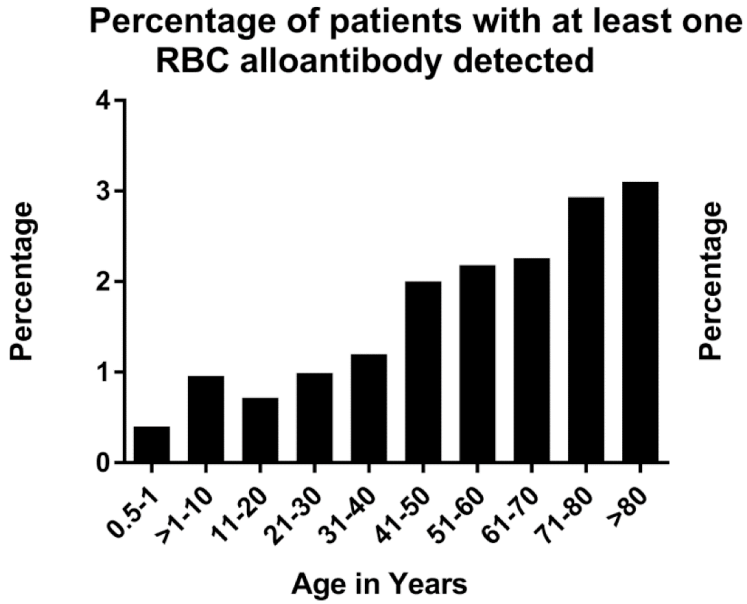
- Increases the risk of immediate as well as delayed hemolytic transfusion reactions.
- Increases the risk of hemolytic disease of the newborn.
- Extra time and cost for workup and finding compatible units.

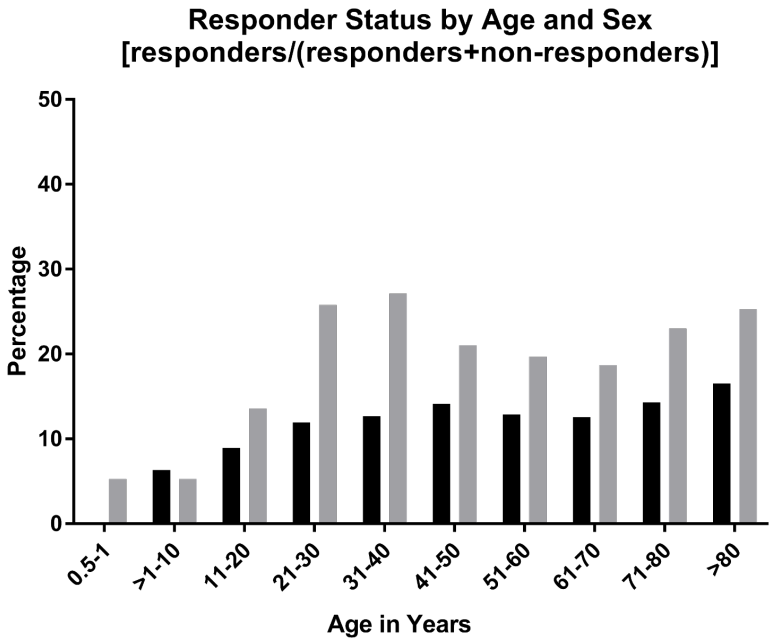


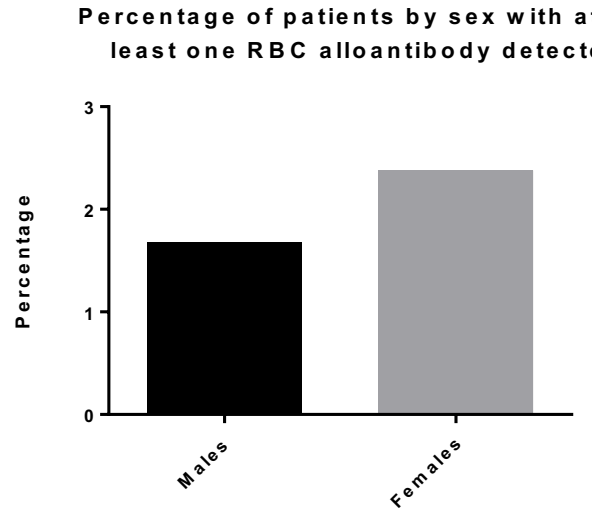
Arthur, Connie M., et al. "Examining the role of complement in predicting, preventing, and treating hemolytic transfusion reactions." Transfusion medicine reviews 33.4 (2019): 217-224.

Prevalence

- Prevalence is approximately 3-5% of “general” transfused adults.
- Prevalence varies by age, sex, underlying disease.





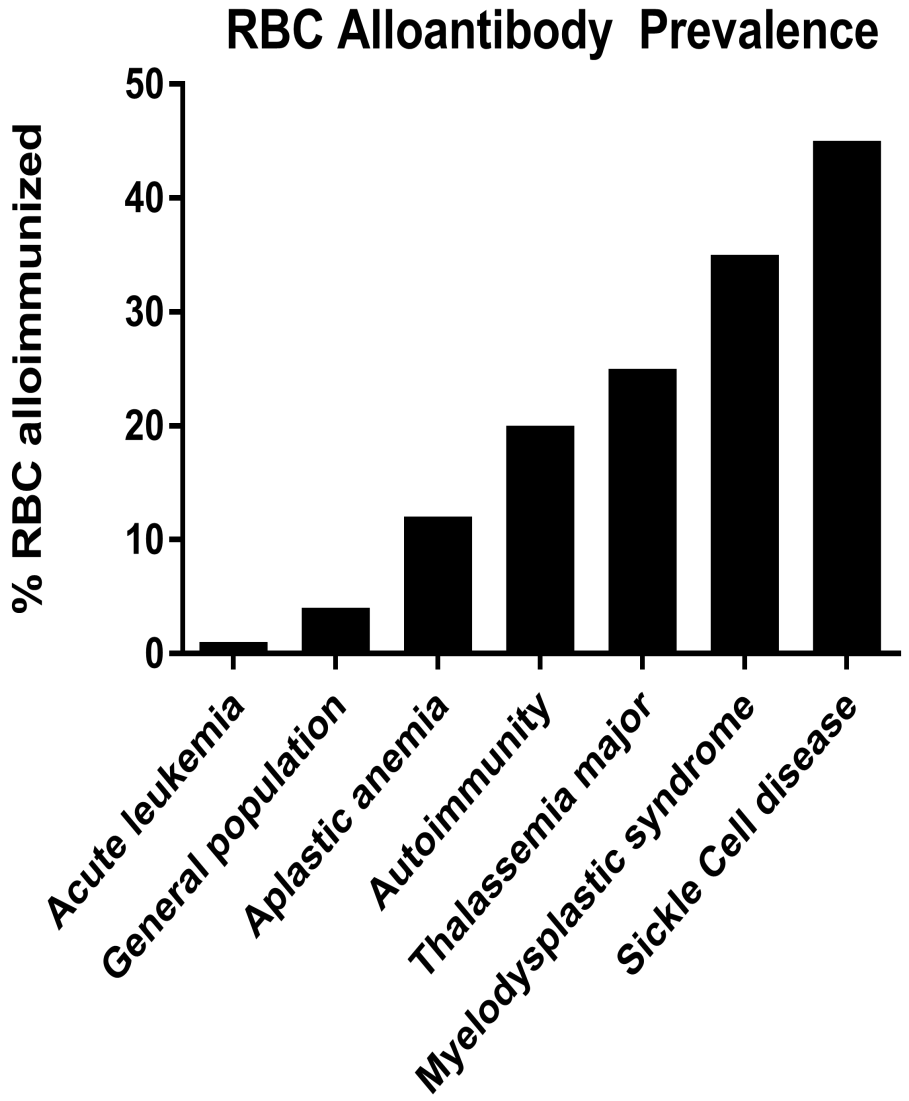


REDS-III Recipient Database, 6,597 alloimmunized patients

Karafin et al, BJH 2018

Prevalence

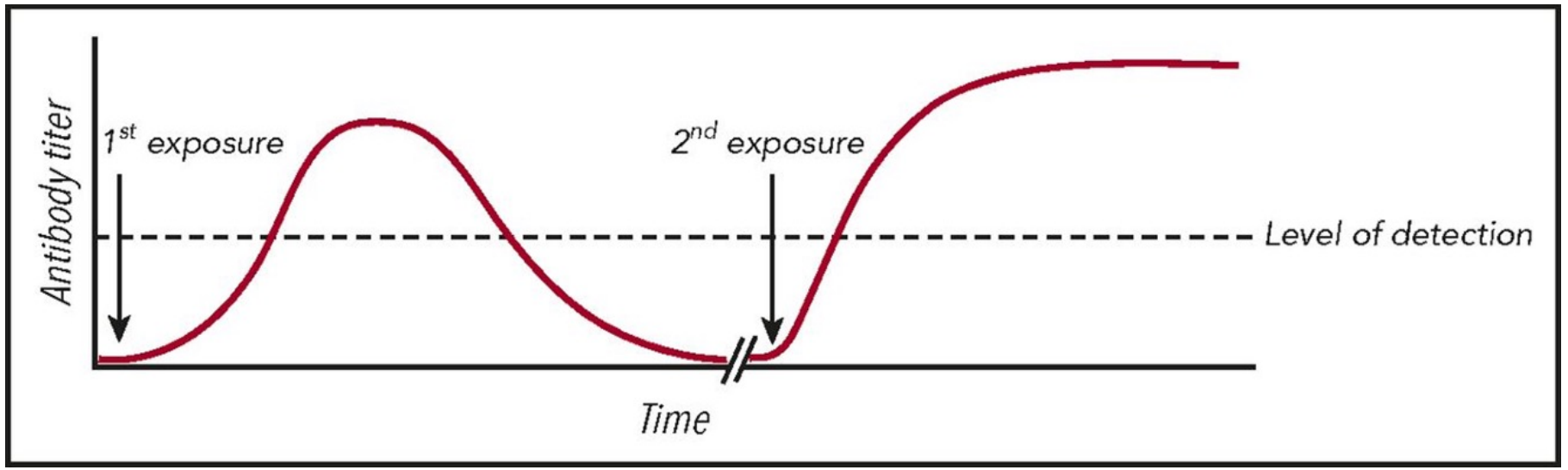
- Chronically transfused patients are at higher risk of red cell alloimmunization.
- And complications associated with alloimmunization.



Hendrickson and Tormey, ASH Education Book 2016 and Blood 2019

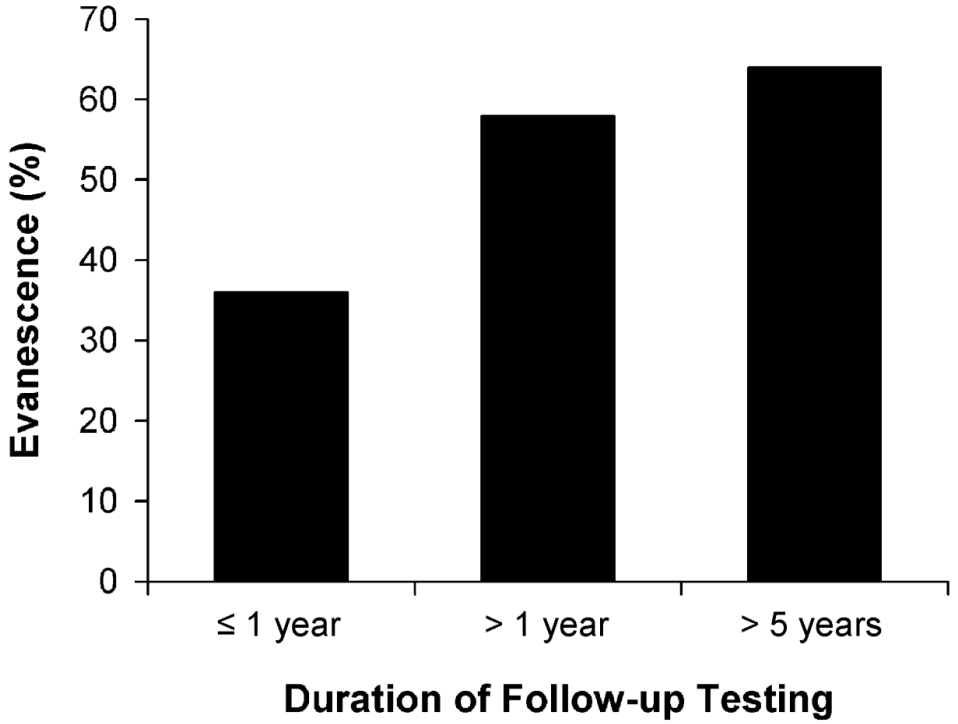
Alloantibody Evanescence

- A decrease in antibody titers to below the limits of detection.
- >60-80% of RBC antibodies show evanescence at some point.

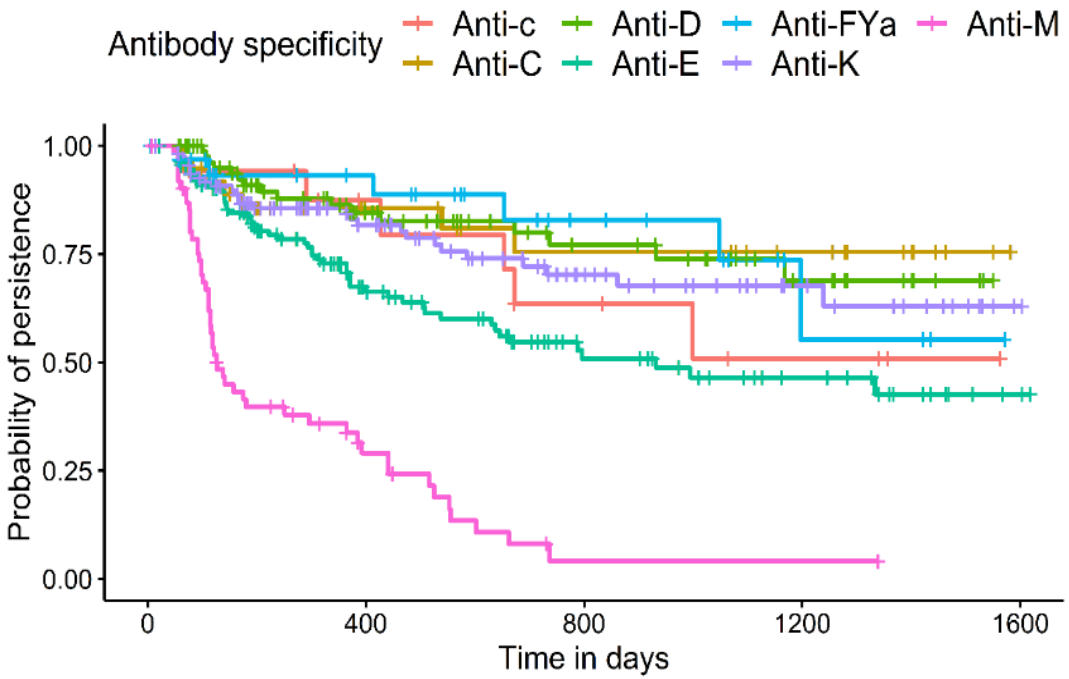


Tormey et al, Blood 2019

Antibody Evanescence Rates



Evanescence Rates Increase Over Time

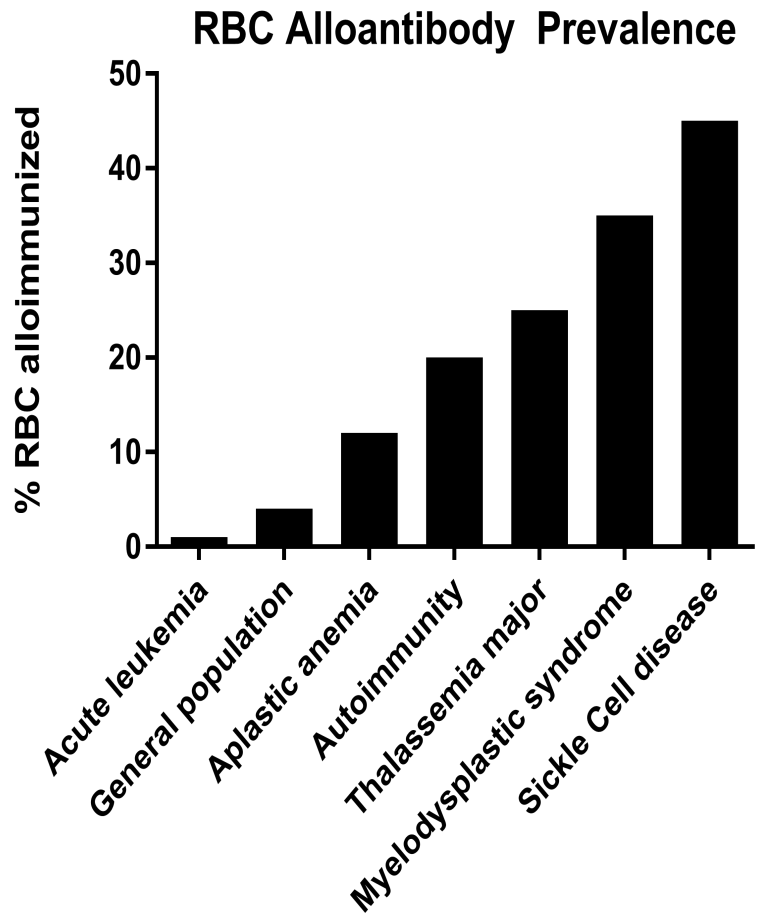


Rates also vary based on antibody specificity

Tormey CA, Stack G. Transfusion 2009;49:505-12.
Williams LA, et al. South Med J 2016;109:588-91.
Hauser RG, et al. Transfusion 2020;60:831-9.

Alloantibody Evanescence

- Prevalence of RBC alloimmunization is significantly underestimated.
- Leads to significant morbidity and mortality.
- Specially in chronically transfused patients.

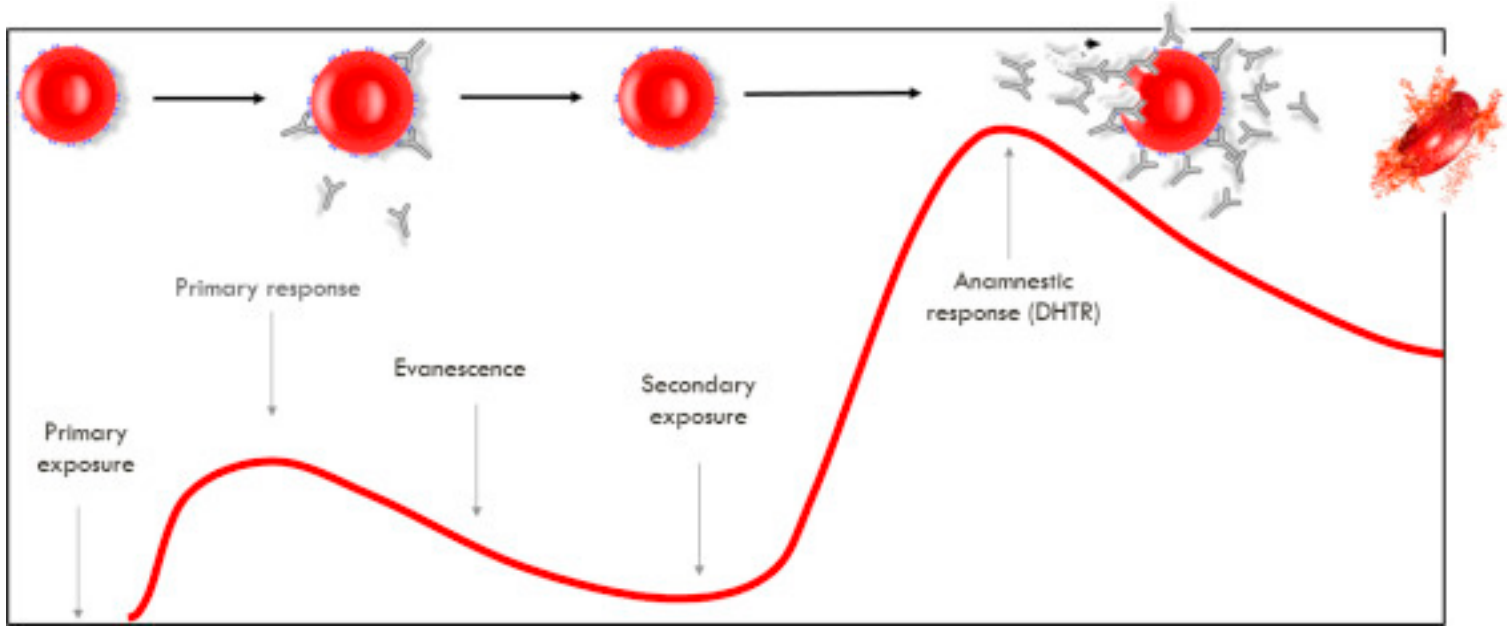


Hendrickson and Tormey, ASH Education Book 2016 and Blood 2019

Hemolysis in Chronically Transfused

- Increases the risk of immediate as well as delayed hemolytic transfusion reactions

- Contributing factors
  - Higher prevalence
  - Evanescence
  - Care fragmentation

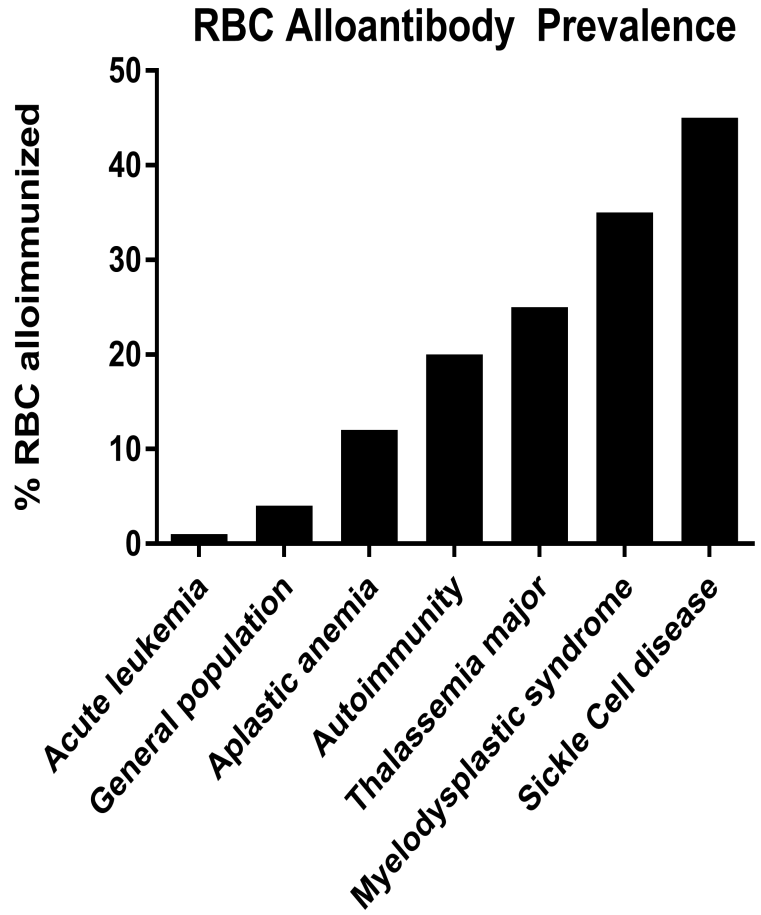


Fasano, R. M., et al. "Clinical presentation of delayed hemolytic transfusion reactions and hyperhemolysis in sickle cell disease." *Transfusion Clinique et Biologique* 26.2 (2019): 94-98.

Care Fragmentation

- Dispersion of an individual's health care across systems and providers.
- Lack of collaboration & standardization.
- A major contributor to low-quality care, negative health outcomes.

- Chronically transfused patients receiving fragmented care are at risk of significant morbidity and mortality due to hemolysis if historical alloantibodies are not honored.



Hendrickson and Tormey, ASH Education Book 2016 and Blood 2019

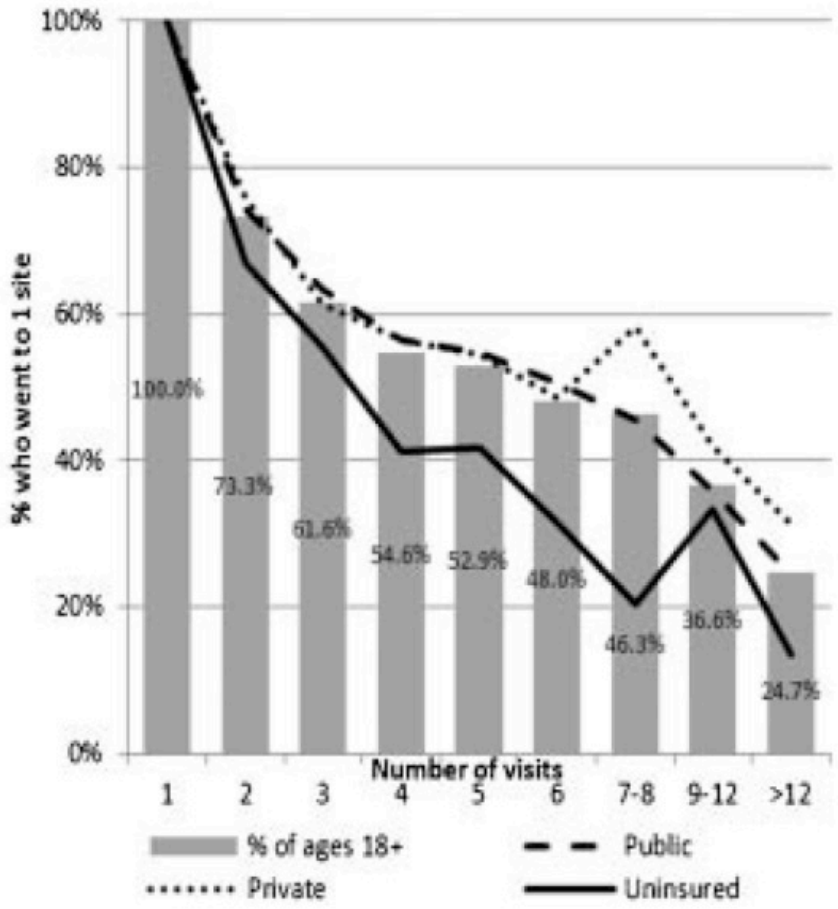
How Prevalent is Care Fragmentation?

Pediatr Blood Cancer 2012;59:685–689

Concentration of Hospital Care for Acute Sickle Cell Disease-Related Visits

JA Panepinto, MD, MSPH,[1,2,4]* PL Owens, PhD,[5,6] AL Mosso, MS,[7] CA Steiner, MD, MPH,[5] and DC Brousseau, MD, MS[1,3,4]

In a 2-year period, most adults with SCD were cared for at more than 1 hospital.



How Prevalent is Care Fragmentation?

901.HEALTH SERVICES RESEARCH-NON-MALIGNANT CONDITIONS | NOVEMBER 13, 2019

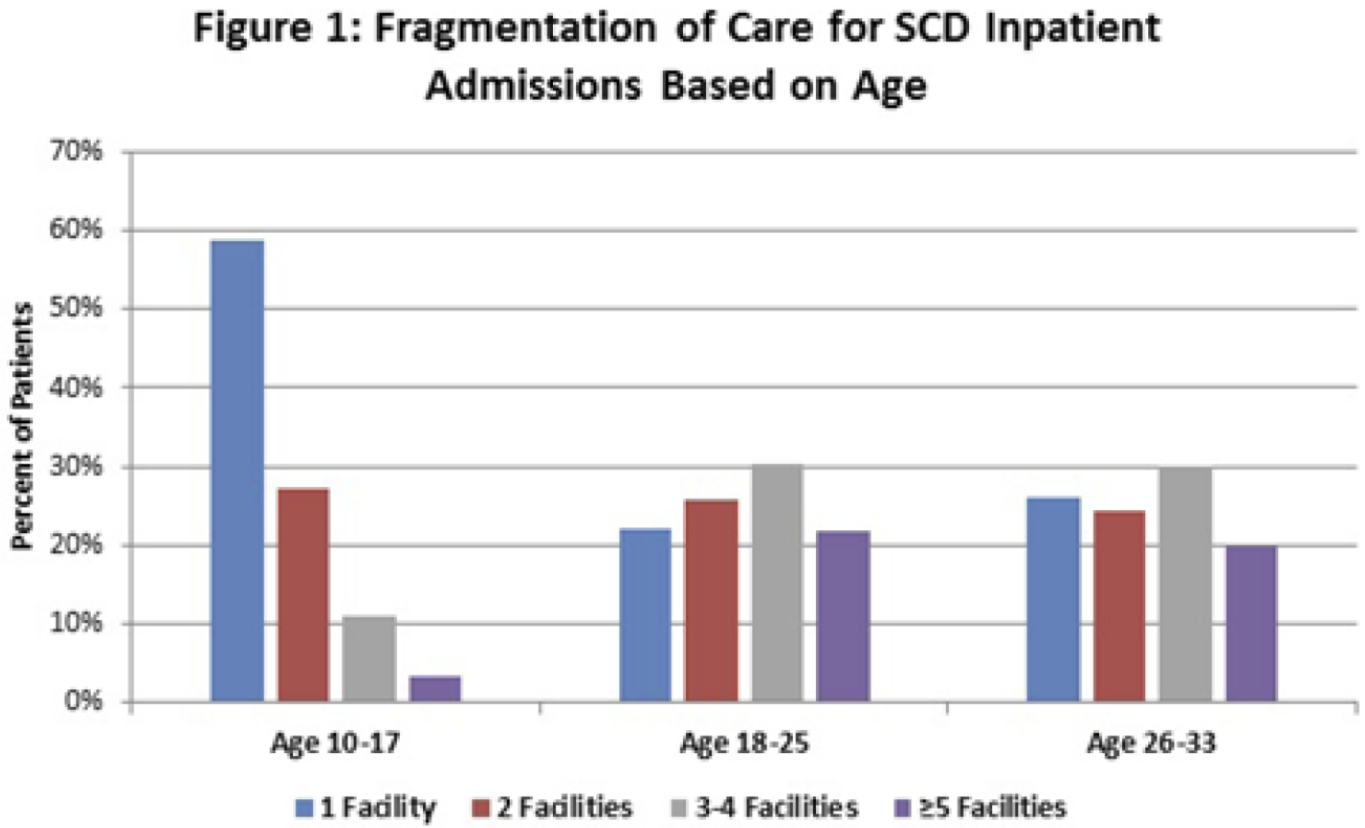
Fragmentation of Care for Young Adults with Sickle Cell Disease in California

Ashley Shatola, Ann M Brunson, MS, Theresa H.M. Keegan, PhD MS, Ted Wun, MD, Anjlee Mahajan, MD

Blood (2019) 134 (Supplement_1): 4667.

https://doi.org/10.1182/blood-2019-121901

78% of young adults with SCD in CA were cared for at more than 1 facility.



73% of adults with SCD in CT were cared for at more than 1 facility (Guarente et al, 2022 AABB abstract submission), most were alloimmunized, and most had evanescent antibodies.

Fragmentation + Evanescence = Danger!!!

- Chronically transfused alloimmunized patients may visit multiple hospitals.
- Between hospitals antibody **record discrepancies found in two-thirds of patients.**

TABLE 2. Number of clinically significant RBC alloantibodies found in 724,584 patients

Number of RBC alloantibodies per patient record	Patients with one hospital record (n = 645,701)	Patients with more than one hospital record (n = 78,883)	p value
1	20,426	4230	<0.005
2	4,104	1033	<0.005
3	847	263	<0.005
4	200	63	<0.005
5	34	18	0.003
6	9	4	<0.005
7	3	0	1.64
Total number of patients	25,623	5611	<0.005

TABLE 1. Discrepancies in alloantibody data between Hospitals A and B

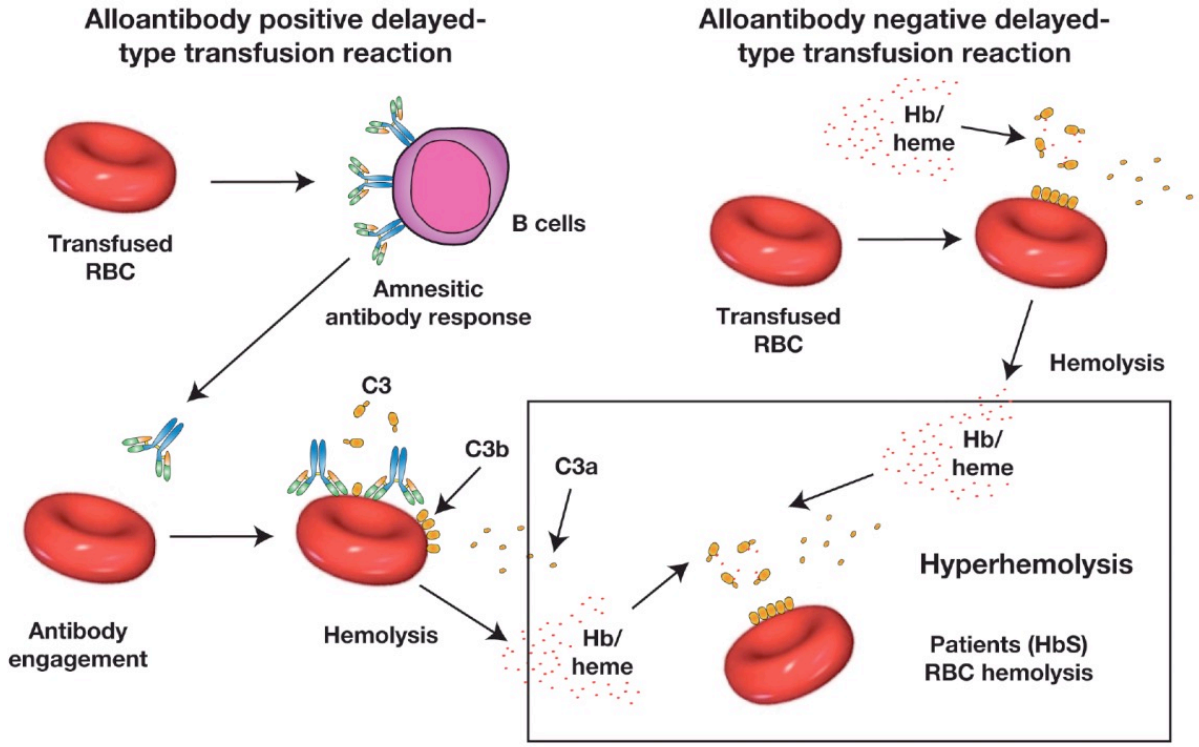
Patient	Antibodies identified at Hospital A	Antibodies identified at Hospital B	Timing of Hospital A testing relative to Hospital B testing
1	E	None	Before
2	E	None	Before
3	E	None	Before
4	E	None	Before
5	E	None	Before
6	K	None	Before
7	K	None	Before
8	K	None	Before
9	S	None	Before
10	Le^a	None	Before
11	HTLA	None	Before
12	Yt^b	Yt^a	Before
13	S, P_1, Kn^a	S, K	Before
14	Jk^a, D, E, C, S	Jk^a, D, E, C	Before
15	E	None	After
16	E	None	After
17	E	None	After
18	E	None	After
19	K	None	After
20	HTLA	None	After
21	Js^a	None	After
22	E, c	None	After
23	Jk^a, Bg^a	None	After
24	K	K, E, c	After
25	E	None	Not known
26	E	None	Not known
27	M	None	Not known

Unni N, et al. Transfusion 2014;54:98-103.
Delaney M, et al. Transfusion 2013;53:771-6.
Harm SK, et al. Am J Clin Pathol 2014;141:256-61.

Dangers of Hemolytic Reactions

- Hemolysis may occur in any previously transfused or pregnant patients exposed to non-self antigens they have been immunized against

- Bystander hemolysis or hyperhemolysis is a cause of morbidity and mortality in patients with sickle cell disease
  - Poorly understood
  - The incidence of DHTRs with bystander hemolysis may be as high as 4.2%
  - Mortality can be as high as 11%



Hemolytic transfusion reactions in sickle cell disease: underappreciated and potentially fatal

Narbet et al, AJH 2017

How Can We Prevent Hemolysis?

1. **Reduce risk of RBC alloimmunization**
   - Prophylactic matching (for Rh (C/c, E/e, K) in patients with SCD and thalassemia.
   - Judicious use of RBC transfusions.
   - Ideally be able to identify Antibody “Responders” from “Non-responders”.
2. **Reduce the risk of missing the detection of a “transient” alloantibody**
   - Follow-up antibody screens at set intervals (4-12 weeks) after every episodic transfusion in patients at highest risk for RBC alloantibody development.
   - Avoid multi-site transfusion.
   - Thorough transfusion history.
   - Reliable inter-institutional blood bank communication.
3. **Reduce the risk of re-exposure to an “evanesced” alloantibody**
   - Avoid multi-site transfusion.
   - Thorough transfusion history.
   - Reliable inter-institutional blood bank communication.

How do we do it?

- Telephone communication for the exchange of alloantibody histories is outdated and inefficient in the information age!

- Patients receiving fragmented care are at risk of significant morbidity and mortality due to hemolysis if historical alloantibodies are not honored.

What should be done?

High Percentage of Evanescent Red Cell Antibodies in Patients with Sickle Cell Disease Highlights Need for a National Antibody Database

Lance A. Williams, III, MD, Robin G. Lorenz, MD, PhD, Absar Tahir, MS, Huy P. Pham, MD, MPH, and Marisa B. Marques, MD

81% of patients had an antibody screen with at least one antibody previously detected antibody now undetected.

Table. Antibody specificity and percent evanescence of alloantibodies identified in at least 10% of study patients

	Rh system					Kell		Duffy		Kidd	MNS	Other
Antibody specificity	**D**	**C**	**E**	**V**	**Go^a**	**K**	**Js^a**	**Fy^a**	**Fy^b**	**Jk^b**	**S**	**AUS**
No. patients	9	30	40	14	7	20	15	18	9	12	17	7
Total antibodies, %	4	14	18	6	3	9	7	8	4	5	8	3
Times not reacting	5	16	21	8	3	12	12	10	7	8	12	3
Evanescent, %	56	53	53	57	43	60	80	56	78	67	71	43

AUS, antibody of unknown specificity. Fy^a = Duffy a; Fy^b = Duffy b; Jk^b = Kidd b.

Williams 3rd, Lance A., et al. "High percentage of evanescent red cell antibodies in patients with sickle cell disease highlights need for a National Antibody Database." South Med J 109.9 (2016): 588-591.

Regional Alloantibody Registry

Community Blood Center (Kansas City) Regional Registry

IMMUNOHEMATOLOGY

Regional registry of patient alloantibodies: first-year experience

Vicki Schwickerath, Mary Kowalski, and Jay E. Menitove

BACKGROUND: Delayed hemolytic transfusion reactions (DHTRs) occur when pretransfusion alloantibody screening tests fail to detect previously formed alloantibodies. Hospital transfusion service records maintain historical alloantibody results. However, patients may receive transfusions at more than one hospital leading to dissociation of current and previous results. As such,

Delayed hemolytic transfusion reactions (DHTRs), caused by alloantibodies formed in response to previous transfusions or pregnancies that are not detected in pretransfusion alloantibody screening, reportedly occur after 1 per 2500 to 13,700 red blood cell (RBC) transfusions. Most are mild and are not life-threatening.[1-3] Approximately one-

TRANSFUSION 2010;50:1465-1470.

Established 2007

"Go live" June 2, 2008

Fulfillment of 1980's concept: Dial an Antibody

goal: reduce incidence delayed hemolytic transfusion reactions

not feasible prior to internet

Based on regional blood center concept

single blood supplier in a geographic region

4% of insured KC patients < 65 y.o. received transfusions >one hospital

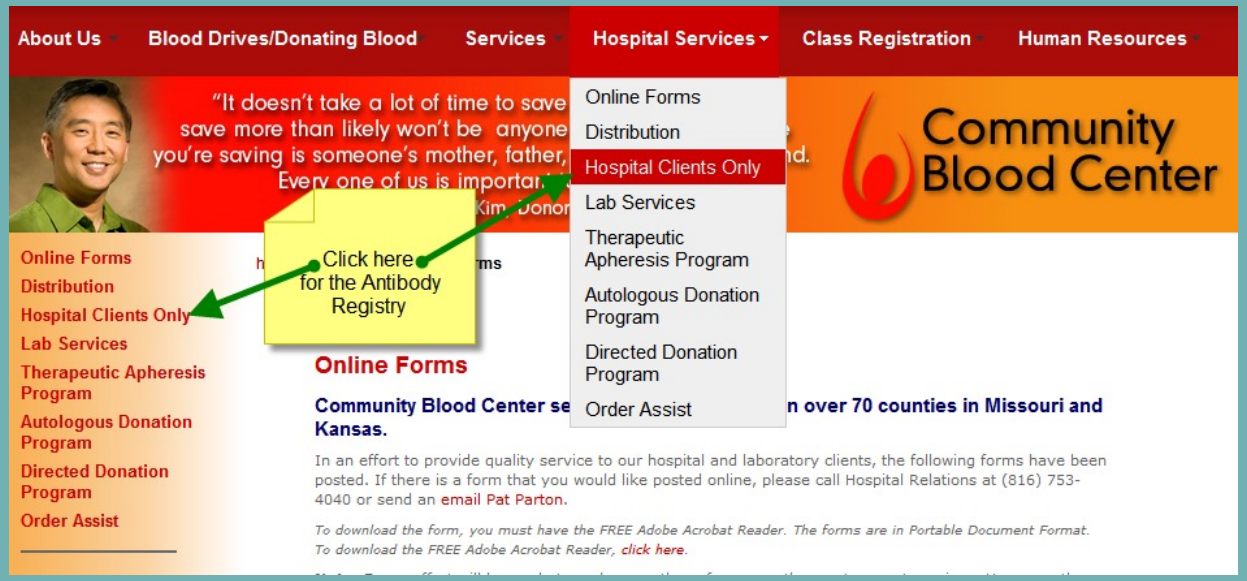
> 65 y.o HRS/CMS study: 14.5% transfused at multiple hospitals

KC Registry

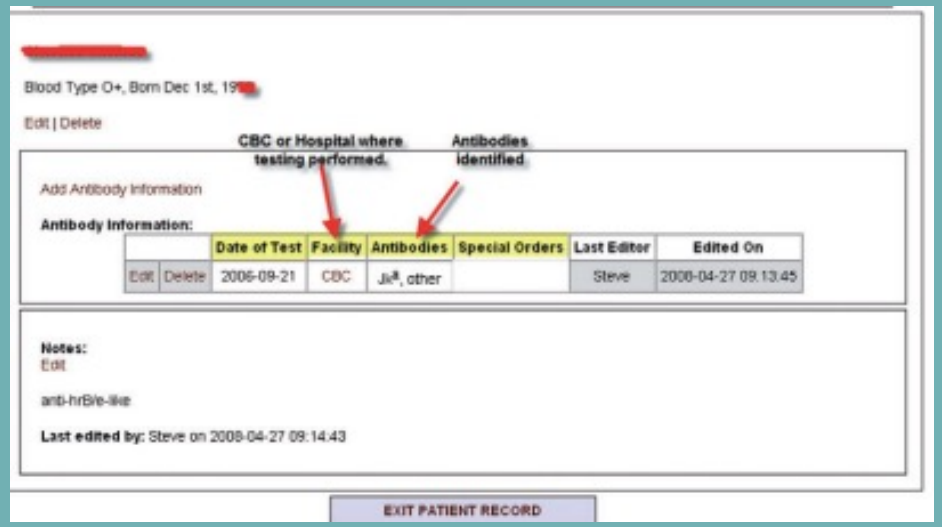
Secure website based

Patients with allo-antibodies identified at IRL entered into data base

Business associate agreements (HIPPA)

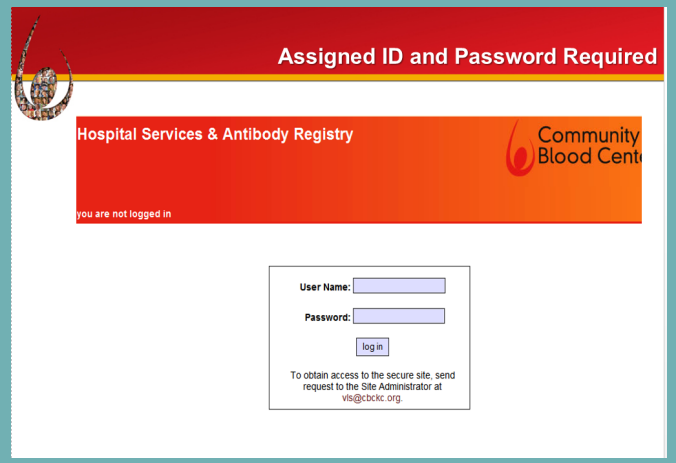


–KC Registry



Data base

- Patient name
- Birth date
- ABO/Rh type
- Antibodies identified
- Comments
- Special Transfusion needs



Hospitals

- unique id and complex password
- access levels assigned
  - registry administrator
  - IRL users
  - hospital administrators
  - hospital users

TABLE 2. User access levels

Access level	Registry administrator	IRL user	Hospital administrator	Hospital user
View patient	Y	Y	Y	Y
Add patient (includes birth date, blood type)	Y	Y	Y	N
Add antibodies and special orders	Y	Y	Y	N
Add notes	Y	Y	Y	N
Edit patients, antibodies, notes	Y	Y	N	N
Delete patients, antibodies, notes	Y	Y	N	N
Add/edit/delete users, facilities	Y	N	N	N

KC Registry

Start-up costs

HIPAA/regulatory	• Business associate agreements • Security regulations 164.308, 164.310 and 164.312 • Assigned user ID and complex password • Daily and weekly usage monitoring	$3,000 (legal fees)
Web design	• Internet accessibility 24/7 • Four access tiers	$11,000 (Web development)
Registry development	• IRL data entered (samples sent to IRL during previous 5 years) • Patient name • Birth date • ABO/Rh type • Antibodies (entered in duplicate) • Special transfusion requirements • Notes	$8,000 (CBC staff time)

KC Registry

During the first year, Registry identified four cases among 1766 patients (0.028% of transfused patients).

Prevention of Delayed Transfusion Reactions Reported by Hospitals

History of Anti-K, C and V
- Current Antibody Screen is Neg

History of Anti-K
- Current Antibody Screen is Neg

History of Anti-K, E and c
- Only Anti-K reacting

History of Anti-E and Fyb
- Only Anti-E reacting

Improved Efficiencies Reported by Hospitals

History of Anti-E and c
- Did not require additional sample to ID Anti-c

History of Anti-E
- Workup went smoother

History of Anti-E and c
- Decreased TAT

History of Anti-E (current sample DAT +)
- Able to obtain transfusion history from previous hospital

Patient Record in the AR but not Accessed by Hospital [Reported by IRL]

History of Anti-Lu^{b} and S
- Current ABSC Neg; two units transfused; TRX RX

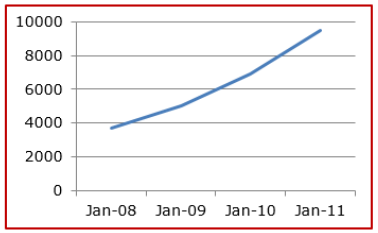
History of Anti-Tc^{a}
- Antibody not Identified; transfused; TRX RX

History of Anti-C, E, Le^{a} and warm auto
- Current ABSC Neg; transfused; TRX RX

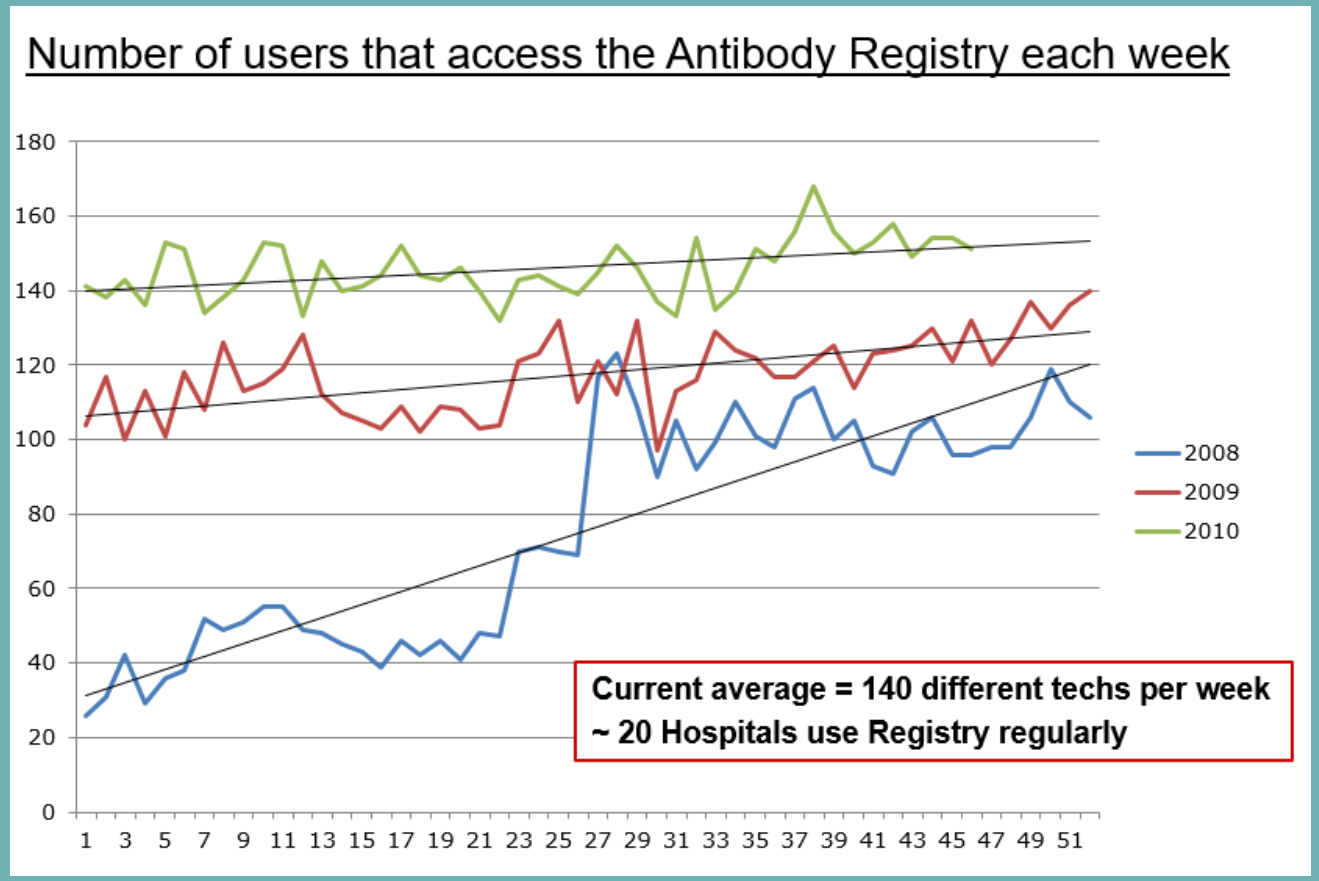
History of Anti-D, E, C^{w}, Fy^{a} and S
- Currently only Anti-D and E reacting

KC Registry

- 3,726 patients entered in the Registry at Go Live on June 2, 2008
- Data entry continues with all current IRL patient results added daily:
  - June 2009: 5,000 patients
  - June 2010: 6,900 patients
  - June 2011: 9,500 patients



- Blood donor antibodies entered January 2009
- 16 hospitals are entering their own patient antibodies



Recent Experience

Recent regional registry experience

Received: 20 September 2021 | Revised: 8 December 2021 | Accepted: 22 December 2021

DOI: 10.1111/vox.13250

SHORT REPORT

Vox Sanguinis ISBT International Society of Blood Transfusion

A case for a national registry of red blood cell antibodies

Gagan Mathur[1,2,3] | Matthew B. Wilkinson[1] | Eddie R. Island[1] | Jay E. Menitove[4] | Lowell Tilzer[1]

Case

- We describe a case where the patient was found to be at high risk of bleeding during liver transplantation.
- Antibody screen on admission was negative but a history of anti-Jka was identified on reviewing patient's history in local registry of RBC antibodies.
- The surgery was pushed back to arrange for antigen negative units.
- The patient received a total of 16 Jk(a-) RBC units during the admission.

Highlights

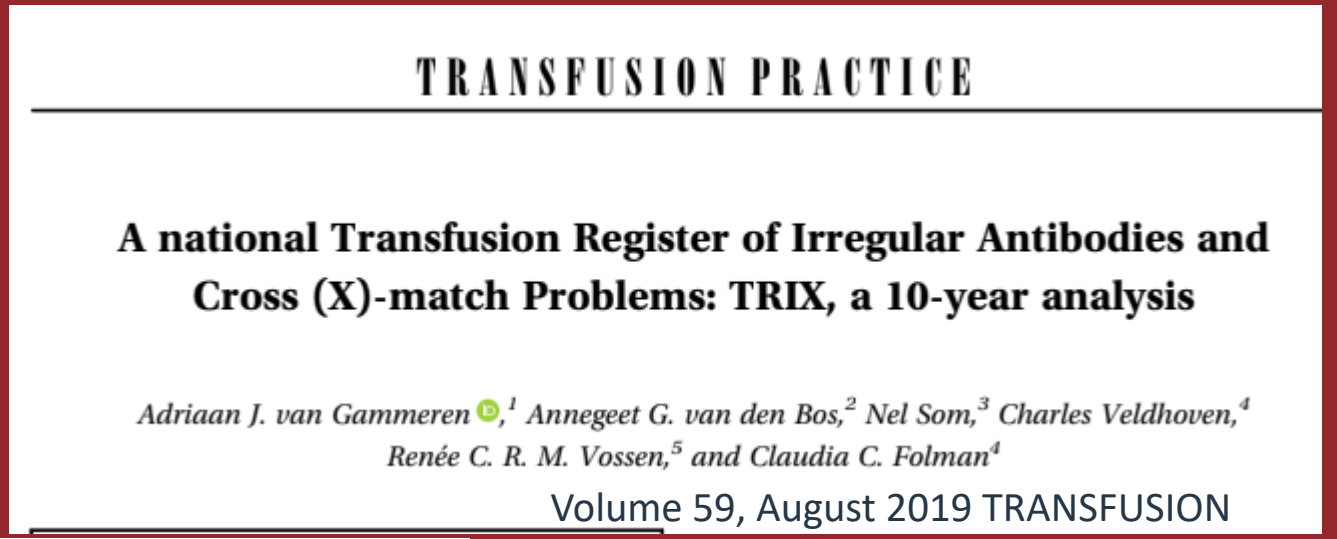
- Most hospitals do not have access to a shared registry of RBC antibodies previously detected at other hospitals.

- In a patient with negative antibody screen but history of RBC antibodies, transfusion of antigen-positive RBC unit can potentially lead to acute and/or delayed hemolytic transfusion reaction which can cause significant morbidity and perhaps mortality.

- A national registry of RBC antibodies can help improve patient safety and outcomes.

Regional Registries as Prototypes

Prototypes



TRANSFUSION PRACTICE

A national Transfusion Register of Irregular Antibodies and Cross (X)-match Problems: TRIX, a 10-year analysis

Adriaan J. van Gammeren,[1] Annegeet G. van den Bos,[2] Nel Som,[3] Charles Veldhoven,[4] Renée C. R. M. Vossen,[5] and Claudia C. Folman[4]

Volume 59, August 2019 TRANSFUSION

EDITORIAL

TRIX with treats: the considerable safety benefits of a transfusion medicine registry

Hauser, Hendrickson, Tormey Volume 59, August 2019 TRANSFUSION

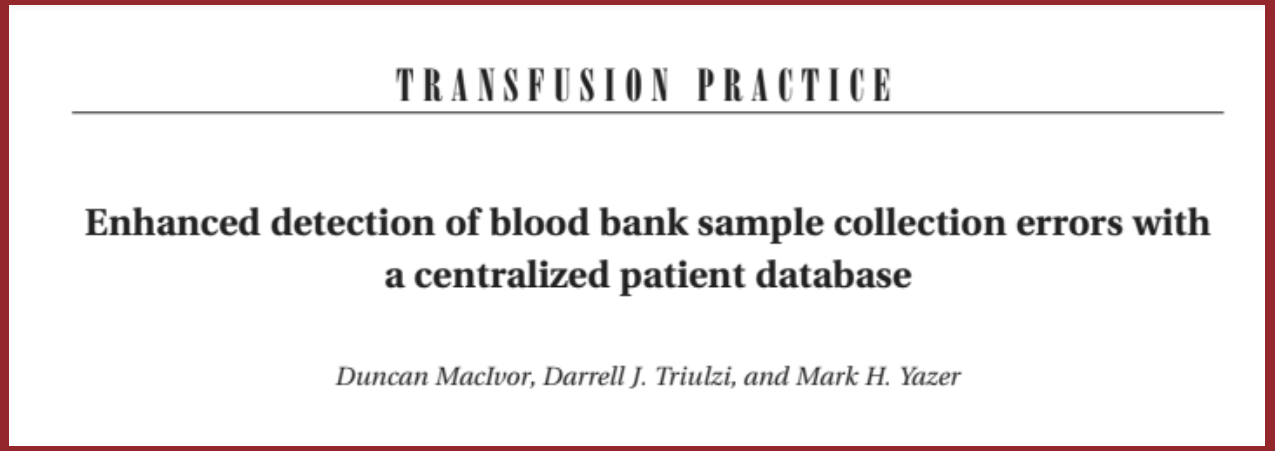
80,000 antibodies

62,000 individuals

Post-2011, DHTR decreased ~50

- Prevention matching
- Restrictive practices
- TRIX Registry

Prototypes



TRANSFUSION PRACTICE

Enhanced detection of blood bank sample collection errors with a centralized patient database

Duncan MacIvor, Darrell J. Triulzi, and Mark H. Yazer

TRANSFUSION 2009;49:40-43.

16 hospitals served by CTS

ABO errors reduced (misidentification)

The immunohematologic and patient safety benefits of a centralized transfusion database

Meghan Delaney, Steve Dinwiddie, Theresa N. Nester, and James A. AuBuchon

Volume 53, April 2013 TRANSFUSION

10.9% of patients receive transfusions at more than one hospital

Patients with allo-antibodies in hospitals

7.11%-- more than one hospital

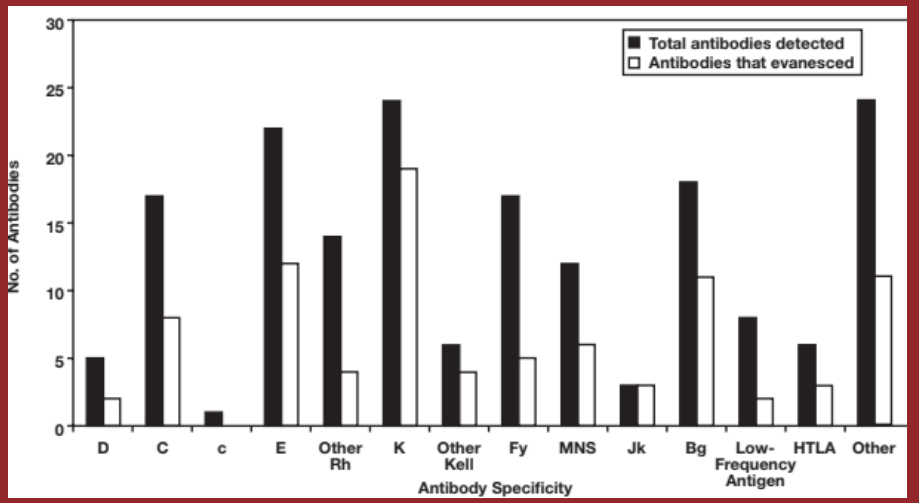
3.07%--one hospital

Prototypes

A Centralized Recipient Database Enhances the Serologic Safety of RBC Transfusions for Patients With Sickle Cell Disease

Sarah K. Harm, MD,[1,2] Mark H. Yazer, MD,[1,2] Grace F. Monis, MD,[3] Darrell J. Triulzi, MD,[1,2] James P. AuBuchon, MD,[3,4] and Meghan Delaney, DO[3,4]

Am J Clin Pathol 2014;141:256-261

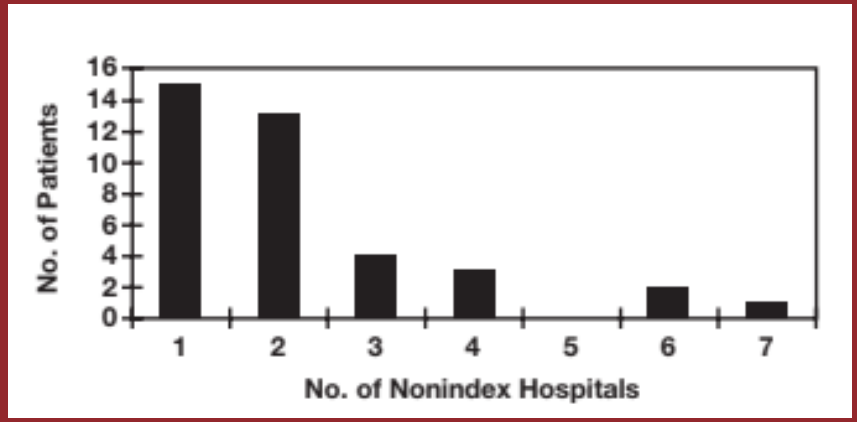


Pittsburgh and Seattle

Patients with Sickle Cell Disease

Receive transfusions at 1-8 hospitals

(Median=2)



Prototypes

Patients with allo-antibodies receive care at multiple hospitals

Common record source (antibody registry) decreases ABO misidentification and DHTR

Regional blood center paradigm evolving

- Hospitals have multiple blood suppliers
- Regional registries (single blood supplier) serve as prototypes for **NATIONAL REGISTRY** (multiple blood suppliers)

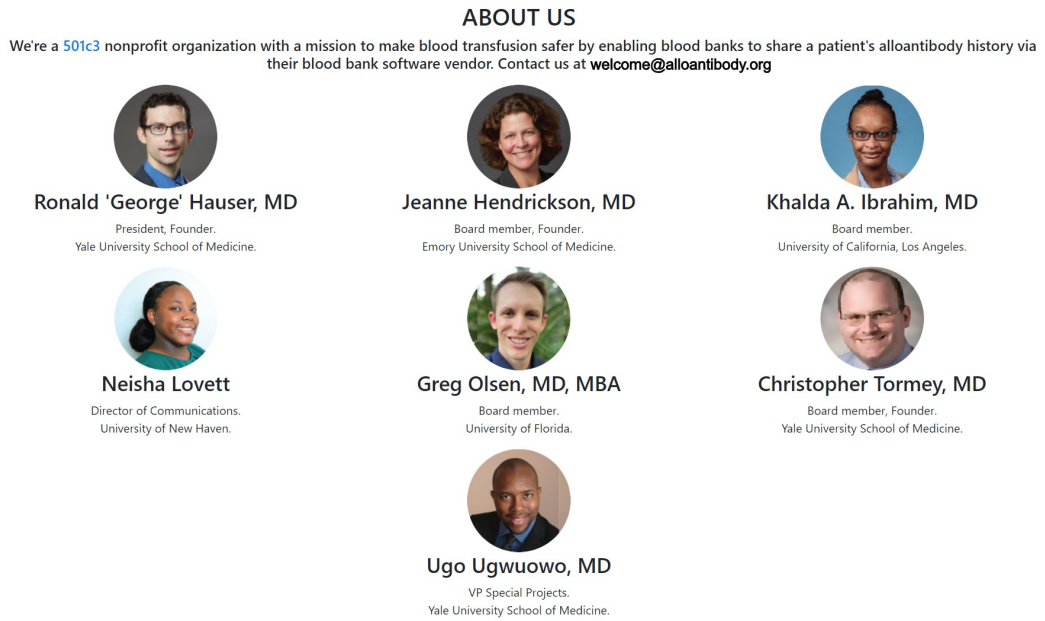
National Registry Proposal

US-wide Red Blood Cell antibody exchange

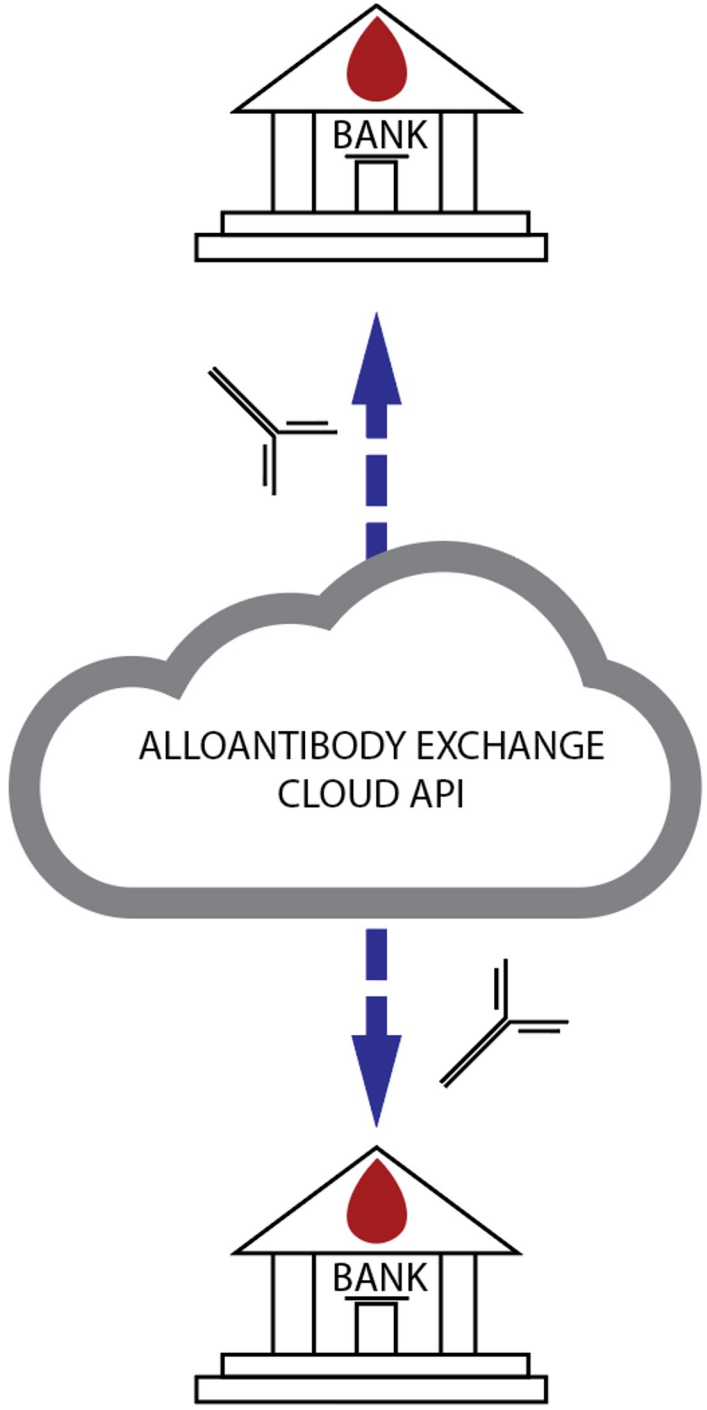
- Improve patient safety by decreasing delayed hemolytic transfusion reactions and…
- Save valuable time

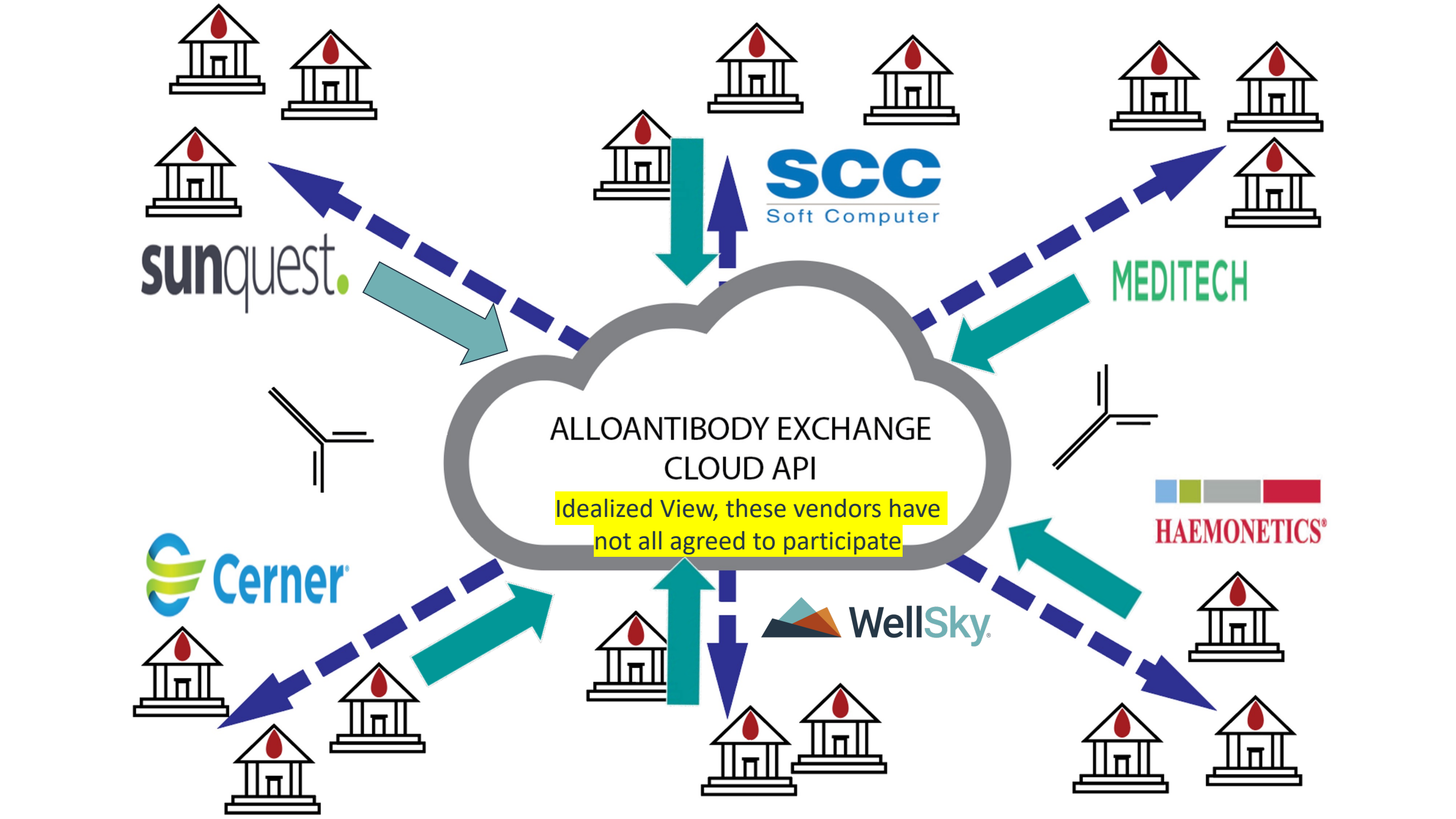
“Red Blood Cell Alloantibody Exchange”

- A project to exchange alloantibody histories between blood bank software vendors in the US.



www.alloantibody.org




SCC
Soft Computer
sunquest.
MEDITECH
ALLOANTIBODY EXCHANGE
CLOUD API
Idealized View, these vendors have
not all agreed to participate
Cerner
HAEMONETICS®
WellSky

Current Thinking/Practical Considerations

- Antibody exchange would be checked directly from the blood bank technologist's workstation, using the blood bank vendor's software
  - Blood bank technologist would decide whether to incorporate an antibody identified by an outside hospital (would be distinguished as an "exchange" antibody)
  - Patient matching algorithm will be similar to that already in use by some blood bank vendors

Association for the Advancement of Blood & Biotherapies

WeeklyReport

MARCH 2, 2022 | Vol. 28, No. 9

IN THIS ISSUE

Top Story

Nationwide Antibody Registry Could Help Further Reduce Risk of Adverse Events Among Patients Receiving Blood Transfusions

Jeanne Hendrickson, MD, professor of laboratory medicine at Yale University, is working with many others on developing a proposal for the creation of a nationwide registry to track patients' antibodies. read more »

ASCP 100 YEARS STRONGERTOGETHER

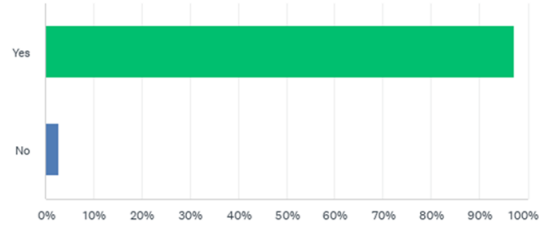
ASCP, Blood Bank Community Developing Nationwide RBC Alloantibody Database to Benefit Patients

Publication Date: Feb 9, 2022

By Henry (Harv) M. Rinder, MD, FASCP, ASCP President

AABB Survey, Jan 2022

Q1 Are you, in theory, interested in a US-wide red blood cell alloantibody registry?



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Thank You…