Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 11 (3—4), pp. 219—229 (1970)

Haemolytic Disease of the Newborn due to Rh-isoimmunization: The Role of Free Anti-D Antibodies in Bilirubin Rebound

By

L. Pataki

Department of Paediatrics, University Medical School, Szeged

(Received April 29, 1970)

Correlations between the free anti-D antibodies contained in the newborn serum, and the phenomenon of bilirubin rebound have been studied. In haemolytic disease caused by Rh-isoimmunization, the presence or absence of anti-D antibodies decisively influenced the extent of bilirubin rebound. This was less serious if the serum of the newborn contained no free antibodies, and in such cases an exchange transfusion was rarely necessary. On the other hand, in the presence of free anti-D antibodies, bilirubin rebound may be so high as to necessitate several transfusions. This high rebound is presumably due to that a considerable portion of the free anti-D antibodies, having escaped from the blood paths is damaging the tissues and inducing haemolysis in the extravascular space. A method of combined blood exchange has been elaborated by which a larger amount of antibodies can be eliminated than by the usual transfusion of Rh-negative blood. Increased elimination of antibodies diminishes the possibility of post-transfusion extravascular haemolysis and so reduces the frequency of repeated transfusions.

Lathe [15] was the first to state that the amount of bilirubin removable from the circulation by exchange transfusion was less than the theoretically calculated volume, further, that the level of bilirubin rose again after the intervention so that this had to be repeated in some cases. Lathe attributed this phenomenon to a reflux of bilirubin from the tissues and to a temporary hepatic disorder. Brown et al. [1] coined the term rebound phenomenon for the reflow of bilirubin.

Subsequent investigations have made it clear that capillary permeability, escape of bilirubin from the blood depots as well as haemolytic factors contributed to the rebound phenomenon [7, 13, 15, 20, 25]. The volume of replaced blood and the duration of transfusion were regarded by most authors as the factors on which the possibility of diminishing the extent of bilirubin reflux depended [1, 5, 6, 10, 11, 12, 14, 20, 23, 25]. Whether the infusion of albumin is able to depress the level of bilirubin is still a debated question [2, 3, 4, 9].

Uniform evaluation of the results obtained by the various authors is difficult because of the diversity of

the material on which their observations were based: some investigators studied the rebound phenomenon in mature, others in premature infants; the material consisted of patients with hyperbilirubinaemia, in others with ABO incompatibility or Rh-isoimmunization. ROSTA and WOHLMUTH [23] demonstrated that the degree of bilirubin rebound varies according to the pathogenesis of icterus gravis, although the exchange transfusion is carried out under identical conditions. The degree of bilirubin rebound may, however, vary even in a homogeneous material; while the bilirubin level is low in some Coombs-positive infants, it is so high in other similarly Coombs--positive babies that several transfusions of blood are needed in order to keep the level below the critical value.

The present material contained patients whose disease was due to Rh-isoimmunization. It had the purpose to study the correlations existing between free anti-D antibodies (to be called antibodies in the following) and the bilirubin rebound in newborn infants.

MATERIAL AND METHODS

In 65 Coombs-positive newborn infants, in addition to the usual pre-transfusion examinations, the free antibodies were determined by the cysteine-papain enzyme method. Since cord blood was not always available, venous blood was used. The patients were divided into

Group I, 27 babies with no demonstrable antibodies in the serum;

Group II, 38 babies with free antibodies in the serum.

RESULTS

Course of the disease and behaviour of bilirubin in Group I

The bilirubin level was below 20 mg per 100 ml during the first five postnatal days in 14 infants. Despite their Coombs positivity, no exchange transfusion was performed in these cases.

As in the other 13 babies the bilirubin level gradually reached the critical level, exchange transfusion became imperative. Six babies received the usual Rh-negative blood (Category 1), whereas 7 babies were given Rh-positive blood (Category 2). The therapeutic use of Rh-positive blood was dealt with in previous communications [17, 18, 19]. Results regarding the bilirubin level in Categories 1 and 2 are illustrated in Fig. 1. Bilirubin values were determined in each patient before, during and after the transfusion; the individual values were then averaged separately for the two categories, and these averages were then compared.

As regards pre-transfusion bilirubin values, there was no significant difference between Categories 1 and 2 ($p > 0.3$). The level of bilirubin fell equally during transfusion, and the degree of rebound was likewise equal in the two categories. In neither of these categories did the level of bilirubin reach the value of 20 mg per 100 ml in the post-transfusion days so that no second intervention was necessary.

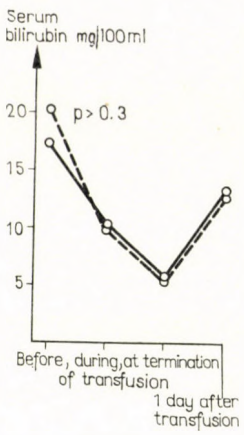

FIG. 1. Changes in serum bilirubin level in patients with no free antibodies. Broken line indicates patients treated with Rh-positive blood, solid line indicates those treated with Rh-negative blood

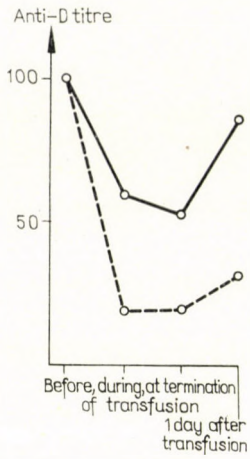

FIG. 2. Changes in free antibody level. Broken line indicates patients treated with combined blood exchange, solid line indicates those treated with Rh-negative blood

Course of the disease and behaviour of bilirubin in Group II

Exchange transfusion had to be carried out in every case; the rapid rise of the bilirubin concentration made it necessary in babies admitted soon after birth, and the high bilirubin level in the babies admitted later.

Nineteen members of this group received Rh-negative blood (Category 1). Blood exchange did not satisfactorily remove the antibodies from the circulation; the antibody titre rose anew after the intervention. The phenomenon was termed antibody rebound [17, 18]. In 9 cases it was necessary to repeat the exchange transfusion once or more than once because of the rapid rise of the bilirubin concentration. Since in the other 10 patients of Category 1 the degree of bilirubin rebound was moderate, no repetition of the transfusion seemed to be indicated. Results in respect of the members of Group II, Category 1, are shown in Table I.

Comparison between the post-transfusion bilirubin values for Groups I and II showed that a high bilirubin concentration and the consequent necessity of renewed exchange transfusion should be excepted if free antibodies are demonstrated in the serum of the newborn. It follows that the serum bilirubin level is often influenced by the presence of such antibodies.

On the reasoning that a more efficient removal of the antibodies would probably reduce the incidence of high bilirubin levels and so also the necessity of repeated exchange transfusions, we elaborated the method of combined blood transfusion

Acta Paediatrica Academiae Scientiarum Hungaricae 11, 1970

TABLE I

Patients with free antibody in the serum, treated with Rh-negative blood

No.	Weight at birth (g)	Time of transfusion (hrs after birth)	Laboratory results	Before first transfusion	After first transfusion	On the post transfusion day	Before second transfusion	After second transfusion	Before third transfusion	After third transfusion	Before fourth transfusion	After fourth transfusion	Number of transfusion
1	2650	8	SeBi mg	15.0	7.3	28.8	28.8	17.5	26.8	9.4			3
			dir. Coombs	++++	++	±	±	0	0	0			
			anti-D	1 : 1	1 : 1	1 : 1	1 : 1	1 : 1	1 : 1	1 : 1			
2	3400	16	SeBi mg	15.8	5.5	14.2							1
			dir. Coombs	+++	0	0							
			anti-D	1 : 1	1 : 1	1 : 1							
3	3400	20	SeBi mg	18.0	7.5	13.0							1
			dir. Coombs	++++	±	±							
			anti-D	1 : 1	1 : 1	1 : 1							
4	2700	8	SeBi mg	14.2	3.2	8.4							1
			dir. Coombs	++++	±	0							
			anti-D	1 : 2	1 : 1	1 : 2							
5	3500	16	SeBi mg	15.8	6.8	10.4							1
			dir. Coombs	++++	±	0							
			anti-D	1 : 4	1 : 2	1 : 2							
6	2900	7	SeBi mg	18.8	7.3	20.5	20.5	17.5	26.8				3
			dir. Coombs	++++	±	±	±	0	0	0			
			anti-D	1 : 4	1 : 1	1 : 1	1 : 1	1 : 1	1 : 1	1 : 1			
7	3800	15	SeBi mg	25.5	10.4	27.2	27.2	9.2					2
			dir. Coombs	++++	++	++	++	0					
			anti-D	1 : 4	1 : 2	1 : 4	1 : 4	1 : 1					
8	2950	77	SeBi mg	35.5	9.9	25.8	25.8	11.0					2
			dir. Coombs	++++	+	+	+	0					
			anti-D	1 : 4	1 : 2	1 : 4	1 : 4	1 : 4					
9	2700	14	SeBi mg	9.3	2.0	19.9	19.9	6.5	20.4	6.5			3
			dir. Coombs	++++	+	±	±	0	±	0			
			anti-D	1 : 8	1 : 4	1 : 8	1 : 8	1 : 4	1 : 8	1 : 2			

10	2600	4	SeBi mg	7.8	3.0	10.1							
			dir. Coombs	++++	0	0							1
			anti-D	1 : 16	1 : 8	1 : 16							
11	3400	13	SeBi mg	13.0	6.2	13.0							
			dir. Coombs	++++	+	±							1
			anti-D	1 : 16	1 : 8	1 : 16							
12	4400	28	SeBi mg	15.3	5.2	9.7							
			dir. Coombs	++++	0	0							1
			anti-D	1 : 16	1 : 8	1 : 16							
13	2900	8	SeBi mg	15.6	7.0	24.0	24.0	9.8					
			dir. Coombs	+++	0	0	±	0					2
			anti-D	1 : 32	1 : 8	1 : 32	1 : 32	1 : 4					
14	3100	12	SeBi mg	12.0	4.5	19.8	19.8	5.9					
			dir. Coombs	+++	±	+	+	0					2
			anti-D	1 : 32	1 : 16	1 : 32	1 : 32	1 : 8					
15	3200	52	SeBi mg	23.8	9.7	14.5							
			dir. Coombs	++++	0	±							1
			anti-D	1 : 64	1 : 32	1 : 32							
16	3000	5	SeBi mg	15.8	3.8	13.5							
			dir. Coombs	++++	0	0							1
			anti-D	1 : 64	1 : 16	1 : 64							
17	3400	16	SeBi mg	7.5	3.0	10.1							
			dir. Coombs	++++	++	0							1
			andti-D	1 : 128	1 : 64	1 : 32							
18	2950	7	SeBi mg	13.2	6.9	28.5	28.5	14.4	36.6	17.2	35.5	17.8	
			dir. Coombs	++++	+	+	+	0	0	0	0	0	4
			anti-D	1 : 128	1 : 64	1 : 128	1 : 128	1 : 64	1 : 128	1 : 32	1 : 64	1 : 32	
19	3200	17	SeBi mg	16.8	7.0	25.1	25.1	7.7	21.6	4.1			
			dir. Coombs	++++	+	++	++	0	0	0			3
			anti-D	1 : 256	1 : 128	1 : 256	1 : 256	1 : 64	1 : 256	1 : 64			
										Total number of transfusions			34

Note SeBi mg = Serum bilirubin, mg/100 m

TABLE II

Patients with free antibodies in the serum, treated with combined blood transfusion

No.	Weight at birth (g)	Time of transfusion (hrs after birth)	Laboratory results	Before (first transfusion)	After (first transfusion)	On the post-transfusion day	Before (second transfusion)	After (second transfusion)	Before (third transfusion)	After (third transfusion)	Before (fourth transfusion)	After (fourth transfusion)	Number of transfusions
1	3200	4	SeBi mg	5.0	1.2	4.7							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 1	0	0							
2	3100	6	SeBi mg	6.3	1.0	8.4							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 2	1 : 1	0							
3	3200	45	SeBi mg	21.7	7.7	15.8							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 2	1 : 1	1 : 1							
4	3300	32	SeBi mg	42.0	17.5	41.0	41.0	15.0					2
			dir. Coombs	++++	++	+	+	0					
			anti-D	1 : 4	1 : 1	1 : 1	1 : 1	1 : 1					
5	3200	32	SeBi mg	18.0	9.7	17.2							1
			dir. Coombs	++++	+	±							
			anti-E	1 - 4	1 : 1	1 : 1							
6	2780	4	SeBi mg	4.5	0.8	3.0							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 8	1 : 1	1 : 1							
7	3500	4	SeBi mg	6.7	1.4	7.8							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 8	1 : 2	1 : 2							
8	3000	4	SeBi mg	7.6	1.2	6.8							1
			dir. Coombs	++++	+	0							
			anti-D	1 : 8	1 : 2	1 : 4							
9	3200	32	SeBi mg	19.2	6.9	15.4							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 16	1 : 2	1 : 8							

10	3100	3	SeBi mg	13.1	4.5								1
			dir. Coombs	++++	0								
			anti-D	1 : 16	1 : 2								
11	3500	4	SeBi mg	9.7	1.6	24.3	24.3	8.0					2
			dir. Coombs	++++	0	0	0	0					
			anti-D	1 : 16	0	0	0	0					
12	2900	45	SeBi mg	37.2	15.0	21.0							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 16	1 : 4	1 : 2							
13	3200	5	SeBi mg	6.7	1.0	6.6							1
			dir. Coombs	+++	+	±							
			anti-D	1 : 32	1 : 4	1 : 8							
14	3510	8	SeBi mg	8.3	3.0	21.5	21.5	7.0					2
			dir. Coombs	+++	++	++	++	0					
			anti-D	1 : 32	1 : 8	1 : 16	1 : 16	1 : 4					
15	2530	4	SeBi mg	9.7	3.2	22.6	22.6	6.7	31.4	9.4			3
			dir. Coombs	++++	0	0	0	0	0	0			
			anti-D	1 : 32	1 : 8	1 : 16	1 : 16	1 : 4	1 : 16	1 : 4			
16	3200	6	SeBi mg	7.5	1.7	6.3							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 32	1 : 2	1 : 8							
17	3000	30	SeBi mg	26.5	8.3	17.5							1
			dir. Coombs	++++	±	±							
			anti-D	1 : 64	1 : 8	1 : 16							
18	2800	17	SeBi mg	22.9	6.8	15.5							1
			dir. Coombs	++++	0	±							
			anti-D	1 : 128	1 : 64	1 : 32							
19	3050	29	SeBi mg	14.2	3.2	12.6							1
			dir. Coombs	++++	0	0							
			anti-D	1 : 128	1 : 32	1 : 64							
												Total number of transfusions	24

Note. SeBi mg = serum bilirubin, mg/100 ml.

[17, 18]; it consists in that the intervention is started with the transfusion of a moderate amount of Rh-positive blood and continued with Rh-negative blood.

Data regarding the 19 patients treated with combined blood transfusion (Category 2) are listed in Table II.

The antibody level of the patients in Group II treated with combined blood transfusion and of those treated with Rh-negative blood are shown in Fig. 2. For comparison, pre-transfusion antibody values were regarded as 100%; the relative values were then determined for each individual during transfusion and on the following day and the individual values were then averaged.

It can be seen from Fig. 2 that the free antibodies were more efficiently removed from the circulation of patients treated with combined blood transfusion than from that of patients treated with Rh-negative blood, and that antibody rebound was less after the combined treatment, while the bilirubin level rose less frequently above the critical value. Twenty-four exchange transfusions were necessary in the 19 cases treated with the combined method (Table II) against 34 transfusions in the 19 cases treated with Rh-negative blood (Table I).

Discussion

The examination of newborns whose haemolytic disease was due to Rh-immunization has made it obvious that the gravity of the disease and the behaviour of the bilirubin level were decisively determined by the presence or absence in the serum of free antibodies.

The course of the disease was milder and the necessity of exchange transfusion did not usually arise if the serum contained no free antibodies, and even if it arose, a repetition was rarely necessary.

An exchange transfusion is, on the other hand, invariably necessary if there are free antibodies in the serum. The bilirubin level often reaches the critical value so that renewed transfusions are frequently needed. The problem regarding the interdependence between free antibodies and bilirubin level requires further elucidation. The observations allowed the following conclusions in this respect.

The fact that the concentration of antibodies diminishes during the exchange transfusion and rises thereafter permits of the assumption that a certain part of the antibodies, after having escaped from the blood paths, passes — like bilirubin — once more into the circulation after the transfusion. Free antibodies, streaming into the extravascular compartment damage the tissues and make it moreover possible for the antigen-antibody reaction and haemolysis to start in the extravascular space, e.g., in the extramedullary haemopoietic foci, the bone marrow. Simultaneous extra- and intravascular haemolysis makes it understandable that the disease is more serious if the serum

contains demonstrable antibodies. Since it is not possible to eliminate all antibodies from the circulation, haemolysis may continue even after transfusion. Haemolysis is presumably more intensive in the extravascular compartment in which Rh-positive erythrocytes are produced at a higher rate provided free antibodies are present. Post-transfusion haemolysis in the vessels is less pronounced because they are filled with Rh-negative blood in the course of transfusion.

It is suggested that, in the presence of free antibodies, bilirubin rebound is fed from two sources, *viz.* the amount of bilirubin reflowing from the tissues and the bilirubin arising in the course of extravascular haemolysis. Haemolysis outside the blood paths and hepatic damage may be more or less pronounced, and the value of bilirubin rebound may vary accordingly.

The extent of bilirubin rebound is always moderate in the absence of free antibodies. This is probably due to that only a smaller amount of antibodies passes from the maternal to the foetal circulation; the erythrocytes of the foetus are capable of neutralizing them so that no extravascular invasion of antibodies occurs, no extravascular haemolysis takes place, and the tissues remain practically unimpaired. If there is no extravascular haemolysis, rebound is caused only by the bilirubin returning from the tissues. The intact or but slightly damaged liver is able to cope with the smaller amount of bilirubin so that the concentration of the latter does not return to the critical pre-transfusion value.

The present investigations failed to provide information as to why the degree of bilirubin rebound was lower in some members of Group II and higher in others (Cases Nos 14, 15, 17, 18 in Table I), although their antibody titre was exactly or nearly equal. It is likewise obscure why there is apparently no correlation between the antibody titre and the extent of bilirubin rebound. While the blood exchange had to be repeated in some cases in which the titre of antibodies was lower (Cases Nos 1, 6, 7, 8 in Table I), no repetition was necessary for other patients with higher antibody titre (Cases Nos 15, 16, 17 in Table I).

Further investigations will have to elucidate the question why the serum of newborn infants contains free antibodies and will have to identify the factors which determine the antibody titre. There are several alternatives in this respect.

(1) Free antibodies may be present in the newborn's serum because the antibodies of maternal origin have not yet been bound by D-antigens, *i.e.*, because the antigen—antibody reaction is still incomplete. Blood transfusion in this condition is more effective. Removal of much antibody decreases the probability of post-transfusion extravascular haemolysis, and the degree of bilirubin rebound will be lower.

(2) Another reason for the presence of free antibodies in the newborn's

serum might be that the red corpuscles are saturated, there is no free D-antigen so that there is nothing to bind the antibodies. The antigen—antibody reaction is complete in such cases, the degree of haemolysis is higher and the effect of transfusions weaker. If the transfusion does not succeed in removing a sufficient amount of antibodies, the degree of post-transfusion extravascular haemolysis will be high and the value of bilirubin may return to the critical level. This would explain the differences in bilirubin rebound at identical antibody titres.

(3) The antibody titre may decisively be determined by the extent to which the foetal organism is able to neutralize antibodies. In cases of increased medullary and extramedullary haematopoiesis a larger amount of antibodies is bound by the red blood corpuscles, and their titre will be accordingly lower. Increased adsorption of antibodies intensifies the process of haemolysis. A low antibody titre is thus by no means incompatible with serious haemolysis. This may be the reason why transfusion has sometimes to be repeated despite the low antibody titre.

It appears from our results that the disease is usually grave if the serum of the newborn contains free antibodies, irrespective of whether their amount is large or small. Repetition of the exchange transfusion can be prevented only by the efficient removal of antibodies. We do not claim that our method of combined blood transfusion is invariably effective; its perfection will be the object of further research work. However, it has already allowed to reduce the number of repeated transfusion. The results of its application point to the significance of the free antibodies.

References

1. Brown, A. K., Zuelzer, W. W., Robinson, A. R.: Studies in hyperbilirubinaemia. II. Clearance of bilirubin from plasma and extravascular space in newborn infants during exchange transfusion. Amer. J. Dis. Child. **93,** 274 (1957).
2. Dieckhoff, J., Theile, L., Theile, H.: Zur Behandlung des Icterus neonatorum Frühgeborener mit Kollidoninfusionen (Periston N.). Z. Kinderheilk. **82,** 539 (1959).
3. Dieckhoff, J., Dietel, V., Künzer, W.: Zur Prophylaxe des Kernicterus Frühgeborener. Dtsch. Gesundh.-Wes. **15,** 949 (1960).
4. Dieckhoff, J., Schneeweiss, B., Schiche, R., Wiegand, U.: Zur Wirkung von Human-Albumin bei Austauschtransfusion. Kinderärztl. Prax. **50,** 337 (1962).
5. Dost, F. H.: Welche sind die günstigsten Bewegungen des Blutes bei der Ausführung von Austauschtransfusionen? Fol. haemat. (Basel) **71,** 322 (1953).
6. Forfar, J. O., Keay, A. J., Elliot, W. D., Cumming, R. A.: Exchange transfusion in neonatal hyperbilirubinaemia. Lancet **2,** 1131 (1958).
7. Giblett, E. R., Varela, J. E., Finck, C. A.: Damage of bone-marrow due to Rh-antibody. Pediatrics **17,** 37 (1956).
8. Gostomzyk, J. K.: Zur Frage der Wirkung von Heparin und Albumin auf die Bilirubinbildung bei der Austauschtransfusion. Z. Kinderheilk. **101,** 136 (1967).
9. Gross, H. P., Michaelis, R., Lüders, D.: Über die Wirkung einer Albuminbehandlung bei Austauschtransfusionen mit größerer Blutmenge. Z. Kinderheilk. **101,** 270 (1967).
10. Haupt, H.: Voraussetzungen und Technik der Austauschtransfusion bei Morbus haemolyticus neonatorum. Kinderärztl. Prax. **29,** 191 (1961).

11. Keuth, U.: Über Zwischenfälle der Austauschtransfusion bei Neu- und Frühgeborenen. Z. Kinderheilk. **81,** 68 (1958).
12. Keuth, U., Partaner, A.: Untersuchungen über den Wiederanstieg des Serumbilirubins nach Austauschtransfusion, sowie zur Frage des optimalen Intervalls bei unterteilter Austauschtransfusion. U. Kinderheilk. **83,** 195 (1959).
13. Kauder, E., Maurer, A. M.: Haemolysis as a contributing factor in the bilirubin rebound after exchange transfusion. J. Pediat. **60,** 163 (1962).
14. Kleint, W.: Untersuchungen über den Bilirubinwechsel bei der Austauschtransfusionsbehandlung des Icterus gravis neonatorum. Z. Kinderheilk. **86,** 632 (1962).
15. Lathe, G. H.: Exchange transfusion as a means of removing bilirubin in haeomlytic disease of the newborn. Brit. med. J. **1,** 192 (1955).
16. Odell, G. B., Cohen, S. N., Gordes, E. H.: Administration of albumin in the management of bilirubinaemia by exchange transfusion. Pediatrics **30,** 611 (1962).
17. Pataki, L., Kaiser, G., Virág, I., Román, F.: Újabb therapiás lehetőségek az Rh-isoimmunisatio okozta Morbus haemolyticus neonatorum kezelésében. Orv. Hetil. **108,** 352 (1967).
18. Pataki, L., Román, F., Kaiser, G., Virágh, I.: Rh-pozitív vér alkalmazásának lehetősége Rh-isoimmunisatio okozta Morbus haemolyticus neonatorum kezelésében. Orv. Hetil, **110** 1968 (1969).
19. Pataki, L., Kaiser, G., Román, F., Virágh, I.: Free anti-D antibody in haemolytic disease of the newborn due to Rh-isoimmunisation. Acta paediat. Acad. Sci. hung. **10,** 245 (1969).
20. Polaček, K.: Factors influencing the effect of exchange transfusion. Acta paediat. scand. **53,** 417 (1964).
21. Rosta, J.: Serum bilirubin during exchange transfusion. The first phase of the rebound phenomenon. Acta paediat. Acad. Sci. hung. **2,** 249 (1961).
22. Rosta, J., Lenkei, P.: Az újszülöttkori vércserék hatásfokáról. Orv. Hetil. **105,** 1301 (1964).
23. Rosta, J., Wohlmuth, G.: A serumbilirubin szint vizsgálata érett újszülöttek és koraszülöttek vércseréje után. Orv. Hetil. **108,** 49 (1967).
24. Walker, W., Murray, S.: The management of haemolytic disease of the newborn. Brit med. J. **4880,** 129 (1954).
25. Walker, W., Neligan, G. A.: Exsanguino-transfusion in haemolytic disease of the newborn. Brit. med. J. **2,** 681 (1955).

Dr. L. Pataki
Gyermekklinika
Szeged, Hungary