Is it time to give up the crossmatch?

J P Wallis

Blood groups A, B, and O were described by Landsteiner in 1901 and the serological crossmatch between the blood donor and the recipient, as a means of preventing ABO incompatibility, was first described by Ottenberg in 1908. In 1941, Rh antibodies were found to be the cause of haemolytic disease of the newborn. The earliest detected forms of anti-D antibodies were very strong and found by saline agglutination. The clinical importance of the discovery quickly led to the development by Coombs and others of the antiglobulin test. In what might be regarded in retrospect as a golden age of red blood cell serology, discovery of other clinically important red cell antigens followed quickly.

Extra effort was then put into the crossmatch, aimed at detection of atypical antibodies, with the result that by the 1960s red blood cell transfusions were being given only after extensive crossmatching performed in saline, at room temperature and body temperature, by enzyme methods, by albumin addition, and by the indirect antiglobulin test. Over the subsequent two decades there has been a slow but steady serological retreat until by the 1990s most laboratories were concentrating on a well performed indirect antiglobulin test alone for the detection of both atypical antibodies and ABO incompatibility.

If we consider the role of the crossmatch as a test for atypical antibodies it is clear that it has limitations. The donor cells, of varying age, are stored at varying haematocrit in a small plastic tag and usually diluted by eye to roughly the right cell concentration. The test is then performed once only and without a positive control.

When serologists were happy that all clinically important red blood cell antigens had been recognised it was possible to choose a red blood cell screening panel that covered all the important antigens and to test for atypical antibodies using these cells rather than donor cells. This logical step was first described by Grove-Rasmussen in 1964. In comparison with the crossmatch, the atypical antibody screen uses carefully chosen cells, optimally diluted, and stored in a preservative solution. It can and should be routinely controlled, preferably with every batch performed, by inclusion of a control antibody such as a weak anti-D.

Technically, the crossmatch is a poor substitute for a well performed antibody screen. Its benefits are that it acts as a double check, should the screen have been performed badly or misread, and that it might pick up antibodies to antigens present on the donor red blood cells but not present on the screening cells. As serologists became confident in the atypical antibody screen, it was possible to revert to the use of the crossmatch for the detection of ABO mismatch alone, the so-called “Quick spin crossmatch”. Large studies of Quick spin crossmatch techniques have confirmed that when the antiglobulin phase of the crossmatch is omitted few, if any, unexpected reactions occur. Those that do are rarely recorded to be of clinical relevance. Schulman, in a postal survey, also noted that most haemolytic reactions occurring after a Quick spin crossmatch were because of missed positives in the antibody screen rather than recipient antibodies to rare donor antigens not present on the screening cells. Despite these findings, most blood banks in the UK still perform an indirect antiglobulin test as part of a crossmatch. Notwithstanding, theory and practice point in the same direction. We can rely on the atypical antibody screen, as long as it is well performed, well controlled, and uses a cell panel covering all relevant red blood cell antigens. It is a matter of argument whether it should include Kp, Lu, and C, but it should not include Wr.

This leaves the crossmatch where it started as a test to exclude ABO incompatibility. Wallace, McClelland and Phillips, and Williamson and colleagues all look at the occurrence of ABO incompatible transfusions and conclude that most occur because of errors of sampling or errors at the point of blood administration. Errors of administration will rarely involve more than one unit. Although they are potentially fatal they are less dangerous than misgrouping of the patient because of sampling or laboratory errors, which can lead to several units of the wrong group being transfused. These laboratory and sampling errors can be virtually removed if we insist on two separate samples, taken on different occasions, from each patient. Assuming that the laboratory information system has the appropriate checks and safeguards inbuilt, discrepancies in the two ABO or Rh groups will prevent acceptance of that record and require further investigation. If the two ABO and Rh groups are in agreement, the chance of persistent error is extremely small. This assumes that the reader and interpreter of the second group is not influenced by a previous result and for this reason it is advisable that groups are read and interpreted electronically, as is often the case now, or that the second group if read or interpreted manually is entered blind to the knowledge of the previous group. This latter might be more difficult to achieve.

Having obtained two concordant ABO and Rh groups, as above, we can be confident that the patient is correctly grouped. Assuming the blood bank computer will only allow the issue of compatible units after bar code entry of donor unit details, the remaining question is...
whether or not the donor has been grouped correctly.

In England the “National Blood Service” (EAE Robinson. Letter on behalf of National Blood Authority, England, 1998) currently assures us of a very high level of accuracy of donor blood grouping. In areas where such an assurance has not been given, or if uncertainty remains in the mind of the hospital blood bankers, it is quite possible to regroup all units of blood on receipt. This is a more efficient and accurate method of ascertaining the donor group than the surrogacy of a crossmatch. The American Association of Blood Banks recommends such checking. It has been suggested that by checking the group, the receiving blood bank assumes product liability that would otherwise rest with the supplier. I am not aware that this particular point has been tested in a court of law, but logic suggests that to change a donor blood group in the receiving laboratory would certainly transfer product liability. Simply to confirm that group would do no such thing. If it does, then the crossmatch, which is in part a test of donor group, would make an equal assumption of product liability. The more important point is whether or not we can trust the supplier to have grouped and labelled the donor units accurately. In this respect, it would help if all suppliers were under obligation to publish error rates on an annual basis, and perhaps inform their customers immediately if more than one error occurred for every, say, million units grouped. At present, I believe we can accept the National Blood Service’s assurances but would like to know that complacency in the future will be guarded against.

Thus, if we have confirmed the patient groups, and have confidence in, or have checked, the donor groups, the crossmatch as a check of ABO compatibility becomes superfluous. Having two patient samples improves the safety of blood provision beyond current requirements and at the same time makes the crossmatch obsolete.

It should be possible to obtain two samples for most patients coming to hospital for elective operations. For those admitted as an emergency it might not be practical or might be prone to manipulation by the sender of the samples. Can we trust a single sample? If an atypical antibody screen is negative and we accept the validity of the donor unit group, what does the current crossmatch achieve? It simply acts as a double check on the ABO compatibility of the recipient with the selected donor group. In the particular case of group O blood selected for a patient grouped as O it adds nothing.

The serological crossmatch is a poor test. Its strength lies in the fact that the result should be negative. A positive result is an alarm bell. A better alternative to the serological crossmatch is to perform a repeat ABO group on the same sample, preferably by a different method from the first group. This is a better technical test but relies on interpretation. Blood bankers who remember the days of two people reading and interpreting results will know only too well how one can be swayed by expectations. Therefore, where a second group on a single sample is to be used in place of a crossmatch, the reading and interpretation of that group should either be electronic or blind to the results of the first group. In addition, the identification of the sample should not be by bar code on both occasions. If the wrong bar code label has been attached a single error will be compounded. One identification should be manual unless a fail safe method of bar coding can be demonstrated. With these safeguards, a good atypical antibody screen and confirmed donor group on a single sample will be as safe as “screen, group, and crossmatch”. Nevertheless, I believe that where practically possible we should aim at the increased safety of two samples.

There are benefits to the electronic selection of blood that should also be weighed in the balance. From the surgeon’s point of view the chief advantage is speed and an almost unlimited supply of blood. If blood can be selected without delay the need for prior reservation of that blood declines. The amount of reserved blood can then be much reduced. Less blood in the issue fringe has several benefits. The less blood that is sitting as reserved stock then the lower the overall stock level, and the more quickly the blood will be used. Not only will outdated or otherwise unsuitable blood be reduced, but the blood will be fresher when transfused. Furthermore, the less blood there is in the issue fringe then the less likely it is that the wrong unit will be collected in error, a common first step in the maladministration of blood.

There is considerable experience with the electronic selection of blood, perhaps for longest in Sweden, where such a system was introduced in 1985 in a group of hospitals and has a near spotless record. There is growing experience elsewhere, although relatively little in the UK at present. A recent report from Hong Kong described a logical progression of the idea by which the user performs the electronic selection of group specific blood at issue. There is no reason why each operating theatre should not have an automatic blood dispenser much like a drinks vending machine. The patients unique identifier is entered by an authorised individual, and assuming the patient matches the requirements, a unit of blood with label is dispensed.

Errors in provision of blood are most commonly the result of mistakes outside the laboratory. Although we must not neglect the laboratory process, there is increasing awareness that the haematologist in charge of blood transfusion, or perhaps the hospital transfusion committee, has responsibility for putting in place a complete process from sample to transfusion that assures a high degree of safety. The crossmatch or its replacement is just part of this process by which we hope to give the right blood to the right patient at the right time. It is important that we do not concentrate overmuch on one small element of that process to the overall detriment of the patient. If the safety of blood transfusion can be greatly improved by the insistence on two pretransfusion samples and the atypical antibody screen is of good quality, then given the safeguards above, the electronic selection of blood is a logical step
Is it time to give up the crossmatch?

The question in our minds should not be whether to increase its use from lack of control. The through knowledge of its rapid availability, as it this is as likely to reduce the use of blood the surgeon’s concerns. Perhaps, unexpectedly, should benefit the patient and certainly eases (fig 1). Quicker supply of blood when required without serological crossmatch. Ab, antibody.

**Figure 1 Flow diagram for electronic issue of blood without serological crossmatch. Ab, antibody.**


---

**Journal of Clinical Pathology - [http://www.jclinpath.com](http://www.jclinpath.com)**

Visitors to the world wide web can now access the *Journal of Clinical Pathology* either through the BMJ Publishing Group’s home page (http://www.bmjpg.com) or directly by using its individual URL (http://www.jclinpath.com). There they will find the following:

- Current contents list for the journal
- Contents lists of previous issues
- Members of the editorial board
- Information for subscribers
- Instructions for authors
- Details of reprint services
- Instructions for use of Pathology Interactive.

A hotlink gives access to:

- BMJ Publishing Group home page
- British Medical Association web site
- Online books catalogue
- BMJ Publishing Group books.

The web site is at a preliminary stage and there are plans to develop it into a more sophisticated site. Suggestions from visitors about features they would like to see are welcomed. They can be left via the opening page of the BMJ Publishing Group site or, alternatively, via the journal page, through “about this site”.

www.jclinpath.com