our knowledge, this is only the nth time in indexed English language literature that. . . ."

CONFLICT OF INTEREST

The author declares that he has no conflicts of interest relevant to the manuscript submitted to **TRANSFUSION**.

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Therapeutic plasma exchange for massive anti-JK3–mediated hemolysis

The Kidd (Jk) antigens, Jk^a and Jk^b, are located on the urea transporter, which is expressed on red blood cells (RBCs) and renal endothelium. Numerous Jk^{null} alleles associated with a Jk(a–b–) phenotype have been described.[1] The null phenotype is rare in most ethnicities, with the exception of Polynesians whose prevalence is 0.9%.[2] After RBC transfusion, individuals with a Jk(a–b–) phenotype are at risk of developing anti-Jk3, an alloantibody that reacts against both Jk^a and Jk^b antigens. Anti-Jk3 is clinically significant and causes severe acute or delayed hemolytic transfusion reactions resulting in the release of free hemoglobin (fHb) into the plasma.[3] Although haptoglobin combines with fHb to create a complex that is not filtered by the kidneys, once plasma fHb exceeds the binding capacity of haptoglobin, it causes kidney toxicity. fHb scavenges nitric oxide causing vasoconstriction and impaired tissue perfusion resulting in organ damage. In addition, fHb and its catabolic products generate reactive oxygen species in renal tubules causing acute renal injury.[4] Removing fHb may help restore organ perfusion and preserve kidney function. We report the case of a patient with an anamnestic anti-Jk3 who received 9 units of incompatible RBCs. Emergent therapeutic plasma exchange (TPE) was performed to remove plasma fHb.

The patient was a 66-year-old Filipino male who underwent transoral incisionless fundoplication followed by exploratory laparotomy, gastrotomy, and hematoma evacuation for bleeding complications at another institution. His initial antibody screen was negative and he received a total of 6 units of RBCs during hospitalization. He was discharged on Hospital Day 6, but returned a few hours later complaining of fever. His Hb at readmission was 7.2 g/dL. Repeat serologic workup now showed pan-reactivity (2+ at anti-human globulin) with a positive direct antiglobulin test (DAT; 1+ for immunoglobulin G and C3d). An eluate was also pan-reactive. Although these results were consistent with a warm autoantibody, the timing was suspect for a delayed hemolytic transfusion reaction. The following morning his Hb had decreased to 5.4 g/dL. The patient now had symptomatic anemia and was transfused with 3 units of least incompatible RBCs. Shortly thereafter, he developed acute dyspnea and hypoxia requiring intubation.

A veteran blood bank technologist phenotyped his pretransfusion sample and noted that he was negative for Jk^a and Jk^b. She believed that he had an amnestic anti-Jk3 based on his ethnicity and clinical history. According to his family, he had received 1 unit of RBCs 5 years earlier. Fortuitously, a donor known to be Jk(a–b–) had just given 2 units of RBCs at the local donor center. The patient's plasma was fully cross-match compatible with these units.

The patient decompensated quickly and was brought by air ambulance to our hospital. Repeat blood bank workup confirmed serologic pan-reactivity with a positive DAT. Initial laboratory analyses were consistent with hemolytic anemia and are shown in Table 1. We performed three daily TPE procedures, exchanging 1.0 plasma volume with thawed plasma, in an attempt to acutely decrease fHb. Thawed plasma was chosen as the replacement fluid to replenish haptoglobin. Figure 1 shows the patient's discarded plasma from each of the three TPE procedures. Daily evaluations of pertinent laboratory values are reported in Table 1. The plasma fHb normalized after the third TPE. The patient required dialysis for several months; however, he has since made a full recovery and is back to his baseline state of health. Should the patient require transfusions in the future there are several frozen RBC units, collected from Hawaiian Jk(a–b–) donors, in storage at our blood supplier's regional facility.

TABLE 1. Laboratory values from treating facility

Variable	Admission	Post-TPE 1*	Post-TPE 2	Post-TPE 3	Reference
Hb (g/dL)	5.8	8.9	7.6	8.8	13.5-17.0
Plasma fHb (mg/dL)	320	90	60	<30	≤40
Haptoglobin (mg/dL)	8	†	5	21	33-271
Lactate dehydrogenase (IU/L)	2565	†	†	531	120-240
Total bilirubin (mg/dL)	4.1	†	†	1.3	0.4-1.4
Direct bilirubin (mg/dL)	2.1	†	†	0.3	0.1-0.3
Blood urea nitrogen (mg/dL)	39	73	81	87	5-22
Creatinine (mg/dL)	2.5	5.2	6.0	7.6	0.7-1.3

* Post-TPE samples were collected the morning after each procedure.
† Testing was not performed at this time.

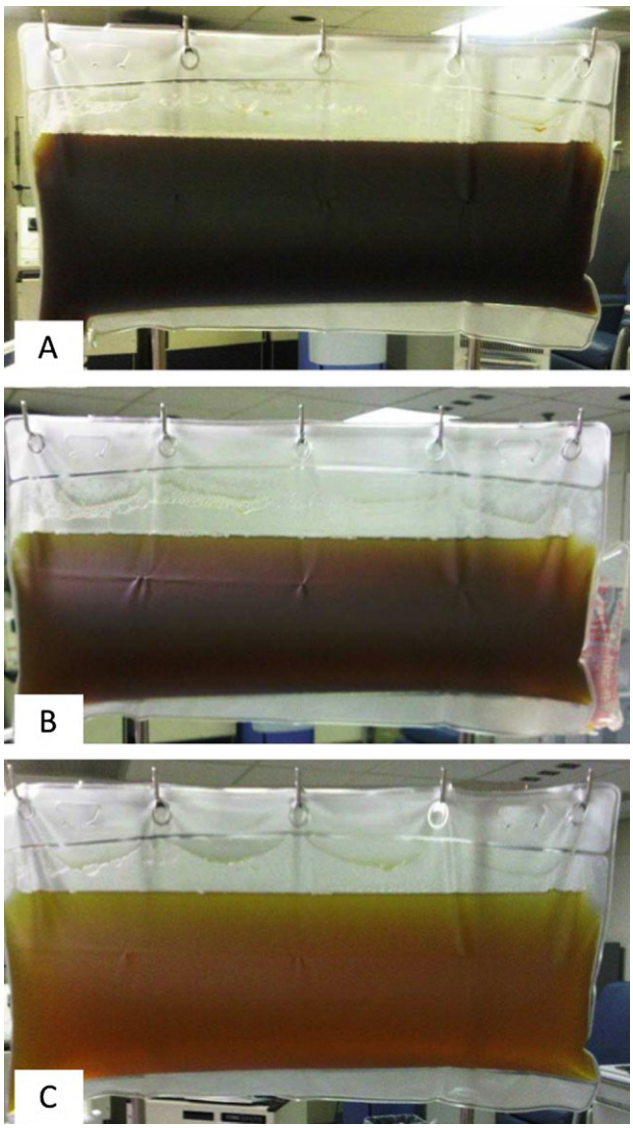

Fig. 1. The patient's plasma that was removed during TPE was dark and tea-colored but lightened considerably with subsequent exchanges. The figure shows removed plasma following the first (A), second (B), and third (C) TPE procedures.

This case illustrates the potential benefit of utilizing TPE in patients with critically high levels of plasma fHb due to massive hemolysis secondary to acute and delayed hemolytic transfusion reactions. Rapid mechanical removal and neutralization of fHb by TPE with plasma replacement may minimize the detrimental clinical effects of fHb by restoring tissue perfusion and limiting the degree of renal injury.[5]

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In search of plentiful universal donor plasma: what might Landsteiner say?

Since the US military experience with aggressive plasma transfusion heralded a new ratio-driven massive transfusion protocol (MTP),[1] subsequently endorsed by an evidence-based review,[2] many transfusion services in the United States have adopted up-front plasma transfusion as part of an institutional MTP. Thawed plasma is widely used for this purpose, and group AB plasma is in great demand since blood component resuscitation in severely injured patients precedes ABO group determination.

Simultaneously, blood centers have adopted strategies to reduce the risk of transfusion-related acute lung injury (TRALI), often by deferring multiparous women from donating plasma for transfusion. This effort has been successful in TRALI mitigation. However, since group AB plasma is in great demand, such mitigation strategies typically exclude group AB donors. A recent study shows that residual TRALI cases disproportionately implicate AB plasma.[3]

A prospective randomized trial studying different plasma:platelet (PLT):red blood cell ratios in MTP is under way. Until the results of this trial are available, the demand for universal donor plasma will continue. In this context, it has been proposed that group A plasma may be seen as "universal plasma" in MTP protocols. In one trauma center[4] with extensive helicopter transport to rural areas, group A plasma has been transfused as the emergency-release "universal" plasma since 2008 during air transport using predefined criteria. Another group found that two-thirds of 100 group A blood donors screened had an anti-B titer less than 64 and proposed that such "low-titer" group A plasma may be explored as universal plasma.[5]

A recent review in **TRANSFUSION**[6] advocates for low-titer group O whole blood in the military environment and eloquently summarizes the risk of hemolysis from the transfusion of blood components containing ABO-incompatible plasma in the context of PLT transfusion. While most such hemolytic reactions have occurred when group O PLTs are transfused to group A patients, severe reactions have been reported when PLTs from a group A donor with a particularly high anti-B titer were transfused to two different patients.[7] In addition, the prevalence of group B patients may be higher than 11% in large urban Level I trauma centers in the United States serving a high proportion of nonwhite populations.

Another approach to providing plasma up-front for trauma resuscitation is the possibility of rapidly determining a patient's ABO group at the bedside, an area that does not appear to have been emphasized. Bedside ABO agglutination tests as the final blood administration safety check have been used in some jurisdictions, notably France.[8] A point-of-care method for Rh(D) typing was evaluated in the United States, although not ultimately approved.[9] Perhaps the development of a bedside ABO point-of-care test in the civilian prehospital setting—where other point-of-care tests are already being used[4]—would complement the options available to blood centers and transfusion services contemplating the imbalance between the supply and demand of group AB plasma.

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