

Editorials

The present and future crossmatch

The crossmatch has been used as the final phase of pretransfusion testing for over half a century.¹ However, during this time, there have been frequent modifications of the procedure, as well as differences of opinion as to the extent of its performance. In recent years, modifications have focused on its abbreviation.

When the American Association of Blood Banks first published its standards in 1958, the crossmatch was described in relatively broad terms. The major crossmatch was specifically required, while the minor crossmatch was characterized as an optional test. The latter never has been a required procedure, although the tendency of many transfusionists to "wear a belt with their suspenders" was illustrated by their reluctance to part with it.² In addition, the major crossmatch was mandated to include two methods: one to demonstrate "serum or saline active" antibodies and the other to detect "incomplete or blocking" antibodies. An appendix to that edition of the standards specified the use of albumin and the indirect antiglobulin test. It must be recalled that this edition predated the general adoption of pretransfusion screening for unexpected antibodies in recipient serum, a procedure that had been introduced almost a decade before.³

By 1962, the standards declared that the antiglobulin phase of the crossmatch was optional, depending upon its inclusion in the antibody screening test. This seemingly casual approach was solidified in the 1970 edition, as demonstration of "agglutinating and coating antibodies" was required, as was performance of an antiglobulin test. The pendulum then swung to a more permissive approach to the crossmatch so that, first, only "significant" and later, "clinically significant" antibodies had to be detected. By 1984, the requirement for routine use of an antiglobulin test was rescinded unless "clinically significant unexpected antibodies were detectable" in the patient's serum.

This change was based on a philosophical modification of the test's purpose. Whereas the crossmatch originally had the dual purpose of providing final verification

of ABO compatibility and detecting unexpected antibodies unrecognized by the antibody screening test, in the revised edition, the latter function was eliminated. This change was permitted by the demonstration of the rarity of detection of clinically significant unexpected antibodies, that were unrecognized by the antibody screening test, by a crossmatch that incorporated an antiglobulin test.⁴⁻⁶ Therefore, the fundamental purpose of the crossmatch currently is to prevent potentially life-threatening acute hemolytic transfusion reactions due to the transfusion of ABO-incompatible red cells.

Elimination of room-temperature incubation of the mixture of the patient's serum with red cells from the donor unit, as well as of antiglobulin testing, resulted in the idiomatic expression "immediate-spin crossmatch." It was acknowledged that there would be instances wherein weakly reactive antibodies, or antibodies against rare antigenic specificities, would be undetected by this procedural modification, and yet these antibodies would be unlikely to result in significant patient morbidity.

While the immediate-spin crossmatch is relied on for final confirmation of ABO compatibility, on rare occasion it has failed this mission. This has occurred because of the combination of a weak ABO antibody in the serum of a patient with donor red cells that represent an incompatible subgroup of A.^{7,8} In even rarer instances, a false-negative immediate-spin crossmatch may result from a prozone phenomenon in tests incorporating very potent ABO antibodies. This can be circumvented by suspending the test red cells in EDTA.⁹ In addition, ABO incompatibility will not be detected by the immediate-spin crossmatch in an infant with weak anti-A or anti-B that reacts only in the antiglobulin test. Transfusion of group O red cells to such infants avoids that situation. It is conceivable that other patients with weakly reactive anti-A or anti-B may be unable to manifest *in vitro* ABO incompatibility.

As was originally anticipated, there have been, during the past decade, isolated instances of unexpected antibodies that eluded detection until they were implicated

in hemolytic transfusion reactions;^{10,11} the reactions were usually of the delayed type, although none were fatal. The article by Pinkerton and his colleagues,¹² in this issue of **TRANSFUSION**, places this issue in proper perspective. It is particularly useful in that it separates those undetected antibodies that had clinical manifestations from those that merely proved to be serologic annoyances. The undetected antibodies that resulted in clinically evident delayed hemolytic transfusion reactions would not have been detected with more extensive pretransfusion testing. While the authors utilized a three-cell screening test, the important considerations are the representation of antigenic specificities on the screening cells and the utilization of a test method that will allow the detection of the majority of clinically significant red cell antibodies, regardless of the number of test cells employed.

In reviewing studies such as the one by Pinkerton and colleagues, one must take care to note the frequency of delayed hemolytic transfusion reactions. Patients with such reactions fail to have the desired hemoglobin increment following a transfusion and may require additional transfusions, which subjects them to increased risk of posttransfusion disease. Only three such clinically manifest reactions occurred over 8 years in the Pinkerton study. While we may consider this to be an acceptably uncommon occurrence, what level of risk is unacceptable to our patients?

The immediate-spin crossmatch has facilitated the ability of transfusion services to respond to the demands of massive transfusions, especially for such surgical procedures as liver transplantation or thoracoabdominal aneurysmectomy. In addition, it may be contended that enhanced speed of blood issuance resulting from the contraction of pretransfusion testing has actually saved lives. Therefore, this has been another area of transfusion medicine wherein the benefits of procedural revision had to be weighed against potential risk to the patient. Although there have been numerous affirmations of the procedure's safety and benefits to patient care, many transfusion services continue to be reluctant to adopt it.^{13,14}

At this time, only testing to detect ABO incompatibility is required of a major crossmatch before a transfusion is given to a patient who lacks or has lacked clinically significant unexpected antibodies.¹⁵ Recent efforts to abbreviate the procedure further, or even to eliminate the serologic test, have stemmed from demands that blood banks contain costs while expediting the provision of blood. However, these corresponding pressures must not be allowed to compromise patient care. It must be the responsibility of those primarily engaged in this subspecialty to be the guardians of this underlying requirement.

While adoption of the immediate-spin crossmatch has been resisted by the majority of transfusion services in

this country, further modification of the procedure is in the offing. The latest "spin" on complying with pretransfusion test requirements in an expeditious manner utilizes computer verification.^{16,17} The computer crossmatch, or electronic crossmatch, may be inferred to be a logical extension of a concept introduced a decade ago, which linked the elimination of the crossmatch to verification of the documentation of the testing that led to the determination of the ABO type and to the results in an extended antibody screening test.¹⁸

It is doubtful whether the saga of the revision of this procedure will cease at this point. The current crossmatch only verifies work performed in the laboratory; however, provision of erroneous blood to the patient as a result of error on the patient-care unit continues to be the major cause of acute hemolytic transfusion reactions. Accordingly, the need continues for better verification of accuracy in all of the steps leading to the transfusion, beginning with the obtaining of the pretransfusion blood sample from the patient. Therefore, the crossmatch, in an expanded sense, should ensure the likelihood of optimal survival of the transfused red cells in the appropriate patient.

HAROLD A. OBERMAN, MD
Professor of Pathology
Director of Blood Bank and Transfusion Service
University of Michigan Medical Center
1500 East Medical Center Drive
Ann Arbor, MI 48109

References

1. Oberman HA. The crossmatch: a brief historical perspective. *Transfusion* 1981;21:645-51.
2. Garratty G. Abbreviated pretransfusion testing (editorial). *Transfusion* 1986;26:217-9.
3. Bove JR, Cedergren B, Davey RJ, et al. Do you think that the crossmatch with donor red cells can be omitted when the serum of a patient has been tested for the presence of red cell alloantibodies with a cell panel? *Vox Sang* 1982;43:151-68.
4. Oberman HA, Barnes BA, Friedman BA. The risk of abbreviating the major crossmatch in urgent or massive transfusion. *Transfusion* 1978;18:137-41.
5. Oberman HA, Barnes BA, Steiner EA. Role of the crossmatch in testing for serologic incompatibility. *Transfusion* 1982;22:12-6.
6. Mintz PD, Haines AL, Sullivan MF. Incompatible crossmatch following nonreactive antibody detection test. Frequency and cause. *Transfusion* 1982;22:107-10.
7. Lamberson RD, Boral LI, Berry-Dortch S. Limitations of the crossmatch for detection of incompatibility between A2B red blood cells and B patient sera. *Am J Clin Pathol* 1986;86:511-3.
8. Berry-Dortch S, Woodside CH, Boral LI. Limitations of the immediate spin crossmatch when used for detecting ABO incompatibility. *Transfusion* 1985;25:176-8.
9. Judd WJ, Steiner EA, O'Donnell DB, Oberman HA. Discrepancies in reverse ABO typing due to prozone: how safe is the immediate-spin crossmatch? *Transfusion* 1988;28:334-8.
10. Judd WJ, Steiner EA, Abruzzo LV, et al. Anti-i causing acute hemolysis following a negative immediate-spin crossmatch. *Transfusion* 1992;32:572-5.

11. Reznicek MJ, Cordle DG, Strauss RG. A hemolytic reaction implicating Sda antibody missed by immediate spin crossmatch. *Vox Sang* 1992;62:173-5.
12. Pinkerton PH, Coovadia AS, Goldstein J. Frequency of delayed hemolytic transfusion reactions following antibody screening and immediate-spin crossmatching. *Transfusion* 1992;32:814-7.
13. Cordle DG, Strauss RG, Snyder EL, Floss AM. Safety and cost-containment data that advocate abbreviated pretransfusion testing. *Am J Clin Pathol* 1990;94:428-31.
14. Shulman IA. The risk of an overt hemolytic transfusion reaction following the use of an immediate spin crossmatch. *Arch Pathol Lab Med* 1990;114:412-4.
15. Widmann FK, ed. Standards for blood banks and transfusion services. 14th ed. Arlington: American Association of Blood Banks, 1991.
16. Butch SH, Judd WJ, Steiner EA, Stoe M, Oberman HA. The computer crossmatch (abstract #S-11). To be presented at the 45th Annual Meeting of the American Association of Blood Banks, San Francisco, CA, November 1992.
17. Judd WJ. Are there better ways than the crossmatch to demonstrate ABO incompatibility? (editorial). *Transfusion* 1991;31:192-4.
18. Winn LC, Svoboda R, Haffleigh EB, Grumet FC. An extended antibody screen to replace the crossmatch. Presented at the 33rd Annual Meeting of the American Association of Blood Banks, Washington, DC, 1980.