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Compatibility testing - past, present, and future

George Garratty

Landsteiner described ABO groups in 1901, but it was almost another decade before it was applied to compatibility testing in the U.S.^{1,2} By 1920, donor and recipient ABO types were determined and patient serum was incubated with saline-suspended donor RBCs at room temperature (RT).^{1,2} Tests were read for hemolysis and agglutination (major crossmatch). In the U.S. a minor crossmatch was also often performed (donor plasma + recipient RBCs). In 1940, Rh was described and crossmatch tests were used at 37°C in addition to RT. In 1945, the use of albumin-suspended RBCs became popular in the U.S. for detection of non-agglutinating antibodies (e.g., Rh).^{1,2} In the same year in the UK, the antiglobulin test (AGT) was described and used for crossmatching. The U.S. did not use the AGT routinely until approximately 1960.^{1,2} In the 1950s and 1960s, many new blood group antigen/antibodies were discovered and the philosophy was to use tests that would detect all antibodies, identify them, and select donors who lacked the putative antigens. From approximately 1976, suggestions were made to abbreviate compatibility testing.^{3,4} Minor crossmatch and crossmatching at room temperature (RT) were shown to have very little clinical value and were gradually deleted from the crossmatch. In the 1970s, use of low ionic strength solutions (LISS) became popular and 37°C incubation times were reduced from 30-60 min. to 10-15 min. In the late 1970s the type and screen (T&S) approach (if antibody screen is negative, no AGT is required in crossmatch) became popular for surgical procedures that did not usually require > 1 unit of RBCs.^{5,6} In the early 1980s after a great deal of controversy, this approach was accepted for all patients, and over the next decade became the most popular approach used in the U.S. The risk of not detecting an antibody (that would be detected by crossmatching) by the antibody screen was estimated to be about 1 per 11 000 crossmatches;⁷⁻¹³ however, when results of using this approach for some years were analyzed risk to the patient was found to be much lower.¹⁴ Data from 20 hospitals in the US, where

blood for transfusions was issued based on 1.3 million negative antibody screens and only an immediate spin crossmatch showed that only five acute, overt hemolytic transfusion reactions occurred: a risk of 1 per 260,000 crossmatches.¹⁴ Thus, in the 1990s the philosophy was to detect only antibodies that had potential clinical importance and to base approaches on cost-benefit-risk calculations.

The major changes occurring in the new century involve computerization and automation. In 1993, AABB standards allowed blood to be issued for transfusion with no serologic crossmatch. If the antibody screen is negative, the blood can be issued using a computer to match the history of donor and recipient ABO and Rh types, and the results of the antibody screen—a so-called computer crossmatch.¹⁵⁻¹⁷ Although this approach is allowed, it has not become popular in the U.S. because of the extensive validation that is required (<20% of hospitals use a computer crossmatch).¹⁵ Automation suitable for hospital laboratories is available and is slowly being used by larger hospitals in the U.S.^{18,19} The future will undoubtedly involve an automated compatibility test. It will probably be composed of an ABO/Rh typing, antibody screen integrated with a computer-generated crossmatch/issue.

In the future, there is a possibility that universal donor/stealth RBCs will be available for transfusion.²⁰ Successful clinical trials have already taken place to show that group B RBCs that have been converted to group O by in vitro treatment with galactosidases (e.g., made from coffee beans) survive normally in recipients. There has been more of a problem with obtaining suitable N-acetylgalactosidases for converting group A RBCs to group O, but clinical trials of group A RBCs converted to group O are soon to take place. Another approach has been to block all RBC antigens on donor RBCs by covalently bonding polyethylene glycol (PEG) to the RBCs.²¹ Such RBCs may not react with any blood group antibodies (including anti-A or anti-B) and may not be immunogenic. If such RBCs do well in clinical trials, compatibility testing may not be essential in the future, but this is more than 10 years into the future.

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