4004

On the Development of Isoagglutinins Following Transfusions.

K. LANDSTEINER, PH. LEVINE AND M. L. JANES.

From the Laboratories of the Rockefeller Institute for Medical Research and the Manhattan State Hospital.

Observations on individual differences in human blood aside from the 4 blood groups[1, 2] support the idea that in transfusion the blood of the donor and recipient is, as a rule, not identical in biochemical constitution even though belonging to the same blood group.

In the literature instances are reported in which the first transfusion was uneventful while a repeated transfusion with the same compatible donor was followed by severe symptoms,[3, 4, 5, 6, 7] and others. There are, however, only casual remarks on the occurrence of atypical isoantibodies under such conditions.

We examined recently the sera of 4 individuals of group 0 and 3 of group A.* In 5 of these individuals, who had been transfused several times with the blood of the same donor of their own group, no abnormal agglutinins were observed. The 6th individual, of group 0, was transfused with blood (500 cc.) of the same group and the transfusion was repeated, using the same donor, since in the routine test no incompatibility was detected. Actually no untoward manifestation followed. On careful observation with a more delicate technique, however, an abnormal isoagglutinin was found in the serum of the transfused individual (after the 1st and 2nd transfusion) that reacted on numerous bloods and stronger on several others than on that of the donor. The reactions took place with bloods of group 0 and, as could be shown after removal by absorption of the common isoagglutinins, also with bloods of the other groups. Some of the results are recorded in the table. The

[1] Landsteiner, K., and Levine, Philip, PROC. SOC. EXP. BIOL. AND MED., 1927, xxiv, 600, 941.

[2] Landsteiner, K., and Levine, Philip, *J. Exp. Med.*, 1928, xlvii, 757.

[3] Lindemann, E. E., *J. Am. Med. Assn.*, 1914, lxii, 993.

[4] Sydenstricker, V. P. W., Mason, V. R., and Rivers, T. M., *J. Am. Med. Assn.*, 1917, lxviii, 1677.

[5] Libman, E., and Ottenberg, R., *Trans. College Phys.*, 1917, xxxix, 266.

[6] Waugh, W. G., *Brit. Med. J.*, 1919, ii, 39.

[7] Bowcock, H. M., *Bull. Johns Hopkins Hospital*, 1921, xxxii, 83.

* The terminology of the 4 blood groups used in this publication is that recommended by the American Association of Immunologists and by a committee of the National Research Council.[8]

[8] Editorial, *J. Am. Med. Assn.*, 1927, lxxxviii, 1421.

tests were made by adding in small test tubes 1 drop each of saline, serum, and 2.5% suspension of washed blood cells. After the mixture stood for 2 hours at room temperature readings were made by withdrawing a drop on a glass slide for microscopic examination. The reactions became distinct after about 30 minutes.

At the end of 2 hours the strongest reactions were similar to common isoagglutination of moderate strength. The reactions persisted at 37° with but little diminution. By adding a sufficient amount of sensitive blood the agglutinin proved to be absorbable.

TABLE I.
Tests with post transfusion serum No. 191.

	Group 0								Group B			
No. of blood specimen	191	195	231	235	248	255	257	261	207	208	1122	1226
Reaction	0	+	0	0	+±	0	+	0	±	0	+	0
	Group A								Group AB			
No. of blood specimen			213	233	520	726	851	1179	614	621	861	1206
Reaction			+	+	0	+	0	0	+±	0	0	0

The blood of the donor was No. 195.

The incidence of the reactions was as follows: Group 0, 20+ reactions, 40— reactions; Group A, 16+, 12—; Group B, 6+, 9—; Group AB, 3+, 6—. With regard to the occurrence in all groups, the reactions recall those obtained with immune agglutinins[1, 2] and the abnormal isoagglutinin recently described by Ottenberg and Johnson[9] (*cf.* 2). When tests were made with numerous individual bloods no parallelism was observed between the effects of the immune sera mentioned and the transfusion serum. On comparing the latter with the serum described by Ottenberg and Johnson corresponding reactions were found in a number of specimens but distinct discrepancies in others.

After observing the abnormal reactions reported, we repeated the test with the serum of the recipient drawn prior to the first transfusion, and the cells of the donor. The results were again negative. On making the tests with the same serum and other bloods a trace of agglutination was noticed with 2 bloods which gave the strongest reactions with a post-transfusion serum. Hence one may conclude that an agglutinin of very slight activity was present originally in the serum of the recipient and that the

[9] Ottenberg, R., and Johnson, A., *J. Immunol.*, 1926, xii, 35.

amount of this agglutinin was increased as a result of the transfusion.

In the serum of another transfused individual (group A)† we found agglutinins which acted weakly on all bloods 0 and AA_2, only faintly on some AA_1‡ thus behaving in a manner similar to the cold agglutinin α^2 described previously.[10] The reactions disappeared at 37°.

On account of the observations reported it will be of interest to make a systematic study of post-transfusion sera in order to establish how frequently atypical agglutinins may occur.

By means of the immune agglutinins referred to above we were able to apply the principle used by Ashby[11] for the demonstration of donor's blood in the circulation of the recipient, also for cases where donor and recipient belong to the same blood group. In this way the foreign blood could be found for as long as 7 weeks after the transfusion. Investigations after a longer interval have not yet been made.

In connection with the reaction of the pretransfusion serum it may be stated that, on examining at room temperature (about 20°) numerous sera, some were found which gave atypical isoagglutination reactions (*Cf.* Unger,[12] Guthrie and Pessel,[13] Jones and Glynn,[14] Landsteiner and Witt.[15]) One of these sera, of group AB agglutinated at room temperature blood of group 0 and AA_2 and to a lesser degree some bloods of group B. The reactions with this serum disappeared at 37°. It is intended to describe these observations in detail.

† For this specimen we are indebted to Dr. M. Lederer of the Brooklyn Jewish Hospital, who noticed some irregularity in grouping this blood. The pretransfusion specimen was not tested by us.

‡ For the terminology see [10].

[10] Landsteiner, K., and Levine, Philip, *J. Immunol.*, 1926, xii, 441.

[11] Ashby, W., *J. Exp. Med.*, 1919, xxix, 267.

[12] Unger, L. J., *J. Am. Med. Assn.*, 1921, lxxvi, 9.

[13] Guthrie, C. G., and Pessel, J. F. P., *Bull. Johns Hopkins Hosp.*, 1924, **xxxv**, 33, 81, 126.

[14] Jones, A. R., and Glynn, E. E., *J. Path. and Bact.*, 1926, **xxix**, 203.

[15] Landsteiner, K., and Witt, D. H., *J. Immunol.*, 1926, xi, 221.