Significance of Some Red Cell Alloantibodies in Blood Transfusion

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ABSTRACT

The detection of in vitro incompatibility between an antibody in a patient's serum and an antigen on a donor's red cells does not always mean the destruction of cells in vivo. It may be costly and time consuming to find a compatible unit in alloantibodies with no clinical significance. It is necessary to review the behaviours, characteristics and specificity to find out the potential significance of antibodies when facilities for their detection are lacking. Knowledge of the frequency distribution of antigen in the population is also necessary. It is possible on many occasions in spite of the shortened survival of red cells to transfuse a patient where delay in the search for antibodies is not acceptable. Evaluation of clinical indications, urgency and consultation with blood bank staff by the patient's physician are important for the satisfactory outcome of transfusion.

Current major crossmatch compatibility testing in vitro employed by most blood banks has proved very sensitive. Pretransfusion screening of donor cells, detailed techniques in identification of antibodies and finding a compatible unit of blood has been the basis of transfusion practice. However, many blood banks with poor facilities or none at all face many problems in identification of antibodies. Most of the time evaluation of crossmatch incompatibility forms the basis for the blood bank staff to decide whether :

Firstly, a blood should be released for transfusion when specificity of antibody cannot be characterized due to limitation of panel cells, lack of antigens, need for urgency of transfusion, non-availability of many donor units to run a series of red cell tests, and inadequate manpower, and

Secondly, whether a crossmatch showing incompatibility in vitro will be harmful in vivo to the patient, since it is known that not all alloantibodies detected in vitro cause destruction of red cells in vivo (5), and should an attempt in recognising these antibodies and finding a compatible unit be carried out. This search may be costly and time-consuming.

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The present article reviews in brief the clinical significance of some red cell alloantibodies and a possible approach to the problem in selection of blood unit.

SIGNIFICANCE OF SOME RED CELL ALLOANTIBODIES

Many blood banks have abolished the crossmatch testing at temperatures other than 37°C, since it is generally known that cold reactive antibodies do not cause destruction of transfused red cells (11). Issitt (10) observed that 70,000 units of red cell products transfused to more than 20,000 patients since abolishing the crossmatch test at temperatures other than 37°C, did not increase the incidence of transfusion reaction and in no case in which a transfusion reaction was reported was a cold-reactive antibody incriminated. On the other hand figures have also been presented to suggest that the cold reacting antibodies such as anti A_1 — P_1, M, N and Lu_a, Le_a, Le_b, H1 seldom, if ever, cause in vivo haemolysis. Similarly, in vitro incompatibility caused by antibodies that are neutralized by the antigenic substances present in plasma of donor blood such as anti-lewis and anti-chido, are very unlikely to cause increased red cell destruction even though they are reacting at 37°C in vitro (1, 5, 16).

Antibodies such as ABO, Rh, Duffy, Kell, Kidd, MNS, react strongly at 37°C and should be regarded as clinically significant. Identification of these antibodies by panel cells is usually straightforward when proper enhancement techniques are employed and if single antibody is present. It is necessary to transfuse antigen negative blood in such patients (9).

It may be logical to consider the situations pertaining to this region where there is frequent need for multiple transfusions in patients with sickle cell anaemia, thalassaemia and other haemoglobinopathies. Blood banks where pre-transfusion testing of donor antigens other than ABO and Rh are not carried out, are frequently faced with the problem of development of multiple antibodies in the patients involved. It may be extremely difficult in a few patients to find a compatible unit of blood. It is necessary therefore in such patients to find which

antibodies are potentially dangerous and which ones could be regarded as insignificant. The chance of a transfusion recipient being exposed to an incompatible blood group antigen, is the product of the frequency of its occurrence in the population times the frequency of its absence. Therefore, if frequency of occurrence of such antigens is known to this population the chance of occurrence of antibodies could be to some extent predicted. Table 1 summarizes the relative immunogenicity of common blood group antigens (7).

TABLE 1

Relative Immunogenicity of Common Blood Group Antigens

Antigen	*Antigenicity (%)*	*Percentage of All Recipients Immunized by First Random Transfusion*	*Percentage of All Recipients with Reaction to Second Random Transfusion*
D	50.0	6.4	5.4
K	5.0	0.4	0.036
c	2.0	0.32	0.26
E	1.7	0.36	0.11
k	1.5	0.003	0.003
e	0.6	0.012	0.012
Fy_a	0.2	0.045	0.030
C	0.1	0.020	0.015
Jk_a	0.07	0.012	0.010
S	0.04	0.010	0.005
Jk_b	0.03	0.0059	0.0043
s	0.03	0.0031	0.0028

Greendyke (7)

A group of such antibodies are those created by high titer, low avidity (HTLA) antibodies directed to high frequency antigens, i.e. YK_a, Cs_a, Kn_a, McC_a, J.M.H, Ch_a, etc. These antibodies react weakly at 37°C invariably showing a weak reaction in antiglobulin, and all panel cells being agglutinated. Many studies of red cell survival using 51 Cr labelled red cells positive for the above said antibodies have shown that in vivo survival of the in vitro incompatible red cells was completely normal (12, 15, 16). However, Valko showed a destruction of a small portion of the Cs (a +) cells (17). Some of another group of antibodies — those reactive at 37°C and which define the high incidence antigen such as Yt_a, Vel, Ge, Gy_a, Sd_a, Hy, Jo_a etc., have been shown to be benign in nature in vivo (2, 4, 14, 15), while other reports suggest that the survival studies resulted in some of the cells being eliminated rapidly while the rest survived normally (6, 13).

Antibodies strongly reactive at 37°C in vitro i.e. Anti-A, Anti-B, Anti A-HI, Pl-Anti D-C, Anti-M, Le_a — Le_b, anti-Jk_a, anti-K and anti Fy_a, cause rapid destruction of red cells labelled with 51 Cr in vivo (11). However, in some cases of anti-Le_a and anti-Le_b, vivo destruction of red cells was shown to be very slow (3, 11). The majority of survival studies suggest that those antibodies strongly reactive at 37°C in an incompatible crossmatch will cause destruction of donor red cells in vivo. Other antibodies although reactive at 37°C but reacting weakly or only in enzyme technique, usually will not cause destruction of red cells in vivo and if at all, bring about a very slow and limited destruction. It may be appropriate, if facilities exist, to carry out red cell survival studies with a smaller dosage in such situations before transfusion (8).

It appears therefore that it may be unnecessary to search for compatible units, which may be costly and time consuming where in vivo destruction of red cells is unlikely. Transfusion indications where surgery is essential without delay, or even in elective surgery where patients do not require totally normal survival or red cells and donors' cells would seem to achieve the objective of transfusion, that it is probably better to transfuse an incompatible unit to these patients rather than to find a compatible unit.

However, it should be remembered that the responsibility is that of the patients' physician in making a decision of transfusion, if compatible blood is not found. Even if transfusion is indicated by progressive severe anaemia, the physician must weigh the risk of withholding the transfusion against the risk of transfusion reaction. It is necessary for the patients' physician to consult with the blood bank staff to find out the nature of the in vitro incompatibility and overall effect of transfusion. If the transfusion is mandatory and serious transfusion reaction is unlikely, the approach is to transfuse 50ml. of blood from an in vitro incompatible unit. It should be transfused very slowly, observing the patient closely for signs of reaction (18). The transfusion is then temporarily stopped while a blood sample is obtained from a different vein to test for a free haemoglobin in plasma. A direct antiglobulin test is next done, and if both the tests are negative, the rest of the unit is slowly transfused.

CHARACTERISTICS OF ANTIBODIES AS AN AID TO IDENTIFICATION

The type and significance of the antibodies can sometimes be identified from the behaviour of the crossmatch alone and a decision can be made as to the need for a further test. Antibodies which have haemolytic characteristics in vitro i.e. anti-A, anti-B, anti Le^a and Le^b will show a rapid destruction in vivo. Most agglutinating antibodies whether or not they bind compliment, e.g. anti-A_1, HI, P_1, anti-D, C anti M, cause extravascular destruction of cells. Antibodies detectable only by enzyme technique do not usually cause immediate destruction of red cells. Anti-P_1 serum is inhibited by adding hydatid-cyst fluid. Agglutination by anti-sd^a gives a mixed-field appearance with discrete clusters of red cells in a field of completely unagglutinated cells. Agglutination by Lewis antibodies gives a peculiar stringy appearance. Anti-sd^a and Lewis antibodies can be inhibited by saliva. Anti-Ch^a is inhibited by addition of serum but not saliva. Antibodies which can be demonstrated by indirect antiglobulin test but not by agglutination in saline are more likely to be Rh, Duffy, Kell and Kidd system. If a reaction is obtained with anticompliment the antibody is certain not to be of the Rh system. Antibodies which react with indirect antiglobulin test but fail to react with enzyme-treated cells are most likely to be anti-Fy^a , anti-S or anti-Chido. Cold autoantibodies often interfere in the identification of alloantibodies and may mask their presence.

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