INDIAN IMMUNOHEMATOLOGY INITIATIVE
CASE OF THE MONTH: February 2009

Answers:

1. What alloantibody appears to be present? Does this seem to be the only antibody present? Why? What would be your next option for testing?

   The negative autocontrol indicates that the reactivity is due to alloantibody(-ies). The patient's sample likely contains allo-anti-c because all the non-reactive cells are c negative. However, there must be additional alloantibodies present since two c neg cells (screen cell I and panel cell 11) are c neg but are reactive. Common, clinically significant alloantibodies that are not ruled out include anti-E, anti-K, anti-Fy^a, and anti-Jk^b. Also anti-Le^b is not ruled out.

   Testing additional c- cells should be informative. Knowing the patient's red cell phenotype would indicate which allo-antibodies the patient can produce.

2. Which antibodies do you now think are present? What alloantibodies cannot yet be excluded?

   The new serum reactions only rule out anti-Le^b. The weak reaction with cell 19 could be due to anti Fy^a or anti-Jk^b, but anti-Jk^b is more likely since another $Fy^{(a+,b+)}$ cell was non-reactive. The strong reactivity with cell 20 could be explained by anti-E, anti Fy^a, or anti-Jk^b, but is most likely due to anti-E in view of the strength of the cell 19 reactivity. Anti-K still cannot be excluded and could explain the reactivity on screen cell I.

   The phenotype indicates that anti-E, -K, -Jk^b, and -Fy^a are all possibilities.

3. Assume that you have an unlimited supply of reagent red cells to select for testing and that your laboratory has the following requirements for antibody identification:
   1) An antibody specificity is confirmed when two antigen positive cells are reactive and 2 antigen negative cells are non-reactive.
   2) An allo-antibody can only be excluded when a double dose cell is non-reactive. One such non-reactive cell is sufficient for exclusion.

   Now:
   - List the phenotypes of panel RBCs needed to prove your hypothesis including any cells required confirm the antibody specificities ("rule in") and exclude any remaining alloantibodies ("rule out").
   - List the purpose of testing the cell (e.g. "rule in anti-c", "rule out anti-Jk^a").
   - Write the cell's Rh phenotype in modified Weiner notation (i.e. "R1R1", "R1Rz", etc.).

   The exact cells chosen may vary somewhat but should have the following characteristics:
   1) All cells would be c negative. Among the cells already tested, there are more than two cells that are positive for c antigen only: c+E-K-Jk(b-). This is sufficient to confirm anti-c.
   2) One cell should be c-E-K-Jk(b-) Fy(a+b-) to exclude anti-Fy^a. The Fy(b-) status would likely indicate that the cell carries a double dose of the Fy^a antigen. This, however, cannot be assured in all populations because of the presence of a silent allele Fy.
   3) One cell should be c-E-Jk(b-) and K+ to confirm anti-K. One cell of this type has already been tested. A second cell of this phenotype would be sufficient to confirm the presence of anti-K.
   4) One cell should be c-Jk(b-)K- and E+. One cell of this type has already been tested. A second cell would be sufficient to confirm the presence of anti-E.
   5) At least one cell should be c-E-K- Jk(b+) to confirm anti-Jk^b. This antibody appears to be very weak even when tested against a double dose Jk(b+) cell (Jk{a-b+}). It would be wise to test more than the minimum number of cells to confirm this antibody.

	Antigen									
Rh phenotype	**c**	**E**	**e**	**Jka**	**Jkb**	**K**	**k**	**Fya**	**Fyb**	**Purpose of testing this cell**
R1R1	*0*	*0*	+	+	*0*	*0*	+	+	*0*	*Rule out anti-Fy^a*
R1R1	*0*	*0*	+	+	*0*	+	+	+	+	*Rule in anti-K*
R1Rz	*0*	+	+	+	*0*	*0*	+	*0*	+	*Rule in anti-E*
R1R1	*0*	*0*	+	*0*	+	*0*	+	*0*	+	*Rule in anti-Jk^b*
R1R1	*0*	*0*	+	*0*	+	*0*	+	+	+	*Rule in anti-Jk^b*

Testing of the above and additional cells indicated that anti-c, anti-E, anti-K, and anti-Jk^b were present. Anti-Fy^a was ruled out. (Note that the laboratory resolving this problem requires 3 "rule-in cells", not 2.)

4. What percentage of donors is expected to be compatible with this recipient given your hypothesis as to the combination of antibodies present? Perform the calculation for European donors.

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The relevant antigen-negative frequencies in European donors are:

c- 20%
E- 70%
K- 91%
Jk(b-) 26%

If these traits assorted independently, the likelihood of compatibility would be:

(0.20) x (0.70) x (0.25) x 100% = 3.3%.

However, there is linkage disequilibrium between c and E which are epitopes on the same protein, and the likelihood of lacking both antigens is not (0.20) x (0.70) = 14%, but instead is about 18.5%. To calculate this one must use a table of Rh haplotypes. The only common c neg, E neg haplotype is R1 at about 42%, so the R1R1 frequency is (0.42) x (0.42).

Based on information obtained from testing Indian blood donors at several locations, it is likely that antigen frequencies are different than European donors for several of the antigens. The incidence of c neg, E neg individuals appears to be higher. Very few Indians are K pos, so the prevalence of K neg RBCs is likely close to 100%.