Meeting the Challenging Transfusion Needs of a Diverse Patient Population

Presented by: Christy P. Beal
Manager, Immunohematology Reference Laboratory
American Red Cross Blood Services
Southern Region, Douglasville, GA

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Objectives

- Understand the role of the Immunohematology Reference Laboratory (IRL)
- Understand the importance of donor phenotyping and genotyping
- Understand that certain blood types are unique to specific racial and ethnic groups
- Recognize the importance of donor diversity

What is the role of the IRL?

The Immunohematology Reference Laboratory (IRL) of the American Red Cross is a specialized laboratory staffed by highly trained clinical laboratory professionals whose primary focus is to assist our customers (hospital blood banks/ transfusion services) with meeting the transfusion needs of their (our) patients.

Two Main Functions of the IRL

1. Provide antigen negative red blood cells (RBCs)
   - The Southern Region IRL provides approximately 200 antigen negative RBCs for hospitals every week
     - Stat antigen negative requests
     - Partners for Life (PFL) program
     - Stock/routine antigen negative orders
     - Exchange transfusions
   - Compatibility testing is then performed by the hospital blood bank/transfusion service

Two Primary Functions of the IRL (Continued)

2. Provide serological investigation of patient samples
   - Antibody Identification work ups, ABO discrepancy resolution and transfusion reaction investigations
   - Testing ranges from simple to high complexity
   - List of services include test of record (TOR) compatibility testing

Serological Investigation

- IRL staff performs the testing that hospitals do not have the resources and/or expertise to perform
  - Warm and cold-reactive autoantibody investigation
  - Multiple specificity antibody investigations
  - Identification of antibodies to high and low prevalence antigens
  - Investigation of antibodies with high titer low avidity characteristics (HTLA)
- Special techniques include: autologous/allogeneic adsorptions, elutions, hypotonic saline wash, microhematocrit cell separation, cell treatments (EDTA glycine, DTT, enzymes etc.)

Which brings us back to….

Most requests require antigen negative red blood cells!

Defining the Challenge

- How do we fill these orders?
- Where do antigen negative units come from?
- Why does it sometimes take so long to fill our request for antigen negative units?

All Inventories are not created equal

- General Inventory
  - Regular stock RBCs
  - Not previously tested or not of interest to IRL
- IRL Inventory
  - Donor RBCs that have been **screened, phenotyped or genotyped** on current or previous donations
  - Code is added to donor record so the next donation is automatically routed to the IRL

Phenotype vs. Genotype

- Phenotype-the assortment of antigens actually detectable on an individual's red cells using selected antisera. In many blood group systems, the phenotype is an exact expression of the genotype
- Genotype-the DNA sequence of the genetic makeup of an individual which determines the specific characteristic (phenotype) of that individual

Phenotype Prevalence

"Prevalence of a blood group antigen is determined by testing red cells from a large random sample of people of the same race or ethnicity with a specific antibody and calculating the percentage of positive and negative reactions."

-Technical Manual, 18th ed. 2014

Prevalence of commonly requested antigen negative RBCs

	Caucasians	Blacks	Asians
C	32%	73%	7%
E	71%	78%	61%
K	91%	98%	*
Fy^a	34%	90%	1%
Fy^b	17%	77%	81.5%
Fy (a-b-)	0%	67%	0%
Jk^a	23%	8%	73%
Jk^b	26%	51%	24%
s	11%	7%	
U	0%	<1%	

Interesting Fact

People of African decent are frequently negative for many antigens that are usually positive in the Caucasian population

Example of a common African American (AA) phenotype:

D+ C- E- c+ e+ K- k+ Fy(a-b-) Jk(a+b-)M+ N+ S- s+

Some Rare Blood Types by Ethnic Group

- African-American- U-, Fy(a-b-)
- Native American, Alaskan Native- RzRz
- Pacific Island, Asian Jk(a-b-)
- Hispanic Di(b-)
- East European/Russian Jews Yt(a-), Dr(a-)
- Caucasian Kp(b-), Vel-

Why is this important?

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Common Antigen Negative Request

O pos C-, E-, K-, Fy(a-), Jk(b-)

- Caucasian Donors
  - 0.32 x 0.71 x 0.91 x 0.34 x 0.26=0.018
  - 0.018 x 100=1.8% (must screen 98 donors to find 1)
- Black Donors
  - 0.73 x 0.78 x 0.98 x 0.90 x 0.50=0.25
  - 0.25 x 100=25% (screen 75 donors to find 1)

Common Antigen Negative Request(s) Continued

O pos C-, E-, K-, **Fy(a-b-),** Jk(b-)

- Caucasion Donors
  - 0.32 x 0.71 x 0.91 x **(0)** x 0.26=0
  - 0 x 100=**0**%
- Black Donors
  - 0.73 x 0.78 x 0.98 x **0.67** x 0.50=0.19
  - 0.19 x 100=19% (must screen 81 donors to find 1)

Antigen Typing Challenges in Hospital

- Limited red cell inventory
- Limited testing staff
- Cost of antisera
- Availability of antisera
- Manual testing is labor intensive

Antigen Typing Challenges in the IRL

- Cost of antisera
- Availability of antisera
- Manual testing is labor intensive
- In the old days (not too long ago)…antigen screening was almost solely manual testing

Meeting the Challenge

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Meeting the Challenge

Combined approach

- Manual testing
- Automated testing
- Molecular (DNA) testing

Meeting the Challenge

- Daily
  - Run report for ethnic donors (critical that donors declare their race/ethnicity)
  - Proactively screen donors for C/E(Ro), e(R2) and c(R1)
  - Perform automated test of record phenotyping on previously screened donors for C, E, c, e
  - Confirm previously screened donors for additional antigens
- Bi-weekly
  - Send 92 pre-screened samples for molecular (DNA) testing
  - Manage RBCs and results for 92 samples that were submitted (34-46 antigen markers/donor)

Advantages of Molecular Testing

- Predict RBC antigen status for identification of donors:
  - Negative for high-incidence antigens
  - Negative for multiple antigens
  - With *RH* variant alleles for matching to patients with *RH* variant alleles who produce *RH* antibody
- Identify genetic determinants of weakly expressed antigens, e.g. Fy^b with Fy^x phenotype
- Determine the predicted phenotype of donors with antigens difficult to characterize serologically, e.g. U, hr^B, hr^S , Do^a, and Do^b
- Aid in resolution of typing discrepancies

Molecular Testing Summary

Total # Samples	hr(B-)	U	Uvar	Hy-	Js(b-)	Lu(b-)	k-	Kp(b-)
15210	248/ **114**	47	88	48	47	5	2	1

Case Study

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Case Study

- BW came to us a 6 year old male with sickle cell disease
- Partners for Life (PFL)program participant
- Transfusions every 4 weeks
- Phenotype: C- c+ E- e+ K- k+ Fy(a-) Fy(b+) Jk(a+) Jk(b-) S- s+ Kp(a-) Kp(b+) **hr(B-)**
- Has produced anti-hr^B,-Kp^a and a warm-autoantibody
- Requires units that are negative for C, E, K, Fy^a, Jk^b, S, Kp^a, hr^B and genotyped matched for optimal results

Case Study (continued)

- Incidence of this phenotype in the Caucasian population= 0%
- In some areas of the country AA donors make up less than 1% of the donor population
- Without an adequate supply of AA donors available to screen, it would be impossible to fill the order for BW's transfusions

Case Study (continued)

- Because of the work that the IRL performs behind the scenes, there is a pool of AA donors that have been screened and determined to be a match for his very rare phenotype
- Thanks to molecular testing, we currently have about 10-12 donors that match BW's phenotype
- Today, BW is a young, energetic 15 year old who doesn't suffer from the debilitating effects of SCD because he has been a part of the PFL program since he was very young

Summary

- Certain blood types are unique to specific racial and ethnic groups.
  - U - and Fy(a-b-) phenotypes are unique to Blacks
  - Recently supported patients with anti-Jk3 and anti-Dib
- To find suitable RBCs for these patients must screen RBCs that are of similar genetic makeup
- **Donor diversity must match patient diversity**

Questions?

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