**HDFN TECHNICAL CASE #3, ANSWERS**

Case study by Jim Perkins, M.D. (©2009)

Indian Immunohematology Initiative

1. What is the probable identity of this antibody? What is the relevance of the patient's ethnic origin?

   *Probable anti-Jk3. Anti-Jk3 reacts as an inseparable form of anti-$Jk^a$ and anti-$Jk^b$. Jk3-negative {Jk(a-,b-)} individuals are rare. This patient presents the classic serologic findings of an antibody directed against a high frequency antigen, serum reactivity against all RBCs except the patient's own. The antigen phenotype then demonstrates that the patient lacks a high frequency antigen, in this case Jk3.*

   *The Jk3 negative phenotype is found most commonly in Polynesian populations (over 1% on certain islands), and it is seen at low frequencies in other East Asian groups including individuals of Philippine descent so, as in other cases of antibodies directed against high prevalence antigens, her ethnicity was a clue.*

2. Is any further workup needed to prove it? What does the alloadsorption study demonstrate?

   *In combination, the antigen phenotype and the adsorption study rule out other underlying allo-antibodies. That is, from the phenotype, the patient could make anti-K, -$Fy^b$, or –M. However, if present these should not have been adsorbed, since the absorbing cell was K negative and ficin treated.*

   *This workup does not prove the identity of the antibody; an antibody directed against another high frequency antigen would also be allo-adsorbed (as long as the antigen was not destroyed by ficin). To prove anti-Jk3 we would like to show that the antibody failed to react with at least 1 and preferably 2 or 3 Jk(a-b-) RBC samples. Nonetheless, given the patient's phenotype, this specificity is highly likely; we can certainly state this is the antibody specificity with greater than 99% confidence, given the rarity of Jk3 negative RBCs.*

   *One would also want to perform a titer. Although there are no standards against which such a titer can be compared, a very high titer, or a significant increase on serial sampling, would prompt measurement of middle cerebral artery blood flow velocity, or even amniocentesis or PUBS, all of which are more specific tests for the presence or absence of fetal hemolysis and anemia.*

3. Does this antibody cause hemolytic transfusion reactions (HTRs)? HDFN?

   *Kidd antibodies cause severe HTRs including some severe delayed hemolytic reactions, but in contrast HDFN is relatively mild and anti-Jk3 has only required phototherapy in a few infants.*

4. How might we find compatible blood for this patient?

   *Test siblings and other blood relatives, or other individuals of Polynesian or Philippine ethnic origin. Also, since the patient's risk for needing transfusion is in the future, she could donate autologous RBCs and have them frozen for future need. Similarly, if her infant required transfusion the frozen cells can be used for the baby.*

5. What is the possible genetic basis of this patient's phenotype?

   *The Kidd blood group system includes 3 antigens, $Jk^a$, $Jk^b$, and Jk3. Family studies show that most Jk(a-b-) phenotypes are inherited on a recessive basis, but there is also a dominant or "inhibitor" form in which Jk antigen expression is decreased. Individuals with inhibitor phenotypes do not form anti-Jk3. There are multiple causes for Jk(a-b-) RBCs on the basis of different mutations, including one occurring in Finns. The most common Polynesian mutation causes loss of one exon.*

6. What is the biochemical nature of the antigen? Are there any health consequences of this phenotype?

   *The Jk antigens are carried by the urea transport protein, which traverses the membrane 10 times. The $Jk^a/Jk^b$ polymorphism is due to a single amino acid substitution. Water reclamation by the kidneys is dependent on urea transport, and Jk3 negative individuals cannot maximally concentrate their urine.*