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THE RESULTS OF ROUTINE INVESTIGATION FOR Rh FACTOR AT THE N.W. LONDON DEPOT*

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Since Oct., 1942, this laboratory has undertaken to supply Rh-negative blood for transfusion purposes and to determine the Rh group of samples submitted for test. In the course of such routine investigations information has been accumulated on the incidence and clinical importance of the Rh factor. This is analysed below under the following headings: (I) The incidence of the Rh factor in Group O donors. (II) Results of examination of samples submitted from families giving a history suggestive of haemolytic disease of the newborn. (III) Routine serological investigation of unselected women attending an antenatal clinic. (IV) Serological investigation of reactions following transfusion reported to the laboratory.

Methods

Test for Rh Factor in Red Cells.—Both cells and serum from samples submitted for test for Rh factor were first examined for their ABO group, using the tile technique (M.R.C. War Memorandum No. 9). The test for Rh factor was carried out in small test-tubes, 2 in. by 1/4 in., using one drop of anti-Rh serum of suitable ABO group or serum neutralized by saliva, and one drop of a weak cell suspension. The tubes were then covered with small glass caps and left in the incubator at 37° C. for two hours. After looking at the cell sediment one drop was carefully removed from the bottom of each tube and spread on a clean slide. If no agglutination could be seen macroscopically, microscopical examination followed. Controls with two known Rh-positive bloods and one known Rh-negative blood were included in each test. From Oct., 1942, until Jan., 1944, the cell suspensions were put up against three different potent anti-Rh sera of appropriate ABO group. The cell suspensions were called Rh-positive if they were agglutinated by one or more of the test sera. After Jan., 1944, the cell suspensions were tested with one known potent anti-Rh serum only. Those which showed no agglutination with this serum were then tested with one known potent anti-Rh' and anti-Rh'' serum.

Tests for Anti-Rh Agglutinins in Serum.—Tests for anti-Rh agglutinins were carried out by putting up the patient's serum in dilutions of from 1:1 to 1:512 against two suspensions of known Rh-positive Group O red cells (Rh,Rh₂ and Rh₂Rh₂ (or Rh₂rh)), one suspension of known Rh-negative Group O red cells, and a suspension of the patient's own cells. In maternity cases the patient's serum was also tested against the baby's red blood cells if these were available and of compatible ABO group. Serum from cord blood was tested for anti-Rh agglutinins whenever possible. Tests for blocking antibodies (Wiener, 1944) or incomplete antibodies (Race, 1944; Race and Taylor, 1944) have been carried out only recently on sera of Rh-negative

patients which contained either weak anti-Rh agglutinins or no anti-Rh agglutinins.

I. Incidence of Rh Factor in Group O Donors

In order to obtain a regular supply of Rh- blood for routine transfusion purposes and to build up a panel of known Rh- donors 5,837 unselected Group O donors have been tested. In the case of the first 2,944 donors tested only anti-Rh serum was used. In this series 2,472 (84%) were Rh+ and 472 (16%) were Rh-. The later 2,893 donors were tested with anti-Rh, anti-Rh', and anti-Rh'' serum: 2,411 (83.3%) were Rh+, 432 (14.9%) were Rh-, 30 (1%) were Rh', and 20 (0.7%) were Rh''. The sera from donors were not tested for anti-Rh agglutinins.

II. Examination of Samples submitted from Families giving a History suggestive of Haemolytic Disease of the Newborn or in whom Anti-Rh Agglutinins were found

Specimens of blood were received from 624 women with a history suggestive of haemolytic disease of the newborn or with a history of repeated stillbirths or miscarriages. In 133 instances the history suggested haemolytic disease of the newborn, as evidenced by the statement that the present or previous infants had anaemia, icterus gravis, hydrops foetalis, erythroblastosis foetalis, kernicterus, haemolytic disease, or early jaundice. In 3 women with a history of repeated miscarriages or stillbirths anti-Rh agglutinins were found; they are therefore included in the following analysis. The complete serological investigation of the remaining 488 specimens will form the subject of a further communication.

The term "Rh-negative" in the following paragraphs includes Rh' and Rh'' subgroups, as the majority of the cases were investigated before the subgroups were recognized. The subgroups have been mentioned in the last column of Table I whenever they have been tested for.

An analysis of the table shows that 120 (88.2%) of the 136 women with either a history or serological findings suggesting haemolytic anaemia in an infant were Rh-negative and 16 (11.8%) Rh-positive. The Rh-negative mothers belonged to the following blood groups: Group O, 46 (38.3%); Group A, 60 (50.0%); Group B, 8 (6.7%); Group AB, 6 (5.0%). It proved possible to test only 85 husbands of the above 120 Rh-negative women; all but one were Rh-positive. The latter father could not be re-tested to determine if he belonged to one of the Rh subgroups. The 84 Rh-positive husbands belonged to the following blood groups: Group O, 50 (59.5%); Group A, 27 (32.1%); Group B, 4 (4.8%); Group AB, 1 (1.2%); unknown, 2 (2.4%). The red cells of only 55 affected babies with Rh-negative mothers were available for examination; 53 were Rh-positive, and 2 belonged to subgroup Rh' (Table I, Cases 59 and 79).

* A report to the Medical Research Council.

TABLE I.—Cases Suggestive of Haemolytic Disease of the Newborn

KEY TO TABLE.—M., Male. F., Female. A.W., Alive and well. D., Died. Surv., Survived. I.G.N., Icterus gravis neonatorum. E.F., Erythroblastosis foetalis. J., Jaundice. S.B., Stillbirth. Misc., Miscarriage. H.F., Hydrops foetalis. Prem., Premature. Prog. an., Progressive anaemia.

Family No.	Mother's Age When Tested	Mother's Group		Father's Group		Mother's Serum		Pregnancies					Notes
		Rh	ABO	Rh	ABO	Anti-Rh	Time When Tested	1	2	3	4	5, 6, 7, and 8	
1	31	—	A	+	O	1:16 1:32 1:4	7 days } 14 days } 2 mths. } after del.	1938 A.W. Gp. O Rh +	1942 E.F.: D. few mins.				
2		—	B	+	O	1:4	9 days after del.	F. 1939 A.W. Gp. O Rh +	1942 I.G.N.: D. 5 days	1943 Therapeut. abortion Gp. O Rh + 10/52	M. 1944 H.F.: D. 15 min.		Mother's anti-Rh 1:16 8 months after 2nd child
3	28	—	A	+	O	1:64	4 mths. after del.	M. 1934 A.W. Gp. A Rh +	M. 1936 J.: D. 10 days	M. 1938 S.B.	M. 1940 J.: E.F. D. 1 day	(5) F. 1942 E.F.: D. 1 hour	
4	39	—	B			1:16	2 yrs. after del.	F. 1923 A.W. Gp. O Rh +	F. 1926 J.: surv. Gp. O Rh +	F. 1928 J.: surv. Gp. O Rh +	F. 1940 J.: surv. Gp. O Rh +		2nd and 4th children had blood trans. 3rd child now deaf and dumb
5		—	A	+	A	1:256	1 mth. after del.	Misc.	1942 I.G.N.: D. 5 days				P.M. report: Kernicterus
6	28	—	A			1:4	14 days after del.	M. A.W. Gp. O Rh +	J.: 1938 D. 7 days	1941 S.B.	1943 S.B.: prem.		Mother's W.R. positive. 4th child: death due to ? syphilis or E.F. (no P.M. to clarify this). 1st child illegitimate
7	35	—	A			1:128	1 mth. after del.	F. 1931 A.W. Gp. A Rh +	M. 1933 J.: D. 4 days	M. 1934 S.B.	F. 1936 J.: surv. Gp. A Rh +	(5) F. 1938 J.: D. 9 days (6) F. 1940 J.: D. 8 days (7) 1941 S.B. (8) 1944 I.G.N.: D. 7 days Gp. A Rh + Convulsions	4th and 8th children had blood trans. No anti-Rh in last baby's cord blood
8		—	AB			1:4	10 days after del.	F. 1935 A.W. Gp. A Rh +	F. 1937 A.W. Gp. A Rh +	1942 I.G.N.: surv. Gp. B Rh +			3rd child had a blood trans-fusion
9		—	A	+	O	1:1	During preg. After del.	F. 1926 A.W.	M. 1928 A.W. Gp. A Rh —	F. 1931 S.B.: ascites	M. 1932 S.B.: J.	(5) F. 1935 S.B. (6) M. 1939 S.B. (7) M. 1940 E.F.: D. soon after birth (8) 1943, A.W. Gp. O Rh —	7th child: P.M. confirmed E.F. Mother's anti-Rh titre 1:32 2 years after 7th pregnancy
10		—	A			1:2	3 wks. before del. 13 days after	F. 1931 S.B.	M. 1932 A.W. Gp. A Rh +	M. 1934 S.B.: prem.	F. 1935 S.B.: H.F.	(5) M. 1936 S.B.: H.F. (6) F. 1940 S.B.: H.F. (7) 1941 S.B. (8) 1944 E.F.: D. 5 hours Gp. O Rh +	1st preg. forceps delivery. 8th preg. blood trans. Enlarged liver and spleen. No anti-Rh in cord blood. Mother's anti-Rh after 7th preg., 1:512
11		—	A			1:8	? mth. after del.	M. 1929 A.W.	M. 1930 A.W.	F. 1939 A.W.	F. 1942 Severe an. Surv.		4th child had blood trans-fusion
12	28	—	A	+	O	1:1	1 mth. after del.	1939 A.W. Gp. A Rh +	1942 Severe an. J. at birth Surv. Gp. A Rh +				
13		—	AB	+	O	—	days after del.	D. few hrs.	D. (dysentery)	1942 I.G.N.: D. 15 days Gp. B Rh +	1944 A.W. Gp. B Rh —		3rd child had blood trans. Mother's anti-Rh at that time 1:4
14	34	—	A	+	O	1:512	11 days after del.	M. 1937 A.W. Gp. O Rh +	1941 I.G.N.: D. 3 days	1943 S.B.: H.F. Gp. O Rh +			Anti-Rh agglutinins present in mother's serum during pregnancy; increasing
15	26	—	A			1:512	8 days after del.	M. 1938 A.W. Gp. O Rh —	M. 1940 A.W. Gp. O Rh +	1942 E.F.: D. few hrs.			
16		—	A			1:8	1 wk. after del.	F. 1927 A.W. Gp. O Rh +	F. 1929 A.W. Gp. A Rh +	M. 1942 I.G.N.: surv. Gp. A Rh +			3rd child had blood trans. This child is by the second husband
17		—	O			1:512	3 wks. after del.	D. melaena	J.: D.	1942 I.G.N.: surv. Gp. O Rh +			3rd child had blood trans-fusions
18		—	O			—	11 mths. after del.	1938 S.B.	Misc.	Misc.	1940 Prem.: D. 4 hours	(5) Misc. (6) 1942 J.: surv.	
19		—	A			1:2048	2 wks. after del.	A.W.	1943 I.G.N.: surv. Gp. A Rh +				2nd child had blood trans-fusion

TABLE I (continued)

Family No.	Mother's Age When Tested	Mother's Group		Father's Group		Mother's Serum		Pregnancies					Notes
		Rh	ABO	Rh	ABO	Anti-Rh	Time When Tested	1	2	3	4	5, 6, 7, and 8	
20	48	—	O			—	9 years after del.	F. 1914 A.W. Gp. O Rh +	M. 1916 J.: D.	M. 1918 A.W. Gp. O Rh —	M. 1920 J.: D.	(5) F. 1924, J.: D. (6) F. 1927, J.: D. (7) F. 1930 J.: surv. (8) F. 1934 J.: D.	First 3 children by 1st husband; 3rd child is reported to have had jaundice as baby. All deaths from jaundice occurred between 3rd and 15th days
21		—	A			Not available		S.B.	S.B.	S.B.	I.G.N.: D.		Sister of No. 16
22		—	A	+	B	—	During and after 2nd preg.	Haemorrh. disease D.	F. 1943 A.W. Gp. B Rh —				
23	36	—	A	+	O	Not available after last preg.		1943 Prog. an.: surv. Gp. A Rh +	1944 A.W. Gp. A Rh — *				Anti-Rh agglutinins in mother's serum after 1st child, 1:4096. *2nd child Rh +
24		—	A	+	O	1:256	6 days after del.	1940 A.W. Gp. A Rh +	1943 Prog. an.: surv. Gp. A Rh +				2nd child had blood transfusion
25	31	—	O	+	O	1:2	During preg.	I.G.N.: D. 5 days	1943 I.G.N.: surv. Gp. O Rh +				2nd child had several blood transfusions
26		—	O	+	O	1:1	Few days after del.	A.W.	A.W.	A.W.	A.W.	(5) 1943, Twins E.F.: D. 3½ hrs. A.W. Gp. O Rh —	
27	23	—	A			1:256	Few days after del.	A.W.	1943 I.G.N.: surv.				Both children are illegitimate by different fathers. 2nd child had blood transfusion
28		—	A	+		1:1	5 days after del.	1935 A.W.	1936 A.W.	1937 D.: transv. pres.	1939 S.B.: H.F.	(5) 1940 S.B.: H.F. (6) 1942 S.B.: H.F. (7) 1943 S.B.: H.F. Gp. A Rh +	Father reported to be Rh +
29	39	—	A			1:1	?	F. 1928 A.W. Gp. A Rh —	Misc.	Misc.	Misc.	(5) 1943 H.F.	Mother's serum tested within first 10 days
30	29	—	A	+	A	1:1	10 days after del.	F. 1936 A.W. Gp. A Rh —	F. 1938 A.W. Gp. A	1941 Misc.	1943 S.B.: prem.		Not enough blood to test 2nd child
31		—	AB	+	O	1:4	19 days after del.	M. 1934 A.W. (prem.) Gp. B Rh +	F. 1934 A.W. Gp. B Rh +	1943 I.G.N.: surv. Gp. B Rh +			Mother: severe rigor after 10 c.cm. of A blood. Maternal grandmother: Gp. B Rh +
32	33	—	A	+	O	1:1	1st week after del.	A.W.	1943 I.G.N.: D. 2 days				
33	23	—	O	+	O	1:2	14 days after del.	M. 1941 A.W. Gp. O Rh +	F. 1943 I.G.N.: surv. Gp. O Rh +				Mother's serum showed zooning. 2nd child had blood transfusion
34	21	—	O	+	A	1:512	1 day after del.	M. 1943 I.G.N.: surv. Gp. O Rh +					Baby's serum contained anti-Rh 1:8. Baby had several blood transfusions, Mother's serum still contained anti-Rh agglutinins 1:256 after 7 months
35		—	A	+	O	1:512	13 days after del.	M. 1936 A.W. Gp. A Rh +	F. 1943 I.G.N.: surv. Gp. O Rh +				2nd child had blood transfusion
36	30	—	A	+	A	1:16	13 days after del.	M. 1937 A.W.	M. 1939 A.W.	M. 1941 Prem. twins D.	1943 A.W. Gp. A Rh —		Mother's serum contained higher anti-Rh agglutinins at end of pregnancy
37	24	—	B			1:32	1 week after del.	D. (vit. K deficiency)	A.W.	1943 Prog. an.: surv. Gp. B Rh +			All children are illegitimate by different fathers
38		—	AB	+	O	1:1	Few days after del.	1942 S.B.	1943 H.F.				
39	30	—	A	+		1:2	3 days after del.	M. 1933 A.W.	M. 1935 J.: D. 3 days	M. 1936 J.: D. 5 days	F. 1937 J.: D. 3½ mths.	(5) M. 1940, A.W. (6) F. 1941, A.W. (7) M. 1943 J.: surv. Gp. A Rh +	7th child had blood transfusion. Father and two children reported to be Rh +. Impossible to get further information
40		—	O	+	A	—	7 days after del.	F. 1930 A.W. Gp. O Rh +	1932 S.B.	1933 S.B.	1935 S.B.	(5) 1936 D. 5 days (6) M. 1938 A.W. Gp. O Rh + (7) 1941, S.B. (8) 1944, A.W. Gp. O Rh +	Mother's serum contained anti-Rh agglutinins (1:2) during preg.; none after del.; also high anti-A titre (1:1024). All living children Gp. O

TABLE I (continued)

Family No.	Mother's Age When Tested	Mother's Group		Father's Group		Mother's Serum		Pregnancies					Notes
		Rh	ABO	Rh	ABO	Anti-Rh	Time When Tested	1	2	3	4	5, 6, 7, and 8	
41	32	-	O	+	O	1:32 1:256	1 day after del. 14 days after del.	F. 1928 A.W.	M. 1930 A.W.	1932 J.: surv.	M. 1935 S.B.: macerated	(5) F. 1938 S.B.: H.F. (6) M. 1943 E.F.: surv. Gp. O Rh+	6th child had blood transfusion. All the other surviving children evacuated to U.S.A.
42		-	A	+	A	1:32	During preg.	S.B.	S.B.	I.G.N.: D. 36 hours	1943 I.G.N.: D. 52 hours Gp. O Rh+		Last baby delivered by Caesarean section; born jaundiced; had 3 blood transfusions
43		-	A			1:32	4½ yrs. after del.	M. A.W.	F. I.G.N.: D.	F. 1939 I.G.N.: surv.			3rd child had blood transfusion
44	35	-	O			-	20 mths. after del.	S.B.	S.B.	1941 I.G.N.: surv.			3rd child had several blood transfusions. Mother had severe reaction after transfusion with blood not tested for Rh
45	29	-	A	+	A	1:32	5 days after del.	M. 1935 A.W. Gp. O Rh+	M. 1936 Twins, A.W. Gp. A Rh+	1943 Prog. an.: D. 4 days			P.M. report on 3rd child: E.F.
46	27	-	O	+	O	1:128 1:64	Before del. 7 days after del.	M. 1938 A.W.	F. 1940 I.G.N.: surv.	M. 1943 I.G.N.: surv. Gp. O Rh+			2nd child has had injections of mother's blood. 3rd child had blood transfusion
47		-	A	+	A	1:4	9 days after del.	S.B.	D. bronchitis	1943 Prog. an.: surv. Gp. A Rh+			3rd child had blood transfusion
48	26	-	A	+	A	1:32	During preg.	F. 1938 A.W. Gp. A Rh+	F. 1939 I.G.N.: D. 12 hrs.	F. 1940 I.G.N.: D. 3 days	M. 1941 A.W. Gp. O Rh-	(5) M. 1943 D. 9 mths. (anaemia) (6) 1943 Therap. misc.	
49		-	AB			1:1	9 mths. after del.	M. 1942 Prog. an.: D. few days	F. 1943 H.F.: D. ½ hr				Mother had toxæmia during last pregnancy
50	28	-	A	+	O	1:512	5 days after del.	M. 1938 A.W.	M. 1943 S.B.: H.F.				
51		-	O	+	A	1:4	9 mths. after del.	Misc.	1943 J.: surv. Gp. O Rh+				
52		-	A	+	A	1:64	8 days after del.	M. 1938 A.W.	1941 M., A.W. Gp. O Rh+ F., A.W. Gp. A Rh+	1943 J.: surv. Gp. A Rh+			Last child had blood transfusion. No anti-Rh agglutinins in cord blood
53	41	-	O	+	O	-	During and after preg.	M. 1922 A.W. Gp. O Rh-	M. 1924 S.B.: E.F.	M. 1928 S.B.: E.F.	1944 A.W. Gp. O Rh-		S.B.s are supposed to be due to E.F. Mother Rh'
54	39	-	A	+	O	1:1 -	14 days before del. 5 days after del.	1934 A.W. Gp. O Rh+	M. 1935 A.W. Gp. O Rh-	F. 1936 A.W. Gp. O Rh-	F. 1937 A.W. Gp. A Rh-	(5) 1940 S.B.: E.F. (6) F. 1944 Anaemia: surv. Gp. O Rh+	6th child: no anti-Rh agglutinins in cord blood. Mother and 3 children Rh'
55	35	-	A	+	O	- 1:2	2 days after del. 1 mth. after del.	1935 A.W.	F. 1944 I.G.N.: surv. Gp. O Rh+				2nd child had blood transfusion
56		-	O	+	O	1:64	2 days after del.	A.W.	1943 I.G.N.: surv.				2nd child had blood transfusion
57	30	-	A	+	O	- 1:2	5 days after del. 12 days after del.	1934 Misc.	M. 1935 A.W. Gp. A Rh+	J.: D. 8 days	1940 S.B.	(5) 1944 D. 24 hrs.	
58	29	-	O	+	O	1:64	10 days after del.	M. 1934 D. 11 mths. (sarcoma)	F. 1935 I.G.N.: D. 5 days	F. 1938 I.G.N.: D. 4 days	1944 Misc.	(5) 1944 5/12 preg.	Anti-Rh titre increasing during pregnancy
59		-	A	+	O	1:8 1:4	1 day after del. 7 days after del.	M. 1936 A.W.	M. 1939 D. 11½ hrs.	F. 1940 I.G.N.: D. 1 day	M. 1942 I.G.N.: D. 7 days	(5) F. 1944 Anaemia: surv. Gp. O Rh-*	*5th child is Rh'; had blood transfusion. No anti-Rh agglutinins in cord blood
60	40	-	A			1:2	?	Repeated misc.					
61	25	-	A	+	O	1:4	Few days after del.	1941 Haemolytic disease, D.	1942 A.W.	F. 1944 Prem. A.W. Gp. A Rh-			Mother suffering from severe anaemia. J. after trans. with blood of unknown Rh factor. Rh- blood given successfully
62		-	O	+	O	1:1 1:4	2 days after del. 11 days after del.	M. 1939 A.W. Gp. O Rh+	1942 S.B.	1944 S.B.: H.F.			

TABLE I (continued)

Family No.	Mother's Age When Tested	Mother's Group		Father's Group		Mother's Serum		Pregnancies					Notes
		Rh	ABO	Rh	ABO	Anti-Rh	Time When Tested	1	2	3	4	5, 6, 7, and 8	
63		-	O	+	A	1:1	?	F. 1942 A.W. Gp. O Rh+	1944 S.B.				Mother Rh'
64		-	A	+	A	1:2	1 day after del.	S.B.	S.B.	1944, S.B.			
65		-	O	+	O	1:32 1:256	6 days after del. 10 days after del.	A.W.	1944 I.G.N.: D. 6 days				
66		-	B	+	B	1:128	?	M. S.B.: prem.	F. 1944 E.F.: D. 15 days				
67		-	O	+	O	1:2	8 days after del.	F. 1937 D. 2 yrs.: pneumonia	F. 1939 S.B.: prem.	F. 1942 S.B.: prem.	1944 E.F.: D. 6 hrs.		
68	38	-	O	+	O	1:4	6 days after del.	M. 1932 A.W. Gp. O Rh-*	F. 1943 Prem. D.	M. 1944 I.G.N.: D. 2 days Gp. O Rh+			*1st child Rh'. 2nd born prem. after car accident: died from haemorrhage from umbilical cord. 3rd child died after convulsions in spite of transfusion with Rh- blood; enormous number of megaloblasts in blood film; serum from cord blood agglutinated baby's own cells
69		-	A	+	O	1:1	9 days after del.	1941 A.W.	M. 1944 I.G.N.: surv. Gp. O Rh+				2nd child had two blood transfusions
70	20	-	O	-	B	Not available		1943 J.: D.					Husband not tested for Rh' or Rh'
71	29	-	O			-	4 days after del.	1943 J.: surv. Gp. A Rh+					Mother's serum anti-A titre 1:16,384
72	34	-	O	+	O	1:128	3 weeks after del.	F. 1936 A.W. Gp. O Rh+	F. 1938 S.B.	1944 S.B.			
73		-	A	+	A	1:128 1:512	3 days after del. 8 days after del.	A.W.	A.W.	A.W.	F. 1944 I.G.N.: surv. Gp. A Rh+		4th child had blood transfusion
74		-	A	+	O	1:128 1:512	6 hours after del. 5 days after del.	F. 1942 A.W. Gp. A Rh+	M. 1944 I.G.N.: D. 3 mths. Gp. A Rh+				2nd child had two blood trans., showing signs of kernicterus. Died 3 mths. old, suffering from spastic paralysis and mental deficiency. Cause of death: pneumonia
75		-	A			1:4	During pregnancy	1931 A.W.	1934 S.B.: prem. (? E.F.)	1935 Misc.	1940 S.B.: prem.	(5) 1944 31/52 preg.	No further information available
76	24	-	O			1:128	3 days after del.	F. 1943 D. of pneumonia	M. 1944 I.G.N.: surv. Gp. O Rh+				2nd child had blood transfusion
77		-	A	+	O	1:512	8 days after del.	M., F. (twins) 1940 A.W. Both Gp. A Rh+	M. 1944 I.G.N.: surv. Gp. A Rh+				
78		-	O	+	A	1:256	7 days after del.	F. 1926 A.W. Gp. A Rh+	A.W.	A.W.	A.W.	(5) D. pneumonia (6) D. 2 weeks (7) 1944 S.B.: H.F.	6th child had enlarged liver
79	22	-	O	+	O	1:256	3 days after del.	F. 1943 A.W. Gp. O Rh+	1944 I.G.N.: D. 2 days Gp. O Rh-*				*2nd child Rh'. Baby's serum contained weak anti-Rh agglutinins
80		-	A	+	A	1:256	7 days after del.	M. 1942 A.W.	M. 1944 Prog. an.: surv. Gp. A Rh+				2nd child had blood transfusion
81		-	B	+	O	-	15 days after del.	1941 D. 2 days: congenital heart	1943 Prem. D. 3 days	1944 Prog. an.: surv.			
82	28	-	A	+	O	1:1	12 days after del.	F. 1935 A.W. Gp. A Rh+	F. 1938 A.W. Gp. O Rh-	F. 1940 S.B.: prem.	F. 1941 A.W. Gp. O Rh-	(5) F. 1943 S.B.: prem. (6) F. 1944 A.W. Gp. O Rh+	6th child reported to be very pale (!) for some time after birth. 2nd and 4th children Rh'
83	38	-	A	+	B	-	17 days after del.	1940 D. 20 days: pneumonia	1942 S.B.	1942 Misc.	1943 Misc.	(5) 1944 H.F.: D. few hrs.*	*Blood in very bad condition: could not be tested

TABLE I (continued)

Family No.	Mother's Age When Tested	Mother's Group		Father's Group		Mother's Serum		Pregnancies					Notes
		Rh	ABO	Rh	ABO	Anti-Rh	Time When Tested	1	2	3	4	5, 6, 7, and 8	
84		—	O	+	A	—	4 days after del.	1931 A.W.	1935 D.: cong. heart	1937 Misc.	1938 S.B.: prem.	(5) 1939 S.B.: prem. (6) 1944 S.B.: H.F.	Impossible to get more information
85		—	O	+	A	1: 512	9 days after del.	F. 1942 A.W. Gp. O Rh +	M. 1944 J.: surv. Gp. A Rh +				Mother's serum has also very high anti-A titre
86		—	B			—	6 mths. after del.	1938 A.W.	1940 S.B.	1944 S.B.: H.F.			
87	28	—	O	+	O	1: 4	9 days after del.	M. 1939 A.W.	F. 1942 Anaemia: surv.	1944 I.G.N.: surv. Gp. O Rh +			3rd child had blood transfusion
88		—	A	+	O	1: 512	14 days after del.	1942 S.B.	1944 I.G.N.: D. 5 hrs.				
89		—	B	+	B	1: 1	3 mths. after del.	S.B.	M. (twins) A.W. Gp. B Rh +	S.B.	S.B.	(5) 1944 S.B.	
90		—	O			1: 1	8 days after del.	A.W.	A.W.	A.W.	M. 1944 I.G.N.: D. 1 mth. Gp. O Rh +		First 3 children by 1st husband. 4th child transfused with Rh— blood when 8 days old, suffering from I.G.N. with rigidity and head retraction (? kernicterus)
91		—	A			—	During preg.	1943 E.F.: D.	1944 5/12 preg.				Mother Rh'
92		—	A	+	A	—	5 days after del.	M. 1944 J.: surv. Gp. O Rh +					Child 10 weeks premature, very anaemic and jaundiced
93		—	O	+	O	1: 64 1: 256	5 days after del. 24 days after del.	M. 1932 A.W. Gp. O Rh +	M. 1944 I.G.N.: D. 2 days				
94		—	O	+	O	— 1: 1	1 day after del. 13 days after del.	A.W. Gp. O Rh +	M. 1944 I.G.N.: surv. Gp. O Rh +				2nd child had blood transfusion
95		—	O	+	A	1: 2	3 days after del.	1942 A.W.	1944 H.F.: D. 15 min. Gp. O Rh +				1st child not by present husband. Mother Rh'
96		—	O	+	O	1: 1	4 days after del.	M. 1928 A.W.	M. 1931 I.G.N.: D. 2 days	M. 1933 S.B.	F. 1936 Prem. I.G.N.: D. 8 days	(5) F. 1941 I.G.N.: D. 2 days (6) 1944 S.B. Gp. O Rh +	6th child: no anti-Rh agglutinins in cord blood
97	37	—	A	+	A	—	9 days after del.	M. 1925 Prem. D. 3 wks.	M. 1933 Prem. A.W.	M. 1941 A.W.	1944 J.: surv. Gp. O Rh +		1st child died of convulsions: ? cause. Mother Rh'
98		—	A			—	During preg.	A.W.	I.G.N.: D. 4 days	1944 7/12 preg.			
99		—	A	+	A	1: 256	? first wk. after del.	M. 1928 A.W. Gp. O Rh +	F. 1930 A.W. Gp. A Rh +	1944 E.F.: surv. Gp. O Rh +			3rd child had blood transfusion
100	30	—	O			1: 2	12 days after del.	F. 1938 A.W. Gp. O Rh +	F. 1941 A.W. Gp. O Rh—	1944 Prog. an.: surv. Rh +			3rd child: specimen too small to group and test for Rh. Group unknown
101	36	—	O	+	O	—	During preg.	F. 1933 A.W.	F. 1941 I.G.N.: D. 4 days	1942 Misc.	1943 Misc.	(5) 1944 6/12 preg.	
102		—	A			1: 16	6 mths. after del.	Twins D.	S.B.	1944 Misc.			
103		—	A	+	A	1: 128	20 days after del.	M. 1944 Prog. an.: surv. Gp. A Rh +					Child had blood transfusion. Mother Rh'
104	35	—	A	+	O	—	12 days after del.	1942 A.W.	1944 J.: surv. Gp. A Rh +				
105		+	A	+	O	—	4 mths. after del.	1942 Severe an.: surv. Gp. A Rh +					Child had blood transfusion
106	20	+	O			—	8 days after del.	1940 ? I.G.N.: D. 12 days	1942 Misc.				
107	29	+	O			—	During preg.	M. 1935 A.W. Gp. O Rh +	1937 J.: D. 3 days	F. 1939 J.: surv. Gp. O Rh +	1943 4/12 preg.		

TABLE I (continued)

Family No.	Mother's Age When Tested	Mother's Group		Father's Group		Mother's Serum		Pregnancies					Notes
		Rh	ABO	Rh	ABO	Anti-Rh	Time When Tested	1	2	3	4	5, 6, 7, and 8	
108	39	+	A			—	During preg.	1931 A.W.	1932 A.W.	1941 J.: D. 14 days	1943 Pregnant		
109		+	O			—	1 day after del.	A.W.	J.: surv. Gp. A Rh +				Mother's anti-A titre after delivery, 1:256
110	23	+	O				Not tested	? E.F.: D. few days	1943 32/52 preg.				
111		+	O	—	A	—	Few days after del.	1 and 2 prem. died soon after birth		D. 10 days	J. and an.: D. 7 days	(5) 1944 A.W. Gp. O Rh +	Mother's anti-A titre during pregnancy, 1: 8192
112		+	A	—	O	—	1st week after del.	1937 A.W.	1943 Prem. J. and an.: surv. Gp. O Rh +				
113		+	O	+	A	—	1st week after del.	1944 J.: surv.					Mother's anti-A titre 1: 1024 after delivery
114		+	A	+	B	—	11 days after del.	J.: D.	M. 1944 J. and haem.: D. Gp. AB Rh +				2nd child had blood transfusion. Mother's anti-B titre 1: 4095 after delivery
115	31	+	B	—	A	—	During preg.	F. 1943 ? E.F.: D. 4 days	1944 Pregnant				Mother's anti-A titre was 1:16,384+ during pregnancy
116	29	+	O			—	4 days after del.	1944 J.: surv. Gp. A Rh —					Mother's anti-A titre 1: 2048 (4 days after delivery) Mother's anti-A titre 1: 256 (11 days after delivery)
117	42	+	A			—	2 mths. after del.	F. 1927 D. pneumonia	M. 1928 A.W.	M. 1931 A.W.	M. 1933 A.W. Gp. AB Rh +	(5) M. 1944 S.B.: ? H.F.	Mother's anti-B titre 1: 512 two months after delivery
118		—	O	+	O	1: 1 1: 1	12 hours after del. 9 days after del.	A.W.	M. 1944 I.G.N.: D. 18 hrs. Gp. O Rh +				2nd child died with convulsions during blood transfusion. Mother's serum incomplete antibodies 1: 1 in two tests
119	30	—	A	+	O	1: 128	During preg.	1940 Prem.: D. 2 days	1943 J.: D. 3 days	1944 Preg.			
120		—	O	+	AB	— 1: 1	1st week after del. 2nd week after del.	M. 1934 A.W. Gp. B Rh +	M. 1937 A.W. Gp. A Rh +	1944 J. and an.			Mother Rh ⁺ , anti-B 1: 8192
121		—	O	+	A	1: 1	10 days after del.	1942 Misc.	1943 Prem. A.W.	1944 S.B.			
122		—	O	+	O	1: 32	During preg.	F. 1939 A.W.	M. 1940 I.G.N.: D. 4 days	F. 1942 J.: D. 19 days	1944 2/12 preg.		
123	26	—	O			1: 1	6 days after del.	F. 1938 A.W.	1940 Ectopic gestation	F. 1944 S.B.: E.F.			Mother: incomplete antibodies 1: 4
124	28	—	B	+	A	—	During preg. 9 days after del.	M. 1942 S.B.	1944 E.F.: surv. Gp. A Rh +				Mother: no incomplete antibodies. Cord serum: no anti-Rh agglutinins
125		—	A			1: 512	6 weeks after del.	1935 I.G.N.: D. 1 week	1944 I.G.N.: D. 5 days				Mother Rh ⁺
126		—	O	+	O	1: 1	During preg.	M. 1936 A.W.	M. 1943 J.: D. 18 days	1944 Misc.	1944 2/12 preg.		Mother: no incomplete antibodies
127		+	B	+	B	—	? some mths. after del.	1944 H.D.: D.					
128	30	—	O	+	A	—	1 day after del. 10 days after del.	M. 1944 I.G.N.: surv. Gp. A Rh +					Mother: no incomplete antibodies in both tests. Child had blood transfusion
129	33	—	O			—	During preg.	M. 1942 I.G.N.: D. 22 days	1944 4/12 preg.				Mother: no incomplete antibodies
130	34	—	O			—	1 day after del.	M. 1940 ? J.: surv.	M. 1942 Misc.	F. 1944 I.G.N.: D. 21 days			Mother Rh ⁺ , no incomplete antibodies. 3rd child had blood transfusion. Died of diarrhoea + vomiting
131	40	—	O	+	O	1: 16	10 days after del.	A.W.	A.W.	F. 1944 I.G.N.: surv. Gp. O Rh +			3rd child had blood transfusion
132	25	+	O			—	6 days after del.	1943 Misc.	1944 Prog. an.: surv. Gp. O Rh —				Child had blood transfusion

TABLE I (concluded)

Family No.	Mother's Age When Tested	Mother's Group		Father's Group		Mother's Serum		Pregnancies					Notes
		Rh	ABO	Rh	ABO	Anti-Rh	Time When Tested	1	2	3	4	5, 6, 7, and 8	
133	25	—	A			1:1	During preg.	1940 A.W.	1942 E.F.: D. 2 days	1944 5/12 preg.			Mother: incomplete anti-bodies 1:16
134		—	A	+	A	1:16	1 week after del.	A.W.	A.W.	A.W.	A.W.	(5) 1944 Haemolytic an.: surv.	5th child had blood transfusion
135	22	+	O	+	B	—	2 days after del.	F. 1944 E.F.: surv. Gp. B Rh—					Child had blood transfusion. Mother: anti-B 1:2048
136	31	—	AB			—	3 mths. after del.	A.W.	A.W.	1944 J.: D. 3 days			Mother: no incomplete anti-bodies

TABLE II.—Transfusion Reactions

Nature of Reaction	Rh + Patients who had:		Rh — Patients who had:		Remarks		
	Previous Transfusions	First Transfusion	Previous Transfusions	First Transfusion	Rh + Patients	Rh — Patients	
						Previous Transfusions	First Transfusion
Anuria ..	0	0	1	1		Mothers of babies suffering from H.D. Both anti-Rh present	
Jaundice ..	0	1	2	3	Anaemia	Anaemia cases. Anti-Rh present	All three women, one of them anaemia of pregnancy. All anti-Rh present
Rigor and high temperature	9	15	5	2	All patients very anaemic. One ulcerative colitis	2 patients: no anti-Rh present. 1 patient had several transfusions, all but the first followed by rigor: anti-Rh present. 1 patient had anaemia (Hodgkins): anti-Rh present	1 P.P.H.: anti-Rh present 1 (see above—jaundice) anti-Rh present
Haemoglobinuria and haematuria	1	0	1	1	Severe anaemia	Steatorrhoea: anti-Rh present	Same case as anaemia (above): anti-Rh present
Urticaria and shock	1	1	0	1	One case of anaemia and one of miscarriage		Eclampsia and anaemia: no anti-Rh present
No rise in haemoglobin	0	0	2	2		Same cases as jaundice (above): anti-Rh present	1 case see above (jaundice). 1 case (woman) of severe anaemia: no anti-Rh present
Pain in back or chest	1	2	0	1	All cases of anaemia		Anaemia (woman): no anti-Rh present
Vomiting ..	0	1	0	0	Ulcerative colitis		
Loss of consciousness	0	1	0	0	Disease unknown		
Undefined ..	0	3	2	4	2 cases of anaemia 1 unknown	1 case of septicaemia 1 case of operation: no anti-Rh present	All women: no anti-Rh present

Anti-Rh agglutinins were found in the serum of 94 (79.6%) of the 120 Rh-negative women. In one of them (Table I, Case 61) the anti-Rh agglutinins may possibly have resulted from the transfusion of Rh-positive blood, as the woman's last baby was Rh-negative. After its birth she had received a transfusion of blood of unknown Rh group. Her first child died of haemolytic anaemia.

Anti-Rh agglutinins could not be found in 26 (21.7%) of the Rh-negative cases. In these the tests were carried out under varying circumstances: (a) after pregnancy with Rh-negative children (4); (b) only during pregnancy (4); (c) only during the first week after delivery (5); (d) during pregnancy and the first week after delivery (1); (e) only during the second week after delivery (2); (f) during the first and second weeks after delivery (1); (g) only during the third week after delivery (2); (h) 1 to 12 months after delivery (3); (i) over one year after delivery (2); (j) serum was not available (2).

Eight sera were tested for incomplete antibodies. Two had a higher titre of incomplete antibodies than of anti-Rh agglutinins; one had the same titre for both; five sera without anti-Rh agglutinins also had no incomplete antibodies. The cord serum of the affected babies was tested in 10 instances: no abnormal agglutinins were found in seven; anti-Rh agglutinins were present in two; one agglutinated the baby's own red cells.

The first pregnancy of the 120 Rh-negative mothers ended with a child normal at birth and during infancy in 80 instances. In 27 cases the child was suffering from haemolytic disease or was stillborn; in 5 the pregnancy ended in a miscarriage; and in 8 cases the child died from unknown causes or from causes other than with haemolytic disease of the newborn. Of the 80 normal first children 33 were Rh-positive, 5 Rh-negative, and 42 were not tested. There were eight Rh-negative normal children in families who had previously had children suffering from haemolytic disease of the newborn (Table I, Cases 9, 13, 20, 22, 23, 48, 53, 61).

The table includes 16 Rh-positive women. Eight of their husbands (5 Rh-positive, 3 Rh-negative) and eight of the affected children (5 Rh-positive, 3 Rh-negative) were tested. The serum of only one of the 16 Rh-positive mothers was put up against the baby's red cells; these were not agglutinated. The serum of one of these women could not be tested; in none of the other 15 were abnormal agglutinins detected.

III. Routine Serological Investigation of Unselected Women Attending an Ante-natal Clinic

Between Jan. 3 and June 5 and between Nov. 1 and Dec. 30, 1944, routine Rh tests were carried out on 433 women attending an ante-natal clinic. These women were unselected except that a large number had been sent to the ante-natal clinic at Univer-

sity College Hospital by outside doctors on account of a difficult obstetric history. This possibly explains the comparatively large number of 96 (22.2%) with histories of miscarriages and/or stillbirths.

339 women (78.3%) were Rh-positive, 79 (18.2%) Rh-negative, 11 (2.6%) Rh', 2 (0.5%) Rh'', and 2 (0.5%) were Rh-negative tested with anti-Rh serum only. Out of 96 women who gave a history of miscarriages and/or stillbirths, 77 (80.2%) were Rh-positive and 19 (19.8%) were Rh-negative, Rh', and Rh'' respectively. The Rh-negative, Rh', and Rh'' women belonged to the following blood groups: Group O, 41 (43.6%); Group A, 44 (46.8%); Group B, 8 (8.5%); Group AB, 1 (1.1%). Of these women 60 had had no children, and 34 were multigravidae.

The sera of the 94 women who were Rh-negative, Rh', or Rh'' were tested for anti-Rh agglutinins. Of these women 53 (36 nulliparae, 17 multigravidae) were tested only during the first 6 months of pregnancy; 22 (13 nulliparae, 9 multigravidae) only between the 3rd and 9th months of pregnancy; 10 women who had had no previous pregnancies were tested some time during pregnancy, but further information was impossible to obtain. The 9 remaining women (1 nullipara, 8 multigravidae) were tested during and after pregnancy. Seven babies of this last group were tested; 6 were Rh-positive and 1 Rh-negative. One of the Rh-positive babies died of icterus gravis neonatorum; the other 6 were apparently normal. No information could be obtained about the remaining two. The mother of the baby who developed icterus gravis had been tested very early in pregnancy and no anti-Rh agglutinins were found then. Her serum contained anti-Rh agglutinins after delivery. Her husband and older child were both Rh-positive. Of the 94 who were Rh-, Rh', or Rh'' this woman was the only one in whose serum anti-Rh agglutinins were detected. The sera of 20 of the Rh-negative women were tested for incomplete antibodies, but none could be found. No abnormal agglutinins were discovered in the serum of the seven babies tested.

Only 33 husbands of the 94 Rh-negative, Rh', or Rh'' women were tested: 31 were Rh-positive; two were Rh-negative.

IV. Serological Investigation of Reactions following Transfusion

Reactions in 48 patients after transfusion of blood of compatible ABO group were reported to the depot director for further investigation: 28 reactions occurred in Rh-positive and 20 in Rh-negative patients. These reactions were not necessarily severe (see Table II). Of the 28 Rh-positive patients who had transfusion reactions six had received Rh-negative blood. No abnormal agglutinins were detected in their serum. A transfusion had been given previously to 10 of these Rh-positive patients. Of the 20 Rh-negative patients included in this series, two had had previous transfusions with known Rh-positive blood without any reactions. A second transfusion—in one case with Rh-positive blood and in the other with blood of unknown Rh factor—was followed by a reaction. Both patients had anti-Rh agglutinins in their serum.

Seven patients had previously been transfused with blood of unknown Rh group without reaction; 3 of them had a further transfusion with Rh-positive blood and with blood of unknown Rh group. The later transfusions were all followed by a reaction. Anti-Rh agglutinins were detected in the sera of two patients known to have had Rh-positive blood and in two who had had blood of unknown Rh group.

In 11 cases the first transfusion was followed by a reaction. One was a young child suffering from haemolytic anaemia and 10 were women, 5 of whom had only recently been delivered. Three of the maternity cases were those of women whose babies suffered from progressive anaemia or jaundice. One had anti-Rh agglutinins in her serum before transfusion, and these increased after the transfusion of Rh-positive blood (Case 23, Table I); the other two women were tested only after the transfusion with blood of unknown Rh group. One had anti-Rh agglutinins in her serum (Case 31, Table I); none could be detected in the serum of the third woman, who was not tested until 20 months after delivery (Case 44, Table I). The two remaining maternity cases were those of women who had been delivered of normal children; one received Rh'' blood, and no abnormal agglutinins could be detected in her serum; the second woman received blood of unknown Rh group after the delivery

of a normal Rh-negative child. Her serum contained anti-Rh agglutinins. She had probably been previously sensitized during a pregnancy ending in the birth of a baby who died of haemolytic anaemia (Case 61, Table I).

The remaining 5 reactions occurring after the first transfusion were in patients not connected with maternity cases. One of these had Rh-positive blood and 4 had blood of unknown Rh group. Anti-Rh agglutinins could be detected in the serum of two of these women. No anti-Rh agglutinins were detected in the serum of the child suffering from haemolytic anaemia. Of these 20 Rh-negative patients 16 received one or more further transfusions with Rh-negative blood without any reaction. Five cases of this series are included in Table I (Nos. 1, 23, 31, 44, 61); anti-Rh agglutinins were found in the serum of each of these patients.

Discussion and Conclusions

The total number of Group O donors tested (5,837) was made up of two series: in the first, 84.0% were Rh-positive; in the second, 83.3% were Rh-positive. These figures are in close agreement with the other large series published in this country (Cappell, 1944).

The series of cases suggestive of haemolytic disease of the newborn has not been selected on as stringent a basis as some previously published series (Levine, 1941; Levine *et al.*, 1941; Potter *et al.*, 1943; Race *et al.*, 1943; Boorman *et al.*, 1944; Cappell, 1944), since it proved difficult to obtain by correspondence complete reports stating the clinical and pathological findings. The wide area served made personal contact impossible. Nevertheless, 88.2% of the total of 136 cases proved to be Rh-negative, and 79.6% of these had anti-Rh agglutinins in their serum.

The 433 ante-natal cases tested showed 78.3% to be Rh-positive—i.e., a lower proportion than occurred in the unselected donors and in other series published from ante-natal clinics (Cappell, 1944; Murray, 1944). There is at present no explanation of this low figure. The relatively high incidence, however, of Rh-negative mothers suggests the importance of routine Rh-testing in ante-natal clinics.

The number of transfusion reactions investigated was not large. The findings, nevertheless, suggest that the transfusion of Rh-negative individuals with Rh-positive blood is a not uncommon cause of relatively mild reactions and may result in more severe reactions. Of the 48 cases examined 20 (41.7%) proved to be Rh-negative, and 11 of these patients had anti-Rh agglutinins in their serum. Nine of the 20 Rh-negative patients had had previous transfusions without reactions, five with Rh-positive blood. It may be of interest that the remaining 11 patients who had a reaction after the first transfusion were all women. Diamond (1942) and Vogel *et al.* (1943) have published 10 cases each of reactions in Rh-negative patients following the transfusion of Rh-positive blood.

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Continuing its campaign for children's nurseries as a permanent feature of our national life, the London Women's Parliament (24, High Holborn, W.C.1) has issued a circular for distribution to mothers telling them how they can help to achieve this end. In an accompanying letter this organization welcomes the Government's recent decision to introduce a national nursery certificate for trained workers, but points out that some other assurance is needed that the nurseries are to remain—such as the continuance of the 100% grant to local authorities, the reopening of the "wartime" training schemes (closed last January), and the opening of the nurseries themselves to all who need them.