CME/SAM

Pathology Consultation on Electronic Crossmatch

Marshall A. Mazepa, MD, Jay S. Raval, MD, and Yara A Park, MD, for the Education Committee of the Academy of Clinical Laboratory Physicians and Scientists

Department of Pathology and Laboratory Medicine, University of North Carolina, Chapel Hill.

Key Words: Electronic crossmatch; EXM; Crossmatch

Am J Clin Pathol May 2014;141:618-624

DOI: 10.1309/AJCPZRQIPGZ2XU4V

ABSTRACT

Objectives: *The full crossmatch is traditionally the final step in compatibility testing, acting as a serologic double check for ABO compatibility and unexpected RBC antibodies. In this review, we discuss the development of electronic crossmatch (EXM), an approach for determining when EXM can be used, and its strengths and weaknesses.*

Methods: *Because EXM relies on highly sensitive screening assays, antibodies are frequently encountered whose clinical significance must be investigated and interpreted. Our approach is to obtain further history, perform enhanced tube testing, and consider tests of immune reactivity or RBC survival.*

Results: *For those without clinically significant antibodies, we found two alternatives: immediate-spin crossmatch (IS XM) and EXM. IS XM is prone to error related to serologic interference, whereas EXM depends on the accuracy of the sample label, accurate data entry, and informatics to avoid errors.*

Conclusion: *EXM is an alternative to the serologic test in patients who have no clinically significant antibodies.*

Upon completion of this activity you will be able to:

- list the required components of an electronic crossmatch (EXM) system.
- describe the circumstances in which EXM may still be considered in patients with a positive antibody screen and, conversely, describe the circumstances in which EXM may not be appropriate despite a negative antibody screen.
- describe the inherent strengths and weaknesses of EXM compared with immediate-spin crossmatch.

The ASCP is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The ASCP designates this journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit*™ per article. Physicians should claim only the credit commensurate with the extent of their participation in the activity. This activity qualifies as an American Board of Pathology Maintenance of Certification Part II Self-Assessment Module.

The authors of this article and the planning committee members and staff have no relevant financial relationships with commercial interests to disclose.

Questions appear on p 753. Exam is located at www.ascp.org/ajcpcme.

Case Report

A 55-year-old woman with chronic cholecystitis had a preoperative anesthesia appointment for an elective open cholecystectomy. She had no prior history of unexpected RBC antibodies. Routine blood typing and screening were performed in preparation for surgery. The patient was found to be blood type A positive, and the antibody screening result was positive. Further testing identified the presence of an anti-M antibody. Does this patient qualify for electronic crossmatch (EXM)?

Table 1
Compatibility Testing to Ensure Safe Transfusions

Term	Clinical Scenario	ABO Confirmation Method	Test for Unexpected ABO Antibodies
Full XM	(1) Clinically significant RBC antibody identified OR (2) history of clinically significant RBC antibody	Serologic: IS phase	Serologic: IAT phase
IS XM	(1) No clinically significant RBC antibodies on current screen AND (2) no history of clinically significant RBC antibodies	Serologic: IS phase	None
EXM	See IS XM	Computer: Historical ABO type OR Serologic: repeat ABO type (same sample by different tester is acceptable)	None

EXM, electronic crossmatch; IAT, indirect antiglobulin test; IS XM, immediate-spin crossmatch; XM, crossmatch.

Questions

1. What are the required components of an EXM system?
2. What are the circumstances in which EXM may still be considered in patients with a positive antibody screening result?
3. Conversely, what are the circumstances in which EXM may not be appropriate despite a negative antibody screening result?
4. What are the inherent strengths and weaknesses of EXM compared with immediate-spin crossmatch (IS XM)?

Background and History

After performing a review of the patient's historical transfusion record, typing for ABO and Rh(D) antigens, and the RBC antibody screening, the full crossmatch has long been the final step in compatibility testing to ensure safe transfusions. Its purpose is dual: first to serologically confirm ABO compatibility and second to serologically detect unexpected RBC antibodies **Table 1**. The first step of the crossmatch, the immediate spin (IS) phase, is the serologic confirmation of the ABO type: donor RBCs are suspended in a saline agent of choice, which is then added to patient serum or plasma, mixed, and then centrifuged for 15 to 30 seconds. The solution is then resuspended; if agglutination or hemolysis is observed, then an immunoglobulin is present with the capacity to bridge RBCs or fix complement. Most frequently, this is an immunoglobulin M (IgM) and is concerning for ABO mismatch. The second step of the crossmatch, the indirect antiglobulin phase, tests for unexpected RBC antibodies: donor RBCs suspended in a potentiating agent of choice are added to patient serum or plasma and incubated at 37°C to allow any immunoglobulins to coat the donor RBCs. After the incubation, the solution is centrifuged, resuspended, and observed for agglutination or hemolysis. Then the RBCs are washed to remove unbound immunoglobulins, after which antihuman globulin (AHG or Coombs reagent) is added to the washed cells and mixed, centrifuged for 15 to 30 seconds, and resuspended. If agglutination occurs, immunoglobulin G from the patient's serum is likely attached to cognate antigens on the donor RBCs, which are then "bridged" by AHG.

The development of the EXM stemmed from the necessity for rapid transfusion testing in the setting of more complex surgical procedures (eg, trauma with massive blood loss or allogeneic liver transplantation) and the need for cost reduction in the clinical laboratory. To implement an EXM testing system that could satisfactorily serve both functions of the manual test, the system required (1) development of sophisticated informatics to prevent ABO-incompatible whole blood or blood components to be issued to patients, (2) an acceptable alternative double check of ABO compatibility, (3) highly sensitive screening tests for RBC antibodies to obviate the need for a second test of non-ABO compatibility, and (4) relatively low costs to ensure a net savings after the initial investment in the automated testing and informatics systems. For ABO compatibility, duplicate testing and repeat checking of records of both patient and donor was recommended[1]; at the same time, improved methods for detection of unexpected antibodies led to greater sensitivity for antibodies that could previously be only detected during crossmatch. Finally, informatics systems were also developed that could meet the requirements for computer crossmatching at an acceptable cost.

The coalescence of these developments then led to the first proposal to replace the full crossmatch in selected individuals with the EXM. It was introduced at the University of Michigan Hospitals (Ann Arbor) Blood Bank in 1992 after the American Association of Blood Banks (AABB) Committee on Standards granted an exemption to implement EXM.[2] The success of EXM was then demonstrated in 1995 with a report of more than 138,000 EXMs performed without an ABO-incompatible transfusion. Since then, several groups have reported similar success with the EXM, even in developing countries.[3-5]

DOI: 10.1309/AJCPZRQIPGZ2XU4V

Since the initial granting of the exemption for the first use of EXM, the Food and Drug Administration (FDA) has developed guidance for the "computer crossmatch."[6] Although these are nonbinding recommendations, this document provides the "practices that we believe satisfy the requirements in 21 CFR 606.151(c) to help ensure detection of an incompatible crossmatch when using a computerized system for matching a donor's cell type with a recipient's serum or plasma type."[6] The following five key elements initially recommended in the seminal report by Butch et al[2] have remained in place since this original description in the AABB Standards.[7]

The computer system must be validated on site to ensure that only ABO-compatible whole blood or RBC components have been selected for transfusion. Two determinations of the recipient's ABO group are made, one on a current sample and the second by one of the following methods: by retesting the same sample, by testing a second current sample, or by comparison with previous records.

The system contains the donation identification number, component name, ABO group, and Rh type of the component; the confirmation of the unit ABO group; two unique recipient identifiers; recipient ABO group, Rh type, and antibody screen results; and interpretation of compatibility. A method exists to verify correct entry of data before release of blood or blood components. The system contains logic to alert the user to discrepancies between the donor ABO group and Rh type on the unit label and those determined by blood group confirmatory test and to ABO incompatibility between the recipient and the donor unit.

EXM With a Positive Antibody Screening Result: Determining the Clinical Significance of RBC Antibodies

Both AABB Standards and the Guidance on Computer Crossmatch require that the recipient have the absence of clinically significant antibodies both on the current sample and on past record.[6,7] Commonly detected, clinically significant antibodies are thus clear indications for exclusion from the use of EXM (eg, against the Rh, Duffy, and Kidd systems). Other detected RBC antibodies can be placed in two groups: antibodies that are rarely clinically significant (eg, Le^b and Bg^a) or antibodies that are potentially clinically significant (eg, M, N, and Vel).[8] Alternatively, we find it useful to group the remaining antibodies into either possibly clinically insignificant or antibodies of undetermined significance (AUS) **Figure 1**. Commonly occurring antibodies that are usually of possible significance include anti-M, anti-Le^a, anti-Le^b, passive anti-D, warm autoimmune antibodies (WAAs), anti-P_1, and "high titer low avidity" (HTLA) antibodies, whereas we consider

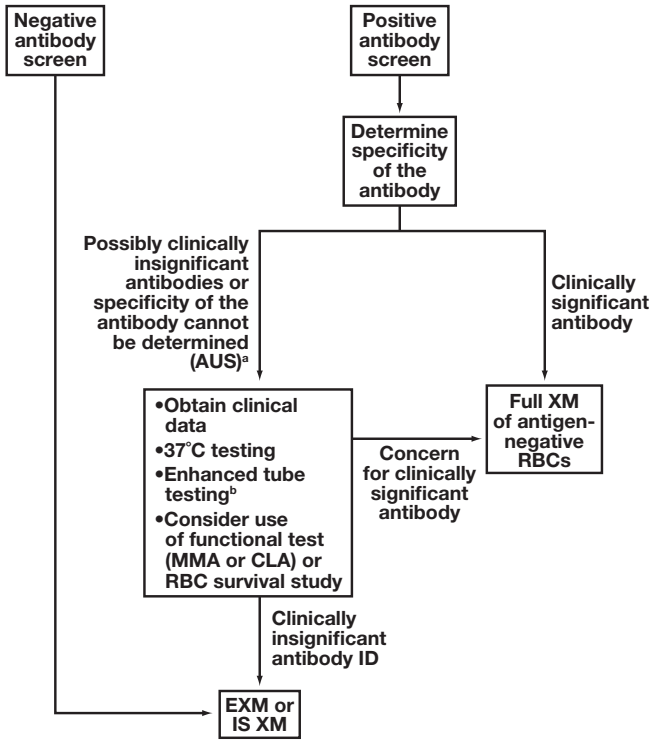

Figure 1 Algorithm for the use of electronic crossmatch (EXM). EXM may be used for patients whose antibody screening result is negative or whose positive antibody screening result is determined to be clinically insignificant. [a]Consider obtaining a second sample several days later for changes in specificity or titer in antibody of undetermined specificity (AUS). [b]Lewis neutralization test for anti-Lewis antibodies or excluding antigen specificity for antigens of known clinical significance with or without low incidence antigen specificity for AUS. CLA, chemiluminescence assay; IS XM, immediate-spin crossmatch; MMA, monocyte monolayer assay.

nonspecific antibodies to be AUS. Importantly, reports of delayed hemolytic transfusion reactions have been reported in both types of antibodies. Although the AABB Standards define a *clinically significant antibody* as an antibody that results in decreased RBC survival,[7] this determination can be challenging to make and is ultimately made by the transfusion service physician.

Highly sensitive screening assays for RBC antibodies have, on one hand, allowed for the elimination of the indirect antiglobulin phase of the full crossmatch in patients with a negative antibody screening result. On the other hand, such assays have also had greater positive results on antibody screening for clinically insignificant antibodies, thus complicating the evaluation of clinical significance of antibodies. The sensitivity for detecting RBC antibodies depends

DOI: 10.1309/AJCPZRQIPGZ2XU4V

on the testing modality, with many centers having adopted the use of the gel microcolumn technique or solid-phase adherence screening assays in place of traditional tube techniques. Automation of these assays offers the advantage of the ability to meet the increasing demands for blood products in modern medicine as well as a more objective interpretation modality. The solid-phase testing modality has been shown to have equivalent sensitivity for clinically significant antibodies at the cost of increased nonspecific reactivity.[9] A recent comparison of gel microcolumn and polyethylene glycol (PEG) tube testing found that, although there were no overall differences in rates of RBC antibody detection ($P \geq .10$), the gel microcolumn technique identified fewer clinically insignificant antibodies (27.6% of positive antibody screens vs 34.8% of positive antibody screens).[10] However, nonspecific antibodies were reported at a much higher frequency with the gel microcolumn assay compared with PEG (3.2% vs 0%).[10] Importantly, these data also reflect the relative frequency with which potentially clinically significant antibodies are detected (>1 in 4 positive antibody screens).

Given that the detection of these antibodies is common and because of their potential to decrease RBC survival or cause overt hemolysis, it is useful to have a strategy to investigate whether the detected antibody is clinically significant or not, with the goal of determining whether the EXM should be used or the crossmatch is required. Our approach is to use both clinical history and enhanced tube testing to gain more evidence for whether the detected antibody is clinically significant (see Figure 1).

Clinical History

The clinical context of the testing often has an important role in determining the significance of the antibody. The transfusion service physician first makes use of the historical transfusion data required by the AABB Standards,[7] that is, whether the patient received a transfusion or was pregnant in the last 3 months and whether this patient has had this antibody previously identified and/or clinical symptoms after transfusion, which would indicate the presence of an acute or delayed hemolytic transfusion reaction. Beyond this first and most critical piece of historical data, review of the patient's medical record or direct communication with the patient's treating physician(s) may also yield critical information in determining the clinical relevance of the antibody. In particular, finding of the administration of anti-D immunoglobulin in an Rh(D)-negative pregnant patient who previously had a negative antibody screening result suggests that passive-D antibodies are identified on such screening as opposed to the development of alloimmune anti-D. Pregnancy is also the time in which patients may develop anti-Le^a or anti-Le^b antibodies; therefore, EXM may still be used at the discretion of the transfusion service physician.

History is also vital in determining the significance of WAAs. Winters et al[10] found WAAs to be the most prevalent clinically insignificant antibody in both PEG and gel microcolumn testing modalities. Although most are clinically insignificant, WAAs cause notable challenges in the detection of underlying clinically significant alloantibodies. If the patient's medical history shows evidence of active hemolysis or autoimmune hemolytic anemia (AIHA), the antibody is likely of critical importance for determining the patient's crossmatch test of choice. In addition, the antibody is important for other testing decisions such as performing an RBC phenotype, direct antiglobulin test, and choice of specialized antibody identification techniques such as adsorptions or elutions. Conversely, a patient with the presence of WAAs without clinical signs of hemolysis could be considered for EXM if underlying alloantibodies can be excluded. Often, weak-reacting WAAs in particular can have alloantibodies excluded after specialized tube testing (eg, use of low ionic strength saline as a potentiator), at which point EXM could be considered. In the case of a more strongly reacting WAA in which simply changing the potentiator is insufficient to completely resolve the WAA's interference, more specialized tube testing may be required (eg, autoadsorption) to exclude underlying antibodies. However, high-potency WAAs will likely yield serologic crossmatch incompatibility with all units, suggesting that a full crossmatch is unlikely to offer any greater assurance of undetected RBC antibodies over EXM. Lee and colleagues[11] reviewed the records of nearly 400 patients with either AIHA or HTLA antibodies in whom over 800 full crossmatches were performed and found that, despite the fact that transfused units were deemed serologically incompatible with full crossmatch, no adverse events were reported. Based on these results, they found that the full crossmatch offered no benefit to these patients over IS XM and suggested that, in patients in whom no underlying alloantibodies were identified, the EXM may be considered.[11]

Enhanced Tube Testing

After obtaining pertinent clinical history, our approach to determining whether the EXM should still be used is to determine the potential clinical significance by investigating the clinical scenario and by performing tube testing, including a minimum testing at body temperature (37°C). We consider the thermal amplitude of the detected antibody to be the test of most singular importance: antibodies that do not react at body temperature have been well studied and found to most frequently have no effect on RBC survival[8]; the caveat is that,

DOI: 10.1309/AJCPZRQIPGZ2XU4V

in rare circumstances, isotype switching after exposure may lead to hemolysis. Most frequently, the test performed at body temperature is the "prewarm" antibody screen, in which the reagents are individually warmed to 37°C before performing tube testing.[12] Warm-reacting antibodies that cause agglutination should raise concern for clinical significance and those that cause hemolysis even more so.

Once warm-reacting, antigen-specific antibodies are excluded, more advanced testing may be considered for determining the likelihood of clinical significance. For example, adding soluble Lewis substance to patient serum may confirm the specificity of antibody by neutralization, which would confirm the presence of only an antibody with low probability of clinical significance. An approach to nonspecific antibodies that react at 37°C is to first exclude antibody specificity to antigens of known clinical significance and then to consider attempting to exclude antigens of low incidence. Nonspecific antibodies, often called *nuisance antibodies*, have become a more common problem since the introduction of gel and solid-phase testing. Importantly, considerable effort is often required to investigate these antibodies, often at what is perceived to be a futile effort; conversely, one may hypothesize that nonspecific antibodies may represent antibodies at the threshold for detection of the assay. The perceived nuisance of these antibodies could actually present clinically relevant antibodies undergoing evanescence or, alternatively, newly emerging clinically significant antibodies. Recently, this hypothesis was investigated by first reviewing the records of patients in whom nonspecific reactivity was initially identified and then identifying whether subsequent testing revealed clinically significant antibodies. This retrospective study found that, among those found to have nonspecific reactivity, a subsequent test revealed the presence of a clinically significant antibody in 15% of repeat samples.[13] This finding suggests that "nuisance" is perhaps too dismissive a term—these antibodies may indeed be harbingers of clinically significant antibodies. An accompanying editorial suggests a systematic approach encompassing thermal amplitude testing, enhanced tube testing, assessment of specificity for low-incidence antigens, patient interviews, and collection of a sample several days later for changes in specificity.[14]

Finally, antibodies determined to have specificity against high-incidence antigens are particularly challenging. Both determining the antigen specificity and then attempting to acquire rare RBC units that lack the high-incidence antigens are resource consuming. Furthermore, the clinical significance of these antibodies may either be unknown, given their rare nature, or thought to be of little clinical significance. Thus, in vitro tests of the immune response anticipated in the patient, such as monocyte monolayer assay and the chemiluminescence test, may be considered (available in reference laboratories only). The 20-year experience using the monocyte monolayer assay found that using a cutoff of 5% or less to define a negative test result could safely predict transfusion of incompatible blood without an overt hemolytic transfusion reaction, but the RBC survival time may be compromised.[15] Another alternative is to consider an RBC survival study of Cr^{51}-labeled RBCs, which may provide further insight into the clinical significance of the detected antibody. However, this test is rarely performed because it is rarely requested, and therefore most nuclear medicine departments lack expertise in performing the test.

When EXM Should Not Be Relied on Despite a Negative RBC Antibody Screening Result

The evanescence of non-ABO blood group antibodies presents a significant challenge in preventing morbidity and mortality associated with transfusion. If a prior immunization event occurred but the antibody screening result is negative, there is false reassurance about the risk for delayed (or, less frequently, acute) hemolytic transfusion reactions. After the transfusion of cells that express an RBC to which the recipient was previously immunized, an anamnestic increase in the pathogenic antibodies would then lead to hemolysis of the transfused cells. Therefore, if a historical clinically significant RBC antibody is identified, the EXM may not be used, even in the presence of a currently negative antibody screening result. In the testing of the ABO/Rh(D) type of the patient, the FDA guidance also notes that an EXM should not be relied upon if an ABO discrepancy exists.[6]

Strengths and Weaknesses of EXM

Based on AABB Standards, in a patient with an antibody screening result that is negative for clinically significant antibodies, at a minimum, a test of ABO incompatibility must be performed: either an IS XM or EXM (see table).[7] Each of these methods has strengths and weaknesses that should be considered when deciding between them. The IS XM consists of a single phase, in which donor RBCs are added to patient serum and mixed, then centrifuged for 15 to 30 seconds, and then resuspended, as in the IS phase of the full crossmatch. Practically, this is a serologic confirmation of ABO compatibility.

Many of the advantages of the implementation of EXM come at the level of the laboratory as whole: a reduction in stress and workload of the laboratory staff, reduced handling of biohazardous materials, cost savings, reduced risk for human error in ABO incompatibility, reduced sample volume requirement, and, most importantly, reduced turnaround time.[16] Disadvantages of EXM include the requirement to repeat ABO typing, initial investment in automation and

DOI: 10.1309/AJCPZRQIPGZ2XU4V

informatics, and the complexity of manipulating the system during downtime.[16] Importantly, although IS XM is considered equivalent to and transposable with EXM, it is important to recall that serologic testing depends on the use of proper technique[17] and the reliability of the interaction between donor antigens and recipient immunoglobulins. For example, false-negative IS XMs have been reported because of the prozone phenomenon,[18] and false-positive IS XMs occur in the presence of interfering immunoglobulins, such as cold agglutinins, or with rouleaux.[19] Because of these inherent weaknesses of the IS XM, some have hypothesized that the XM may be safer than the IS XM.[20] Therefore, in institutions with high transfusion volumes, a need for rapid turnaround time for high-risk surgical or trauma patients, and where the initial capital investment is feasible, the IS XM has essentially been replaced by the EXM.

One final, but notable, problem that is common to all of the current crossmatch tests as they are currently implemented is that the second ABO type needs to be performed on the same patient sample. Although this ensures against laboratory error in the blood bank or transfusion service, it does not ensure that the label correctly identifies the sample. The phenomenon known as "wrong blood in tube" has recently been reported as a cause for ABO-incompatible transfusions, drawing light onto this issue.[21-23] Historical ABO typing offers protection against this error. However, in patients who have never been ABO typed by the blood bank or transfusion service receiving the sample, the wrong blood in tube problem is possible; this is true regardless of whether the sample is collected in an error-prone setting or by a distracted health care provider, both of which are common in modern medicine. Introduction of a check-type sample, which again increases workload to a small degree, offers enhanced protection against the wrong blood in the tube, although this additional sample is not currently required by the AABB or FDA.[24]

Case Summary and Conclusion

In determining the pretransfusion testing strategy for the present case, we first determined that the anti-M antibody is typically a clinically insignificant antibody. The patient did not receive a transfusion nor was she pregnant in the preceding 3 months. She reported two prior pregnancies and no prior blood transfusions as potential immunizing events. Testing was then performed at 37°C, which confirmed the presence of a cold-reacting antibody (not agglutinating at body temperature), likely a naturally occurring IgM antibody of no clinical significance. This patient was deemed appropriate for EXM, and 1 unit of RBCs was ultimately issued and transfused to the patient without evidence of hemolysis or shortened RBC survival after the transfusion.

In summary, the demands for rapid turnaround time, increased blood product utilization, and cost reduction pressure ultimately resulted in the widespread implementation of EXM. The five key elements first described in the seminal report still hold true as requirements for the EXM system by AABB Standards. For EXM to be used in a specific patient, he or she must not have a clinically significant antibody identified either previously on history or on the current antibody screen. In the presence of an ABO discrepancy, the use of EXM is not recommended. Highly sensitive screening modalities were a requirement for the EXM to replace the full crossmatch because the EXM serves as a double check for both ABO compatibility and non-ABO antibodies. The enhanced screening modalities lead to the challenge of determining the clinical significance of antibodies that are identified. We use a system of gathering clinical history, "prewarm" testing, and enhanced tube testing to further determine an estimation of clinical significance and consider specialized testing in particularly challenging cases. Finally, EXM has largely replaced IS XM because of its efficiency and cost benefits to the laboratory as a whole, and serologic testing is confined to samples of patients with complex transfusion needs. Notably, the primary disadvantage of EXM comes in its reliance on automation, informatics, and up-front capital investment. The current safeguards of the EXM system provide excellent protection against ABO incompatibility; however, recent attention to the wrong blood in tube phenomenon has led some institutions to implement a check-type sample in patients who lack historical ABO types in that blood bank or transfusion service, which is currently not a requirement by accrediting and regulatory bodies.

Address reprint requests to Dr Mazepa: 101 Manning Dr, Memorial Hospital, 1021 East Wing, Campus Box 7525, Chapel Hill, NC 27599; mmazepa@unch.unc.edu.

References

1. Svoboda R. Passing the crossmatch by screening antibodies. *Lab World*. 1981;32:26-32.
2. Butch SH, Judd WJ, Steiner EA, et al. Electronic verification of donor-recipient compatibility: the computer crossmatch. *Transfusion*. 1994;34:105-109.
3. Arslan O. Donors' blood group declaration before donation can be used as a tool for electronic crossmatching. *Transfus Med*. 2005;15:487-492.
4. Chan AH, Chan JC, Wong LY, et al. From maximum surgical blood ordering schedule to unlimited computer crossmatching: evolution of blood transfusion for surgical patients at a tertiary hospital in Hong Kong. *Transfus Med*. 1996;6:121-124.
5. Kuriyan M, Fox E. Pretransfusion testing without serologic crossmatch: approaches to ensure patient safety. *Vox Sang*. 2000;78:113-118.

DOI: 10.1309/AJCPZRQIPGZ2XU4V

6. US Food and Drug Administration. Guidance for industry: "computer crossmatch" (computerized analysis of the compatibility between the donor's cell type and the recipient's serum or plasma type). Silver Spring, MD: US Food and Drug Administration; 2011.
7. Carson TH, ed. *Standards for Blood Banks and Transfusion Services*. 28th ed. Bethesda, MD: AABB; 2012.
8. Garratty G. Evaluating the clinical significance of blood group alloantibodies that are causing problems in pretransfusion testing. *Vox Sang*. 1998;74(S2):285-290.
9. Yamada C, Serrano-Rahman L, Vasovic LV, et al. Antibody identification using both automated solid-phase red cell adherence assay and a tube polyethylene glycol antiglobulin method. *Transfusion*. 2008;48:1693-1698.
10. Winters JL, Richa EM, Bryant SC, et al. Polyethylene glycol antiglobulin tube versus gel microcolumn: influence on the incidence of delayed hemolytic transfusion reactions and delayed serologic transfusion reactions. *Transfusion*. 2010;50:1444-1452.
11. Lee E, Redman M, Burgess G, et al. Do patients with autoantibodies or clinically insignificant alloantibodies require an indirect antiglobulin test crossmatch? *Transfusion*. 2007;47:1290-1295.
12. Roback JD, Grossman BJ, Harris T, et al, eds. *Technical Manual*. 17th ed. Bethesda, MD: AABB; 2011.
13. Liu C, Grossman BJ. Antibody of undetermined specificity: frequency, laboratory features, and natural history. *Transfusion*. 2013;53:931-938.
14. Tormey CA, Hendrickson JE. Antibodies of undetermined significance: nuisance or near miss? *Transfusion*. 2013;53:926-928.
15. Arndt PA, Garratty G. A retrospective analysis of the value of monocyte monolayer assay results for predicting the clinical significance of blood group alloantibodies. *Transfusion*. 2004;44:1273-1281.
16. Arslan O. Electronic crossmatching. *Transfus Med Rev*. 2006;20:75-79.
17. Shulman IA, Calderon C. Effect of delayed centrifugation or reading on the detection of ABO incompatibility by the immediate-spin crossmatch. *Transfusion*. 1991;31:197-200.
18. Judd WJ, Steiner EA, O'Donnell DB, et al Discrepancies in reverse ABO typing due to prozone: how safe is the immediate-spin crossmatch? *Transfusion*. 1988;28:334-338.
19. Meyer EA, Shulman IA. The sensitivity and specificity of the immediate-spin crossmatch. *Transfusion*. 1989;29:99-102.
20. Chapman JF, Milkins C, Voak D. The computer crossmatch: a safe alternative to the serological crossmatch. *Transfus Med*. 2000;10:251-256.
21. Dzik WS, Beckman N, Selleng K, et al. Errors in patient specimen collection: application of statistical process control. *Transfusion*. 2008;48:2143-2151.
22. MacIvor D, Triulzi DJ, Yazer MH. Enhanced detection of blood bank sample collection errors with a centralized patient database. *Transfusion*. 2009;49:40-43.
23. Varey A, Tinegate H, Robertson J, et al. Factors predisposing to wrong blood in tube incidents: a year's experience in the North East of England [published online ahead of print July 3, 2013]. *Transfus Med*. 2013.
24. Figueroa PI, Ziman A, Wheeler C, et al. Nearly two decades using the check-type to prevent ABO incompatible transfusions: one institution's experience. *Am J Clin Pathol*. 2006;126:422-426.

DOI: 10.1309/AJCPZRQIPGZ2XU4V