HEMOLYTIC TRANSFUSION REACTION DUE TO ANTI-Di\textsuperscript{b} 
ANSWERS

1. What is the differential diagnosis of a pan-agglutinin, an antibody that reacts with all allogeneic RBCs tested?

Agglutination of all (or most) allogeneic RBC samples suggests the presence of an autoantibody, an alloantibody directed against a high frequency antigen, or the presence of multiple antibodies. A negative DAT suggests one of the latter two possibilities. Variation in the strength or phase of reactivity suggests a mixture of antibodies. In this case the demonstration of anti-Di\textsuperscript{b} was consistent with the patient’s apparent ancestry, as Hispanic-surnamed individuals in the United States often are from Central or South America where the Di\textsuperscript{b} negative phenotype is more common.

2. How might one attempt to find blood for this patient in an emergency? Over the long term? (Hint: What is the significance of her ethnicity?)

When confronted with a need for transfusion in a patient with an antibody directed against a high frequency antigen there are generally four potential sources of compatible RBCs. If transfusion is urgent family members, particularly siblings, may be tested for compatibility and a rare donor registry can be contacted. In this case family members were not compatible with the patient’s antibody. The local blood center contacted the American Rare Donor Program (ARDP) which identified the one unit of Di\textsuperscript{b} negative RBCs which was transfused. Compatible blood may also be obtained from the patient him or herself. Red blood cell salvage can be performed during many operations and even in trauma surgery. When there is time to prepare the patient can deposit his or her own blood prior to surgery, or even in pregnancy. In the latter case the RBCs can be frozen in advance of need. Patients and families have created frozen supplies of rare units through the ARDP which are available for themselves or for others through the program. Finally, blood donor drives can be targeted to specific populations in which high frequency antigen negative RBCs are more common. In this case an appeal was made to Native Americans; 130 individuals responded, but none were found to be Di\textsuperscript{b} negative.

3. What manifestations of a hemolytic transfusion reaction did this patient present? Is there anything else that might have been done? What treatment might be available for this patient in the future?

No obvious signs or symptoms of an immediate hemolytic transfusion reaction (IHTR) were evident, and the hematocrit determined on the morning of the 8th hospital day at the end of transfusion of the 3rd unit of incompatible blood, had increased to 10.1 gm/dL. Of note, however, the prothrombin and partial thromboplastin times (PT and PTT) were elevated at 21 and 68 seconds, and the patient’s creatinine level, which had previously been at the upper limit of normal, had increased from 1.5 to 2.9 mg/dL. By the following morning hemolysis was evident as the hemoglobin level had fallen to 7.9 gm/dL. Bilirubin, haptoglobin, and plasma free hemoglobin levels were all normal one day after completion of the incompatible transfusion, but the LDH level was very elevated and renal function had deteriorated further. Of note, the platelet count dropped to 85,000. Together with the abnormal clotting times this suggests the presence of a consumption coagulopathy.

In summary, the patient showed multiple manifestations of a hemolytic transfusion reaction including a falling hematocrit increased LDH, consumption coagulopathy, and worsening renal failure. The patient had abnormal renal function on admission, presumably due to her longstanding and severe diabetes, and the hemorrhagic shock which necessitated the transfusion may well have contributed, but the latter was relatively short lived. Hemolysis appears to have been largely by the “intravascular” mechanism on the basis of the haptoglobin and plasma free hemoglobin measurements.
With hindsight one might wish that the blood removed from her thorax could have been collected, washed, and the RBCs immediately re-infused, but this would have required superhuman forethought and immediate coordination among clinical and laboratory services.

In the future hemoglobin-based oxygen carriers, or some other form of oxygen carrying agent, may be available to tide such a patient over until compatible RBCs can be found.