AABB Annual Meeting Education Program 2014

October 25-28, 2014 | Pennsylvania Convention Center | Philadelphia, PA

Presentation Handouts

(9106-TC-PBM) Uncommon Donors in the Cloud

October 25, 2014 ✧ 10:30 AM - 12:00 PM

Advancing Transfusion and Cellular Therapies Worldwide

Event Faculty List

Event Title: **(9106-TC-PBM)** Uncommon Donors in the Cloud
Event Date: October 25, 2014
Event Time: 10:30 AM - 12:00 PM

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New York Blood Center
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Disclosure: No

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Disclosure: No

Outline

- RBC therapy for sickle cell disease
- Alloimmunization and current challenges
- Case studies of patients who need uncommon donors

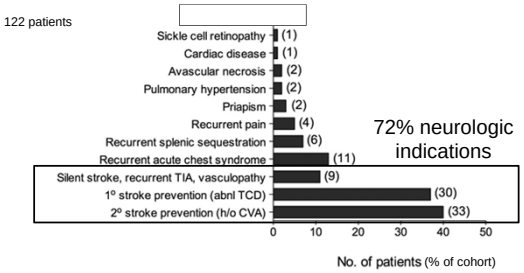
No disclosures

RBC therapy for sickle cell disease

- Remains a primary treatment for patients with sickle cell disease
- RBC usage is rising
  - ↑ indications for chronic therapy
  - ↑ use of erythrocytapheresis
  - availability of oral iron chelator

Smith-Whitley K, Pediatr Blood Cancer, 2012.Chou ST, BJH 2012.
Drasar E, BJH 2011. Raphael JL, Pediatr Blood Cancer 2013.

Indications for chronic transfusion in patients with SCD at a single center



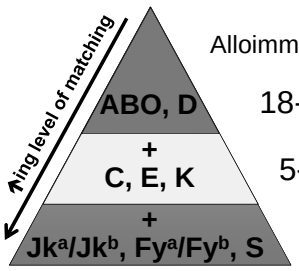
72% neurologic indications

Currently, no therapeutic equivalent to blood transfusion for many complications of SCD

Alloimmunization: current challenges

- Remains problematic despite phenotype matching strategies
  - Anti-Rh and -K antibodies most common
- Shortens RBC survival
  - Delayed hemolytic transfusion reactions (DTHRs) can be life-threatening
- Many patients form multiple antibodies
  - Therapy becomes impossible for some
- Complicates crossmatching
  - ↑difficulty finding blood, delays transfusion
  - ↑ labor and costs

Increased level of antigen matching reduces alloimmunization



Alloimmunization rates

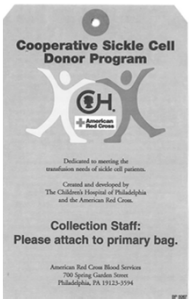
18-76%

5-27%

7%

O'Suoji, Pediatr Blood Cancer 2013; Sakhalkar, Ann N Y Acad Sci 2005; Lasalle-Williams,Transfusion 2011; Tahhan, Transfusion 1994; Vichinsky, NEJM 1990;

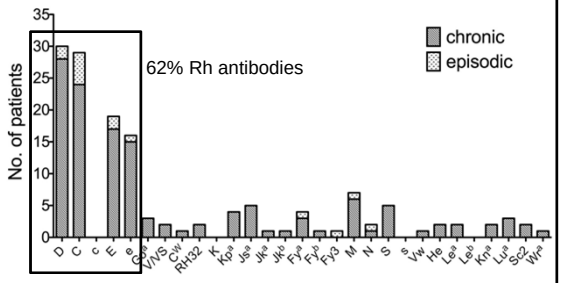
Alternative strategy: transfusion from minority donors



- Blue Tie Tag Program (1995)
  - Directs blood from African-American donors to children with SCD
  - Combined with CEK matching
- Episodically transfused:
  - 9 of 59 patients
  - Mean exposures: 4.6 (1-15)
  - 15% alloimmunized
- Chronically transfused:
  - 71 of 123 patients
  - Mean exposures: 354 (10-1460)
  - 58% alloimmunized

Chou & Westhoff, Blood, 2013

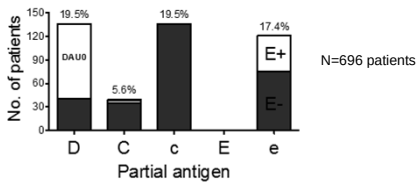
Antibody specificities formed with CEK matching and minority donor units



Chou & Westhoff, Blood 2013

Rh serologic phenotype-matched transfusions does not prevent all Rh alloimmunization

- Variant RH genes are common in patients with SCD and contribute to Rh alloimmunization
- Many patients' RBCs express partial Rh antigens and are at risk of allo- anti-Rh antibodies



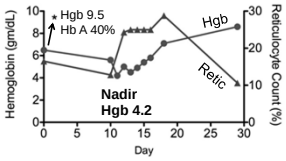
Case 1: 5 yo boy with SCD

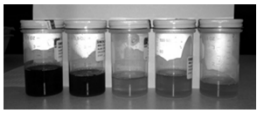
- Presented with fatigue, jaundice and pain
- Transfused 1 unit PRBC 10 days prior
  - Pretransfusion hemoglobin 6.5 gm/dl, Ab screen negative
  - RBC phenotype: O+, C-, c+, E-, e+, K-, Jka+, Jkb-, Fya-, Fyb-, M+, N+, S-, s+
  - On protocol to receive C, E, K negative PRBCs

Hemoglobin	5.6 gm/dl
DAT	Negative
Antibody screen (gel)	weak reactivity to all cells except one
Antibody screen (tube)	Negative

- **Suspected delayed hemolytic transfusion reaction**

Delayed hemolytic transfusion reaction





Urine collected every 6 hrs

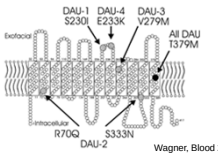
- Admitted to ICU, treated with IVIG and steroids
- Anti-D identified in subsequent antibody screen

Ipe et al, JPHO 2014

DHTR due to anti-D in patient with partial D

High resolution RH - partial D antigen and at risk for allo anti-D

RHD	*RHCE*
DAU4	*ce48C*
DAU4	*ce48C*



Wagner, Blood 2002

<u>Goal: transfuse antigen matched units: D-, C-, E-, K- RBCs</u>
13 in 100 from general donor pool
7 in 100 from African-American donor pool
By providing D- units, more likely from Caucasian donor

Case 1: 5 yo boy with SCD

- 6 months later transfused 1 unit PBRC (Nov 2012)
  - Pretransfusion hemoglobin 7.0 gm/dL
  - Crossmatch compatible D-, C-, E-, K- RBCs
- 6 days later presents with pain, jaundice, dark urine
- Suspected delayed hemolytic transfusion reaction
  - Transferred to ICU and treated with steroids and IVIG
  - Hemoglobin 6.7 → 4.5 gm/dl within 12 hours
  - Anti-Jkb identified
  - Transfused 5 ml/kg D-, C-, E-, K-, Jkb- RBCs
- Rec: C-, E-, K-, D-, Jkb-, Fya-, S- for future transfusions

Finding blood: D- C- E- K- Jkb- Fya- S-

Antigen	General donor pool		African-American donor pool	
	Frequency	Cumulative Donor frequency	Frequency	Cumulative Donor frequency
rr	0.15		0.07	
K-	0.91		0.98	
Jk(b-)	0.26	**0.54%**	0.51	**2.2%**
Fy(a-)	0.34		0.90	
S-	0.45		0.69	

Blood Group Antigen Facts Book 2012

Goal: transfuse antigen matched units
1 in 200 from general donor pool
1 in 50 from African-American donor pool

Case 1: follow-up

- 18 months later presents with acute stroke
  - Transfused, Hgb 6.8 gm/dl → Hgb 10.5 gm/dl
  - 8 days later presents with diffuse pain, hgb 7.0 gm/dL
  - DAT negative
  - Ab screen: anti-D, no new identifiable antibody
  - Low frequency panel: anti-Wra
- Seeks hematopoietic stem cell transplant as option
  - Transplant team recommends chronic transfusions until transplant
  - Treated with Rituximab
- Returns for transfusion after third dose Rituximab
  - D-, C-, E-, K-, Jkb-, Fya-, S- RBCs
  - Hgb 5.4 gm/dL → Hgb 8.9 gm/dL
- 6 days later presents with symptoms of DHTR
  - Hemoglobin 5.7 gm/dL → 4.1 gm/dl
  - DAT and antibody screen negative
  - NOT transfused

Case 1: untransfusable?

- Hemolysis of RBC units despite antigen matching with no additional antibodies apparent
- D-, C-, E-, K-, Jkb-, Fya-, S- RBCs homozygous for *RHCE*ce(48C)* unavailable
  - 94 AA donors, 94 hispanic donors
- Dombrock, Cromer, and Knops sequencing

Knops

Sla	KCAM
-	-

* Knops antibodies usually not clinically significant
Sl(a-) RBCs: 50-60% AA donors, 2% Caucasians

Dombrock*

Doa	Dob	Hy	Joa
+	+	+	+

*** Dombrock 898C>G change**
- reported in Brazilian Blacks, *DO*B > DO*A*
- not associated with antibody formation but data limited
- could consider Do(b-) units

- **1 unit of D-, C-, E-, K-, Jkb-, Fya-, S-, Do(b-) identified**

Case 2: 11 yo boy with SCD

- Presented with back pain, jaundice
- Transfused 1 unit PRBCs 5 days prior (pre-op)
  - Pre-transfusion hgb 6.7 gm/dl, 87% hgb S, Ab screen negative
  - RBC phenotype: O+, C+, c+, E-, e+, K-,
  - On protocol to receive E, K negative PRBCs

Hemoglobin	7.1 gm/dl → 6.2 gm/dl
LDH	932 u/L
Total bilirubin	6.9 mg/dl
DAT	Negative
Antibody screen (solid phase)	Negative
Antibody screen (tube)	Negative

- **Suspected delayed hemolytic transfusion reaction**

Case courtesy of Steve Sloan
Boston Children's Hospital

Case 2: 11 yo boy with SCD

- Transfused 2 units crossmatch compatible D+E-K- PBRC
  - Hgb 6.2 → 8.1 gm/dl
  - Hgb 6.5 gm/dl three days after PRBCs
- Suspected delayed hemolytic transfusion reaction
  - Antibody screen + (solid phase)
  - Antibody panel shows positive and negative reactions
  - No clear pattern/specificity
  - DAT negative
  - 14 of 14 units crossmatch incompatible
- Reference laboratory antibody evaluation
  - Found anti-Kn system antibody
  - Kn antibodies are not usually associated with DHTR
  - Another unidentified specificity below detection levels ?

Case courtesy of Steve Sloan
Boston Children's Hospital

Case 2: DNA testing

High resolution RH - partial c antigen and at risk for allo anti-c

RHD	*RHCE*
RHD	Ce
RHD	ce(254G)

HEA Beadchip - at risk for Fy^a and Do^b

K	k	Jka	Jkb	Fya	Fyb	M	N	S	s
-	+	+	+	-	- *	+	+	+	+

*GATA mutation present, not at risk for anti-Fyb

Kpa	Kpb	Jsa	Jsb	Lua	Dia	V	VS	Doa	Dob
-	+	-	+	-	-	-	-	+	-

→ **All 3 units received Do(b+)**

Knops

Yka	Kna	Knb	McCa	McCb	Sl3	Vil	Sla	KCAM
+	+	-	+	+	-	+	-	-

DHTRs due to anti-Dombrock antibodies

- Two antithetical antigens: Do^a, Do^b

RBC phenotype	Caucasian (%)	African American (%)
Do(a+b-)	**18**	**11**
Do(a+b+)	49	44
Do(a-b+)	33	45

- Hemolytic transfusion reactions caused by anti-Do^a or –Do^b reported but likely under-reported
- Antibodies often difficult to identify
  - Usually IgG but weakly reactive
  - Can be undetectable
  - DAT usually negative
- Provision of Do(a-) or Do(b-) blood as predicted by DNA analysis has improved RBC survival in patients with antibodies
  - No reliable antisera

Finding blood: E- K- Do(b-) Fy(a-)

Antigen	Caucasian donors		African-American donors	
	Frequency	Cumulative Donor frequency	Frequency	Cumulative Donor frequency
R1R1	**0.20**	**3.3%**	**0.04**	**0.43%**
K-	0.91		0.98	
Do(b-)	0.18		0.11	
Fy(a-)	0.34	**1.1%**	0.90	**0.39%**

Blood Group Antigen Facts Book 2012

Goal: transfuse antigen matched units

1 in 30 from general donor pool
- 1 in 100 if also Fy(a-)

1 in 230 from African-American donor pool
- 1 in 250 if also Fy(a-)

Has 3 frozen antigen-matched units reserved at local BB

DNA-based extended RBC typing for patients with SCD

vs

- DNA-based typing has been implemented as the primary method for extended RBC typing at our institution
  - Status on 35 antigens which can guide new antibody evaluations
  - Highly accurate, including chronically transfused patients with SCD
- Donor RBC typing by DNA tests at blood centers rising
  - Potential to match patients and donors for clinically significant antigens for which serologic reagents are limited or lacking

Summary

- Avoiding a first alloimmunization event is important
- Obtain pre-transfusion extended RBC phenotype for all individuals with SCD
  - C, E, K antigen match at a minimum
- Access to antigen-matched units can be challenging for patients with multiple alloantibodies
- Improved methods for identifying antigen-matched RBC units are needed
- Donors in the Cloud, an initiative to provide real-time electronic access to antigen-typed units may help locate antigen-matched units more quickly

Uncommon Donors in the Cloud

Meghan Delaney, DO, MPH
Medical Director, RBC Genomics, Puget Sound Blood Center
Assistant Professor, Laboratory Medicine & Pediatric (Adjunct)
University of Washington

Focus on access to units to help improve transfusion safety for patients

- Objective
  - To describe efforts to develop an open and real-time online system for sharing uncommon donor red cell units and platelets throughout the U.S.
- Goal
  - Improve access to antigen negative units for all patients throughout the nation

The Problem

- When a blood bank does not have access to specially typed (uncommon) blood units, the results are:
  - Reaction to poorly matched blood
  - More severe response the next time transfusion needed
  - Delay of needed blood transfusions and delayed medical procedures
  - Death
- The current methods for finding and accessing multiply antigen negative blood units are
  - ad-hoc
  - manual phone calls to neighboring centers
  - fax and paper based

Project Supporters

"The Foundation for America's Blood Center's believes that no one should die (or suffer) from lack of access to a safe and available blood supply. Indeed the information is there, but access requires a modern and open IT solution "in the cloud" to provide highly typed units in a timely and efficient manner to patients that need them, when and where they need them."

Dr Chris Hillyer, MD, President & CEO New York Blood Center

"This project [will] modernize, simplify and accelerate the process to identify and make red blood cells available for alloimmunized patients."

Karen L Shoos, JD, (CEO, AABB, retired)

"…A request that will provide the last piece of the puzzle: How to share the availability of specially typed units. A large, diverse pool of [typed] donors must be available to connected with potential recipients to complete the perfect match that is necessary for many patients."

Dr James P AuBuchon, MD, President & CEO, Puget Sound Blood Center

Uncommon donors in the cloud

Blood Suppliers

Hospitals/ Blood Center Recipients

Donations Management

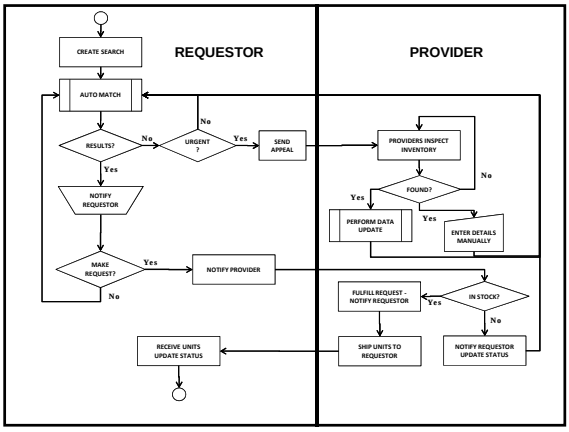
- Post units that are available for sharing
- Respond to specific requests
- Tracking / trending
- Improve resource sharing

Communication

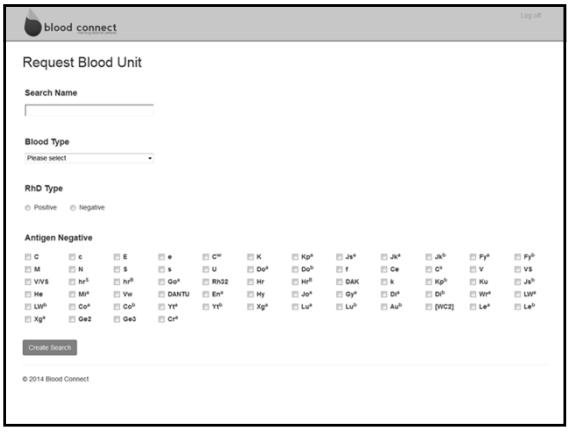
- Documented communication between suppliers and recipients
- More specially typed units go where needed with less effort resulting in better patient care

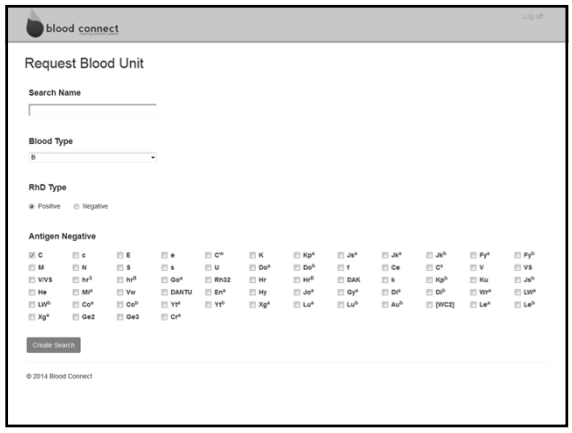
Recipient Technology Enablement

- Post needs online
- Search available products
- Request products from suppliers



Requestor initiated flows

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Log off
Request Blood Unit
Search Name
Blood Type
B
RhD Type
Positive
Negative
Antigen Negative
C
c
E
e
C^w
K
Kp^a
Js^a
Jk^a
Jk^b
Fy^a
Fy^b
M
N
S
s
U
Do^a
Do^b
f
Ce
C^x
V
VS
V/VS
hr^S
hr^B
Go^a
Rh32
Hr
Hr^B
DAK
k
Kp^b
Ku
Js^b
He
Mi^a
Vw
DANTU
En^a
Hy
Jo^a
Gy^a
Di^a
Di^b
Wr^a
LW^a
LW^b
Co^a
Co^b
Yt^a
Yt^b
Xg^a
Lu^a
Lu^b
Au^b
[WC2]
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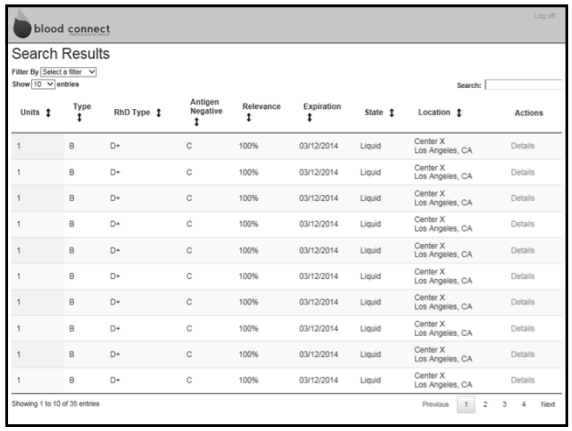
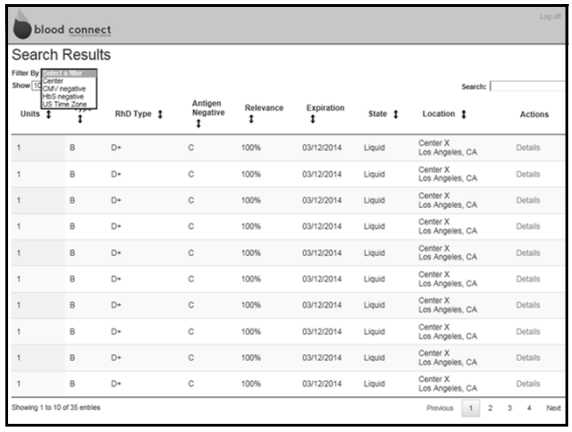
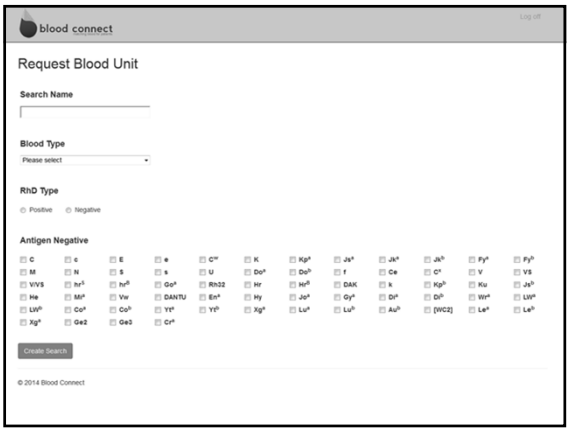
Le^b
Xg^a
Ge2
Ge3
Cr^a
Create Search
© 2014 Blood Connect


blood connect
Log off
Search Results
Filter By Select a filter
Show 10 entries
Search:
Units
Type
RhD Type
Antigen Negative
Relevance
Expiration
State
Location
Actions
1 B D+ C 100% 03/12/2014 Liquid Center X Los Angeles, CA Details
Showing 1 to 10 of 35 entries
Previous 1 2 3 4 Next


blood connect
Log off
Search Results
Filter By Select a filter
Center
CMV negative
HbS negative
LR Time Zone
Show 10 entries
Search:
Units
Type
RhD Type
Antigen Negative
Relevance
Expiration
State
Location
Actions
1 B D+ C 100% 03/12/2014 Liquid Center X Los Angeles, CA Details
Showing 1 to 10 of 35 entries
Previous 1 2 3 4 Next


blood connect
Log off
Request Blood Unit
Search Name
Blood Type
Please select
RhD Type
Positive
Negative
Antigen Negative
C c E e Cʷ K Kpᵃ Jsᵃ Jkᵃ Jkᵇ Fyᵃ Fyᵇ
M N S s U Doᵃ Doᵇ f Ce Cʷ V VS
V/VS hr¹ hr⁵ Goᵃ Rh32 Hr Hr⁶ DAK k Kpᵇ Ku Jsᵇ
He Miᵃ Vw DANTU Emᵃ Hy Joᵃ Gyᵃ Diᵃ Diᵇ Wrᵃ LWᵃ
LWᵇ Coᵃ Coᵇ Ytᵃ Ytᵇ Xgᵃ Luᵃ Luᵇ Auᵇ [WC2] Leᵃ Leᵇ
Xgᵃ Ge2 Ge3 Crᵃ
Create Search
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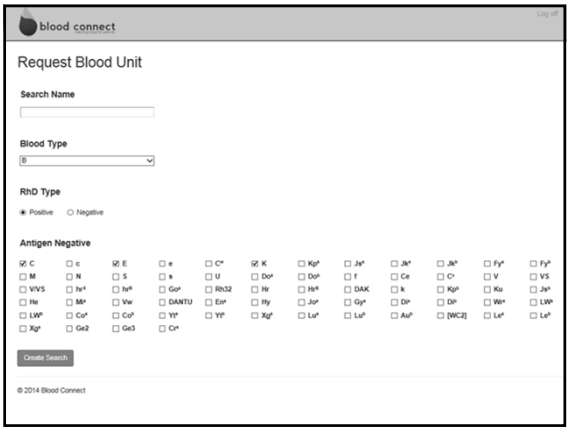
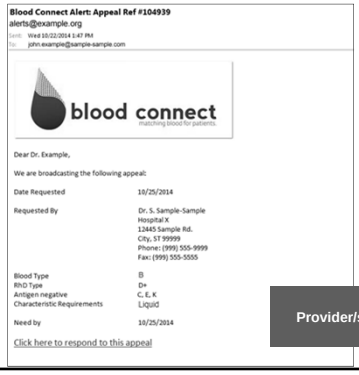

blood connect
Log off
Request Blood Unit
Search Name
Blood Type
B
RhD Type
Positive
Negative
Antigen Negative
C c E e Cʷ K Kpᵃ Jsᵃ Jkᵃ Jkᵇ Fyᵃ Fyᵇ
M N S s U Doᵃ Doᵇ f Ce Cʷ V VS
V/VS hr¹ hr⁵ Goᵃ Rh32 Hr Hr⁶ DAK k Kpᵇ Ku Jsᵇ
He Miᵃ Vw DANTU Emᵃ Hy Joᵃ Gyᵃ Diᵃ Diᵇ Wrᵃ LWᵃ
LWᵇ Coᵃ Coᵇ Ytᵃ Ytᵇ Xgᵃ Luᵃ Luᵇ Auᵇ [WC2] Leᵃ Leᵇ
Xgᵃ Ge2 Ge3 Crᵃ
Create Search
© 2014 Blood Connect


blood connect
Log off
Search Results
None of the units available in the system match your search criteria. You can broadcast your appeal to all blood suppliers. Please enter any additional information below and submit this form to broadcast appeal.
Blood Type: B
RhD Type: D+
Antigen Negative:
C, E, K
Need by:
11/12/2014
Characteristic Requirements:
Leukoreduced only
CMV neg
HbS neg
Unit Preferences:
Frozen
Liquid
Either
Comments:
Broadcast this appeal
Cancel
© 2014 Blood Connect

Broadcast email to suppliers



Blood Connect Alert: Appeal Ref #104939
alerts@example.org
Sent: Wed 10/22/2014 1:47 PM
To: john.example@sample-sample.com

blood connect
matching blood for patients.

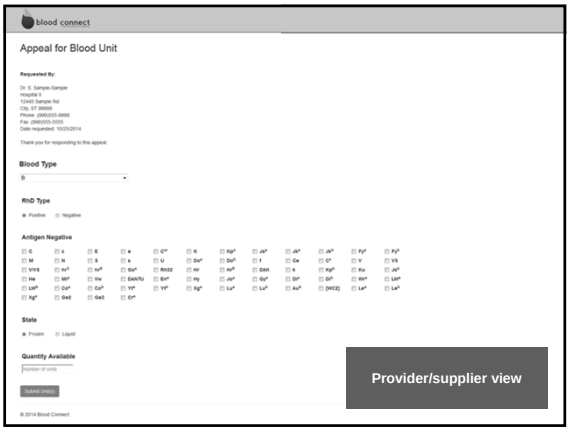
Dear Dr. Example,

We are broadcasting the following appeal:

Date Requested	10/25/2014
Requested By	Dr. S. Sample-Sample Hospital X 12445 Sample Rd. City, ST 99999 Phone: (999) 555-9999 Fax: (999) 555-5555
Blood Type	B
RhD Type	D+
Antigen negative	C, E, K
Characteristic Requirements	Liquid
Need by	10/25/2014

Click here to respond to this appeal

Provider/supplier view



blood connect

Appeal for Blood Unit

Requested By:

Dr. S. Sample-Sample
Hospital X
12445 Sample Rd.
City, ST 99999
Phone: (999)555-9999
Fax: (999)555-5555
Date requested: 10/25/2014

Thank you for responding to this appeal.

Blood Type

B

RhD Type

Positive Negative

Antigen Negative

C E c e C^w K Kp^a Jk^a Jk^b Fy^a Fy^b
M N S s U Do^a Do^b f Cw Cˆ V VS
V^VS Hr^S Hr^B Gy^a Rh32 Hro Hr^B DAK k Kp^b Ku Js^a
He Mi^a Vw GAL^U Er^3 Hg Js^b Sl^1 Sl^2 (WC2) Lw^a Lw^b
Lb^A Cs^a Cs^b Yt^a Yt^b Xg^a Lu^a Lu^b Au^b (WC2) Lw^a Lw^b
Xg^a Ge2 Ge3 Cr^a

State

Frozen Liquid

Quantity Available

Number of units

Submit Unit(s)

© 2014 Blood Connect

Provider/supplier view

blood connect

Log off

Requestor Dashboard

Requestor
Contact
Address
Phone/Fax/Email

Edit Profile

Actions:

View My Appeals View My Searches

Search

© 2014 Blood Connect

Provider(supplier) initiated flows


blood connect
Log off
Please upload your data sheet.
(CSV files only. Thank you.)
File:
Browse...
No file selected.
Upload Data Sheet
© 2014 Blood Connect


blood connect
Log off
Your file has been successfully uploaded. Thank you.
BCavailable_10_10_2015.csv
Continue
© 2014 Blood Connect


blood connect
Log off
Provider Dashboard
Provider Name
Contact
Address
Phone/Fax/Email
Edit Profile
Manage Inventory
Upload CSV
Add Unit
Manage Transactions
View Open Appeals
View All Transactions
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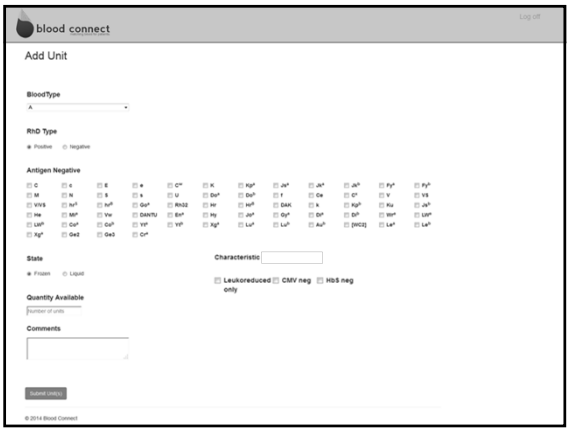

Anticipated Results

- Better matches for patients
- More units available in faster time frame
- Access to typed units increased to smaller medical facilities
- Less delays for vital procedures

It takes a village

- Collaborators
  - Connie Westhoff, PhD
  - Keith Thode
  - Anthony Feldman
- Volunteers
  - Jim Palmeri
  - Toddy Mladenov
  - Paul Osborn
  - Oscar Martinez
  - Nabil Sutjipto
  - Christine van Egeren
  - David Corona
  - Suhas Joshi
  - M Navali
- Support
  - ABC Foundation
  - PSBC
  - NYBC
  - Microsoft
  - AdvanceNet Labs
  - Accenture
  - Agitare Technologies

Microsoft

AdvanceNet Labs

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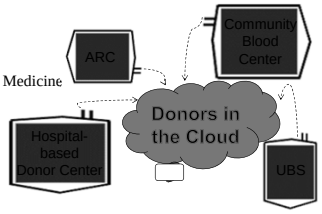
Thank you

- Please come up and sign up to be on the mailing list

Uncommon Donors in the Cloud: RBC Selection for Patients with Warm Autoantibodies

Alyssa Ziman, MD
Medical Director, Transfusion Medicine

AABB Annual Meeting 2014
Philadelphia



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Objectives

- Highlight challenges for the transfusion service in patients with warm autoantibodies
- Discuss RBC selection strategies for patients with warm autoantibodies

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Warm Autoantibodies & Autoimmune Hemolytic Anemia

- Account for the majority of cases of autoimmune hemolytic anemia (~ 80% of all AIHA)
- Most cases are idiopathic; also distinct disease associations
  - Chronic Lymphocytic Leukemia
  - Lymphoma
  - Autoimmune Diseases
  - Chronic Inflammatory Conditions
- All ages are affected – increase in incidence throughout life, particularly after 50 yo
- Incidence higher in women than men

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Warm Autoantibodies

- Positive Indirect Antiglobulin Tests
  - Panreactive
  - May demonstrate relative specificity (most commonly "Rh" specificity)
- Positive DAT
  - IgG + complement (67%)
  - IgG only (20%)
  - Complement only (13%)
- WAA does not always equal AIHA

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Challenges for the Transfusion Service

1. Detection of underlying alloantibodies
   - Given WAA potential to mask alloantibodies
   - Prevalence of clinically significant red cell alloantibodies is higher in patients with WAIHA than in other patients.

Patient Population	Alloimmunization Rate (varies with degree of antigen matching)
WAIHA	12 - 56%
Sickle Cell Disease (SCD)	5 - 46%
Non-AIHA/SCD	~5%

Petz and Garratty, Immune Hemolytic Anemias; O'Suoji, Pediatr Blood Cancer 2013; Lasalle-Williams, Transfusion 2011; Castro, Transfusion 2002;Vichinsky, NEJM 1990

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Challenges for the Transfusion Service

2. Provision of appropriate RBC units for transfusion
   - Crossmatch = incompatible
     - Transfusion of RBCs incompatible with autoantibody will not cause clinically severe transfusion reaction
     - Transfusion of RBCs incompatible with alloantibody will cause a reaction as clinically severe as in any other patient
   - Phenotype/genotype requirements
     - Prophylactic matching
     - Antigen negative for WAA that demonstrate specificity

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RBC Selection Practices

UCLA

vs.

Community (BEST Collaborative)

UCLA: RBC Selection for Patients with WAA

- Perform phenotype with identification of WAA
  - Limited to Rh and Kell antigens
  - Extended with presence of underlying alloantibodies, unable to rule out clinically significant alloantibodies, need to perform alloadsorption
- Rh and Kell phenomatched RBCs
  - Prevent future alloimmunization
  - Decrease performance of alloadsorptions
- Do not provide antigen-negative units for autoantibody demonstrating relative specificity

Petz, Br J Haematol. 2004; Shirey, Transfusion 2002; El Kenz, Transl Res. 2014

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Community: RBC Selection for Patients with WAA

- BEST Collaborative – Survey of 52 sites
  - US, Canada, Europe, Brazil, New Zealand
  - Affiliated with BEST, ABC, CAP, EBA
  - Tremendous variability in RBC selection as well as testing practices (methodology and phases of a work-up)
- 68% provide phenotype or genotype antigen matched RBC units for transfusion
  - These policies have been in effect since as early as the 1970's.

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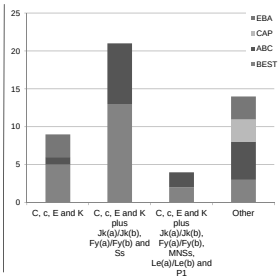
BEST Collaborative Survey

- Phenotype:
  - 54% perform with initial detection of WAA
- Genotype:
  - 18% perform genotyping with initial detection of WAA



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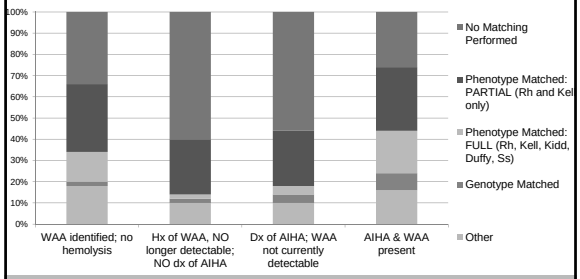
Antigen Matching Policy for Patients with WAA: NO Underlying Alloantibodies



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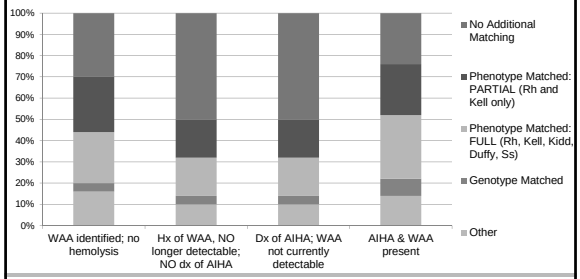
Antigen Matching Policy for Patients with WAA: 1 or More Underlying Alloantibodies



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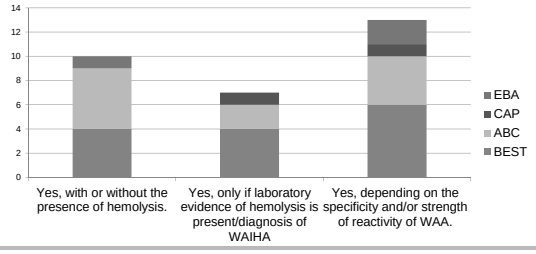
BEST Collaborative Survey

- 60% provide antigen negative units when patient has a WAA demonstrating specificity



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BEST Collaborative

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Case Studies

Case #1

- 59 yo ♂ presents w/ recent respiratory infection, fatigue and dark urine.
  - CLL, s/p rituximab and bendamustine x 6 cycles (completed 4/2010)
  - Evan's Syndrome, s/p rituximab and prednisone with restoration of counts.
- ➢ Recurrent Evan's, likely after recent infection vs CLL progression

Labs	Day of Admission
Hemoglobin	7.2
Hematocrit	22.5
Platelet Count (x10E3/uL)	308
Reticulocyte Count (%)	16.16
Haptoglobin (mg/dL)	<8
LD (U/L)	479
Bilirubin, total (mg/dL)	2.1

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Case #1 – Type and Screen (Admission)

Blood Type: A negative

Last transfusion: 5 years ago

	Rh - Hr						Kell						Duffy		Kidd		Lewis		P	MN				Luth-eran		X_g	
	D	C	c	E	e	Cw	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P1	M	N	S	s	Lu^a	Lu^b	Xga	
I	+	+	0	0	+	0	0	+	0	+	0	+	+	0	0	+	0	+	+	+	0	+	0	+	+	+	4+
II	+	0	+	+	0	0	0	+	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	4+
III	0	0	+	0	+	0	+	+	0	+	0	+	0	+	+	0	+	0	+	+	0	+	+	0	+	+	4+
Positive Control																											4+

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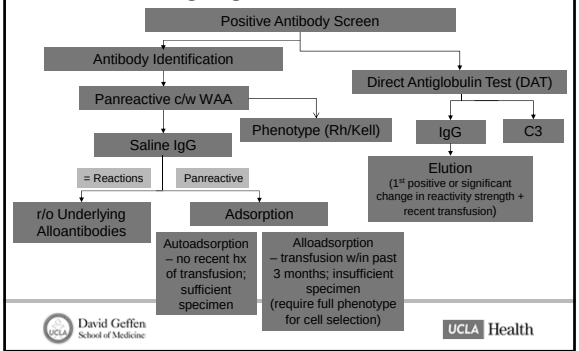
UCLA Testing Algorithm



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Case #1 – Antibody ID (SPRCA → CAT)

	Rh - Hr							Kell						Duffy		Kidd		X_g	Lewis		MN				P	Luth-eran		NEAT
	D	C	E	c	e	f	Cw	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Xga	Le^a	Le^b	S	s	M	N	P1	Lu^a	Lu^b	
1	0	0	0	+	+	+	0	0	+	0	+	0	+	0	+	+	+	0	0	+	+	0	+	+	+	0	+	4+
2	0	0	0	+	+	+	0	+	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+	4+
3	0	0	0	+	+	+	0	0	+	0	+	0	+	+	0	0	+	0	+	0	+	+	+	+	+	0	+	4+
4	+	0	+	+	0	0	0	+	+	0	+	0	+	+	+	+	0	0	0	+	0	+	+	+	+	0	+	4+
5	+	0	+	+	0	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	0	+	0	+	4+
6	+	0	+	+	0	0	0	0	+	0	+	/	+	0	+	+	0	+	0	+	0	+	+	+	+	0	+	4+
7	+	+	0	0	+	0	0	0	+	0	+	0	+	0	+	+	0	+	+	0	+	0	+	+	+	0	+	4+
8	+	+	0	0	+	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	+	0	+	4+
9	+	+	+	0	+	0	0	0	+	0	+	0	+	+	+	+	+	+	0	+	+	+	+	+	+	0	+	4+
10	0	+	0	+	+	+	0	0	+	0	+	/	+	+	+	+	0	+	0	+	+	+	+	0	+	0	+	4+
11	+	+	0	0	+	0	0	+	0	0	+	/	+	0	+	+	+	+	0	+	0	+	0	0	0	0	+	4+
Patient Cells																											4+

Case #1 – Saline IgG

	Rh - Hr							Kell					Duffy		Kidd		Lewis		P	MN				Luth-eran		X_g	Saline IgG
	D	C	c	E	e	V	Cw	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P1	M	N	S	s	Lu^a	Lu^b	Xga	
I	+	+	0	0	+	0	0	0	+	0	+	0	+	+	0	0	+	0	+	+	+	0	+	0	+	+	+	2+
II	+	0	+	+	0	0	0	0	+	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	2+
III	0	0	+	0	+	0	0	+	+	0	+	0	+	0	+	+	0	+	0	+	+	0	+	+	0	+	+	2+

Case #1 – Adsorption (x5) (CAT)

	Rh - Hr							Kell					Duffy		Kidd		X_g	Lewis		MN				P	Luth-eran		NEAT
	D	C	E	c	e	f	Cw	K	k	Kp^a	Kp^b	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Xga	Le^a	Le^b	S	s	M	N	P1	Lu^a	Lu^b	
1	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	+	0	0	+	+	0	+	+	+	0	+	4+
2	0	0	0	+	+	+	0	0	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+	4+
3	0	0	0	+	+	+	0	0	+	0	+	0	+	+	0	0	+	0	+	0	+	+	+	+	0	+	4+
4	+	0	+	+	0	0	0	0	+	0	+	0	+	+	+	0	0	0	+	0	+	+	+	+	0	+	4+
5	+	0	+	+	0	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	0	+	0	+	4+
6	+	0	+	+	0	0	0	0	+	0	+	/	+	0	+	0	+	0	+	0	+	+	+	+	0	+	4+
7	+	+	0	0	+	0	0	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	+	0	+	4+
8	+	+	0	0	+	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	+	0	+	4+
9	+	+	+	0	+	0	0	0	+	0	+	0	+	+	+	+	+	0	+	+	+	+	+	+	0	+	4+
10	0	+	0	+	+	+	0	0	+	0	+	/	+	+	+	0	+	0	+	+	+	+	0	+	0	+	4+
11	+	+	0	0	+	0	0	0	+	0	0	+	/	+	0	+	+	+	0	+	0	+	0	0	0	+	4+
Patients Cells																											4+

Case #1 – Adsorption (x5) (CAT)

	Rh - Hr							Kell					Duffy		Kidd		X_g	Lewis		MN				P	Luth-eran		NEAT
	D	C	E	c	e	f	Cw	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Xga	Le^a	Le^b	S	s	M	N	P1	Lu^a	Lu^b	
1	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	+	0	0	+	+	0	+	+	+	0	+	4+
2	0	0	0	+	+	+	0	0	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+	4+
3	0	0	0	+	+	+	0	0	+	0	+	0	+	+	0	0	+	0	+	0	+	+	+	+	0	+	4+
4	+	0	+	+	0	0	0	0	+	0	+	0	+	+	+	0	0	0	+	0	+	+	+	+	0	+	4+
5	+	0	+	+	0	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	0	+	0	+	4+
6	+	0	+	+	0	0	0	0	+	0	+	/	+	0	+	+	0	+	0	+	0	+	+	+	0	+	4+
7	+	+	0	0	+	0	0	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	+	0	+	4+
8	+	+	0	0	+	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	+	0	+	4+
9	+	+	+	0	+	0	0	0	+	0	+	0	+	+	+	+	+	0	+	+	+	+	+	+	0	+	4+
10	0	+	0	+	+	+	0	0	+	0	+	/	+	+	+	0	+	0	+	+	+	+	0	+	0	+	4+
11	+	+	0	0	+	0	0	0	+	0	0	+	/	+	0	+	+	+	0	+	0	+	0	0	0	+	4+
Patients Cells		=	=	+	+				=						+	+	+	=				=	+					4+

Case #1 – Adsorption (x5) (CAT)

	Rh - Hr							Kell					Duffy		Kidd		X_g	Lewis		MN				P	Luth-eran		NEAT	rr	R2R2
	DU	D	E	C	e	f	Cw	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Xga	Le^a	Le^b	S	s	M	N	P1	Lu^a	Lu^b			
1	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	+	0	0	+	+	0	+	+	+	0	+	4+	=	=
2	0	0	0	+	+	+	0	0	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+	4+	=	=
3	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	0	+	0	+	+	+	+	0	+	4+	=	=
4	+	0	+	+	0	0	0	0	+	0	+	0	+	+	+	+	0	0	0	+	0	+	+	+	+	0	+	4+	=	=
5	+	0	+	+	0	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	0	+	0	+	4+	=	=
6	+	0	+	+	0	0	0	0	+	0	+	/	+	0	+	+	0	+	0	+	0	+	+	+	+	0	+	4+	=	=
7	+	+	0	0	+	0	0	0	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	+	+	0	+	4+	=	=
8	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	+	0	+	4+	=	=
9	+	+	+	0	+	0	0	0	0	+	0	+	0	+	+	+	+	+	0	+	+	+	+	+	+	+	0	+	4+	=	=
10	0	+	0	+	+	+	0	0	0	+	0	+	/	+	+	+	+	0	+	0	+	+	+	+	0	+	0	+	4+	=	=
11	+	+	0	0	+	0	0	0	+	0	0	+	/	+	0	+	+	+	+	0	+	0	+	0	0	0	+	4+	=	=
Patients Cells		=	=	+	+			=						+	+	+	=				=	+						4+		

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Transfusion Service

- A negative
- Last transfusion – five years ago

	Day of Admission
Antibody Screen	Positive
DAT, IgG	2+
DAT, C3	3+
Adsorption	Allo (x5)
Elution	NP
ABID	Warm auto
Transfusion Instructions	C, E, K =

- Order for 2 RBC units
  - C, E, K negative
  - Frequency of 13:100
- No transfusion given adequate hemoglobin

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Transfusion Service

- A negative
- Last transfusion – five years ago

	Day of Admission	2 weeks later
Antibody Screen	Positive	Positive
DAT, IgG	2+	3+
DAT, C3	3+	1+
Adsorption	Allo (x5)	NP
Elution	NP	NP
ABID	Warm auto	
Transfusion Instructions	C, E, K =	

- Hgb: ↑10.3g.dL

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Transfusion Service

- A negative
- Last transfusion – five years ago

	Day of Admission	2 weeks later	3 ½ months later
Antibody Screen	Positive	Positive	Positive
DAT, IgG	2+	3+	2+
DAT, C3	3+	1+	m+
Adsorption	Allo (x5)	NP	NP
Elution	NP	NP	NP
ABID	Warm auto		Warm auto, e specificity
Transfusion Instructions	C, E, K =		C, E, K =

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UCLA RBC Selection Policy: Case #1

- Rh and Kell phenomatched RBCs
  - Prevent future alloimmunization
  - Decrease performance of alloadsorptions
- Do <u>not</u> provide antigen-negative units for autoantibody demonstrating relative specificity
  - Reserved for patients with an alloantibody
  - Impact on prophylactic policy
  - If policy to give pheno-matched when specificity, challenge to identify e= units

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Case #2

- 52 yo ♂ with Myelofibrosis with JAK2 positive mutation diagnosed in 2010 with transfusion dependent anemia
  - At the time of diagnosis, underwent splenectomy

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Case #2 – Transfusion Service

- A positive
- Transfusion History: ~8 units in 2008 (outside hospital)

	Antibody Screen	Antibody Identification	RBC Selection	Frequency
Admission	Positive	Weakly reactive antibody of no apparent specificity		
9 months later	Positive	Anti-C, Anti-Fya, Anti-K	C, Fya and K =	9.8%
12 months later	Positive	**WAA** + Anti-C, Anti-Fya, Anti-K	C, E, Fya and K =	4.6%

- RBC Phenotype

C	E	c	e	K	Jk^a	Jk^b	M	S	s	Fy^a	Fy^b
=	=	4+	4+	=	4+	=	4+	3+	3+	=	=

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Case #2 – Transfusion Service

	Antibody Screen	Antibody Identification	RBC Selection	Freq.
Admission	Positive	Weakly reactive antibody of no apparent specificity		
2 months	Positive	Anti-C, Anti-Fya, Anti-K	C, Fya and K =	9.8%
12 months	Positive	**WAA** + Anti-C, Anti-Fya, Anti-K	C, E, Fya, K =	4.6%
18 months	Positive	WAA + Anti-C, Anti-Fya, Anti-K, **Anti-Jkb**	C, E, Fya, K, Jkb =	1.2%
19 months	Positive	WAA + Anti-C, Anti-Fya, Anti-K, Anti-Jkb, **Anti-Fyb**	C, E, Fya, Fyb, K, Jkb =	0.2%

- RBCs transfusions: every 2-3 weeks, maintain Hgb 7-8g/dL
  - RBC Transfusions: 79 units
  - Once antibodies present, all but 2 units were imported.

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UCLA RBC Selection Policy: Case #2

- Provide antigen negative units for all alloantibodies
- Rh and Kell phenomatched RBCs
  - Prevent future alloimmunization
  - Decrease performance of alloadsorptions

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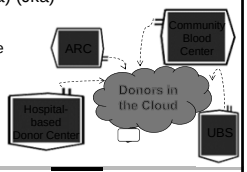
Conclusion

- Phenotype/genotype all patients when WAA initially identified
- Exclude underlying alloantibodies (various strategies available based on transfusion history, utilization of pheno/geno-matched for transfusion)
- Select matched units for Rh, K, (Fya) (Jka)
  - Prevent future alloimmunization
  - Decrease performance of labor-intensive immunohematology work-ups (i.e. alloadsorptions)
  - Computer based platform would be beneficial



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