The Significance of Maternal—Foetal Blood Group Incompatibility in Premature Infants

By

R. Backhausz, Gertrude Wohlmuth and P. Kiss

Institute for Vaccine Production and Research "Human", and Schöpf-Merei Hospital for Premature Infants, Budapest

(Received October 19, 1960)

A few years ago kernicterus had a prominent place in the mortality statistics of premature infant departments throughout the world. Isoimmunisation processes within the ABO, Rh and other blood group systems have been found to have a decisive role in the genesis of the condition. This observation has at the same time shown the way to be followed in prevention and therapy: the development of isoimmunisation kernicterus may be prevented by the timely exchange of blood. Success depends greatly on early diagnosis, so that early, precise and detailed serological studies are essential [29, 30, 1, 26].

Jaundice is more common, usually more severe and longer in duration in the premature infant than in the mature newborn. However, grave jaundice of the premature infant may be due not only to isoimmunisation processes. Avascularity of the liver, anoxic lesion, listeriosis, cytomegaly, syphilis, etc. may also be the cause.

In order to ensure early diagnosis and to avoid lesions due to isoimmunisation, at admission to our Department each mother and premature infant is tested for blood group and D (Rh_0) factor. On the basis of a statistical comparison of the results with those obtained for mature newborns we shall attempt to answer the questions,

(i) has blood group incompatibility a role in the pathogenesis of premature births?

(ii) what is the significance of blood group incompatibility in the genesis of jaundice of premature infants?

Methods

(i) *Organisation of studies.* A total of 1441 test pairs (mother-infant), representing 88 per cent of the patient material, were performed in the period of from January 1, 1956, to December 31, 1959. The number of patients admitted was 1640. In 199 cases no parallel (mother—child) tests could be made, either because there was no maternal blood available, or owing to the moribund state of the infant at admission.

The patients were premature infants, most of them from Budapest and its surroundings. Ninety-three per cent weighed less than 2000 g. The blood taken from the mothers at the maternity wards was brought to us by the nurse transporting the baby.

(ii) *Blood typing.* The ABO blood groups were determined by the slide technique,

using human A (anti-B), B (anti-A) and O (anti-AB) sera with titres not lower than 1 : 64. To demonstrate the D factor (Rh_0), also by the slide technique, human sera of at least 1 : 64 titre containing incomplete haemagglutinins were used. In doubtful cases the indirect antiglobulin (Coombs') test was also carried out.

(iii) *Studies in suspected cases of maternal isoimmunisation.* When ABO or Rh incompatibility was revealed, or when the clinical picture suggested haemolytic disease of the newborn, the maternal and foetal bloods were subjected to detailed serological studies. A direct antiglobulin reaction was done with the newborn's erythrocytes.

To demonstrate ABO isoimmunisation we determined the titre of anti-A and anti-B haemagglutinins and that of the haemolysins. To demonstrate isoimmunisation against the D factor, D-negative mothers were tested for complete and incomplete anti-D haemagglutinins. When both ABO and D isoimmunisation could be ruled out, erythrocytes from the newborn were added to the serum of the mother and Coombs' indirect test was carried out. In the case of agglutinophilia the maternal serum was neutralized with previously dissolved group antigen.

(iv) *Calculation of gene frequency.* The formulae of FISHER (as cited by KHÉRUMIAN, 13) were used:

$$\text{O gene} = \frac{s}{v}; \quad \text{A gene} = \frac{t-s}{v};$$

$$\text{B gene} = \frac{u-s}{v} \quad \chi^2 = \frac{t \cdot u}{w \cdot x} z^2, \text{ where}$$

$s = \sqrt{O}$, $t = \sqrt{O + A}$, $u = \sqrt{O + B}$, $v = t + u - s$, $w = v^2$, $x = w - (O + A + B)$, $y = AB$, $z = x - y$;

where A, B, O and AB represent the absolute number of individuals belonging to the corresponding blood group. FISHER's method has the advantage over that of BERNSTEIN [5] that the total of the percentage gene frequencies is invariably 100.0.

(v) *Calculation of the blood group combinations of the mothers and their premature newborns* was made by the formulae of SCHIFF and HASELHORST (as quoted by STEFFAN [22]).

When the mother is blood group	Expectable frequency of newborns of blood group			
	O	A	B	AB
O	$\overline{O}^3$	$\overline{O}^2\overline{A}$	$\overline{O}^2 \cdot \overline{B}$	—
A	$\overline{O}^2 \cdot \overline{A}$	$\overline{A} \cdot ((\overline{O} + \overline{A})^2 + \overline{O} \cdot \overline{A})$	$\overline{O} \cdot \overline{A} \cdot \overline{B}$	$\overline{A} \cdot \overline{B}\,(\overline{O} + \overline{A})$
B	$\overline{O}^2 \cdot \overline{B}$	$\overline{O} \cdot \overline{A} \cdot \overline{B}$	$\overline{B}((\overline{O} + \overline{B})^2 + \overline{O} \cdot \overline{B})$	$\overline{A} \cdot \overline{B}(\overline{O} + \overline{B})$
AB	—	$\overline{A} \cdot \overline{B}(\overline{O} + \overline{A})$	$\overline{A} \cdot \overline{B}(\overline{O} + \overline{B})$	$\overline{A} \cdot \overline{B}(\overline{A} + \overline{B})$

where $\overline{A}$, $\overline{B}$, and $\overline{O}$ represent the frequency of the corresponding gene, as calculated according to FISHER.

RESULTS and DISCUSSION

(i) *Blood group frequency of the premature newborns and their mothers.* The results of blood typing for the mothers and their premature newborns and the number of combinations are presented in Table I. The blood group and gene frequencies are shown in Table II.

As controls, the results of two Budapest series are presented, one [4] mainly for the VIIIth district of Budapest and the other [3] for suburban areas: districts IV and XVIII. There was no statistically significant

TABLE I

Blood Group Relations between Mother and Child in Cases of Premature Birth

Maternal blood type	Blood type of the child				Number of mothers
	O	A	B	AB	
O	247	116	52	—	415
A	127	406	37	43	613
B	67	41	126	31	265
AB	—	74	42	32	148
Number of children	441	637	257	106	1441

difference in blood group frequency between the test and the control groups, either with the mothers or with the premature infants. The frequencies of A and O genes were between the values for series I and II [4, 3]. The frequency of gene B was somewhat higher in our material than in the controls. This might have been due to the fact that 27.9 per cent of those admitted (457 premature infants) had come from areas other than Budapest; for example, 8.1 per cent from Pest county, 2.9 per cent from Szolnok county, and 1.4 from Heves county, In all these parts of Hungary the frequency of gene B is somewhat higher than in Budapest (15.07, 15.63 and 14.33 per cent, respectively).

The value of χ^2, as computed according to FISHER did not exceed the limit for one degree of freedom ($\chi^2_{0.05} = 3.841$) in any of the groups. Higher χ^2 values indicate an error in calculation or are due to selection. Thus, in our premature newborn material there was no selective factor involved that would have caused a shift in favour of some blood group from the mean blood group frequency for Budapest

(ii) *Frequency of ABO blood group*

TABLE II

Percentage Incidence of Blood Groups and Gene Counts

Blood type	Mothers	Premature infants	Total	Budapest studies	
				series I	series II
O	28.30	30.60	29.70	29.87	32.87
A	42.54	44.21	43.37	45.24	42.04
B	18.39	17.83	18.11	17.00	17.76
AB	10.27	7.36	8.81	7.88	7.32
gene O	53.94	54.90	54.69	54.40	57.12
gene A	30.95	30.93	31.09	31.86	29.11
gene B	15.11	14.17	14.22	13.74	13.79
χ^2	0.923	2.297	1.018	0.639	0.968
Number of subjects tested	1441	1441	2882	1041	2966

TABLE III

Combinations Calculated on the Basis of Percentage Incidence of Blood Type Gene Counts and of those Observed in the Case of Premature Infants

Blood type of		Percentage incidence, calculated	Percentage incidence, observed				
			total	jaundice			
mother	child			none	slight	moderate	grave
O	O	16.4	17.1	19.4	15.2	17.3	15.1
A	O	9.3	8.8	9.6	10.3	8.8	6.9
A	A	28.2	28.2	28.4	30.9	26.7	27.8
B	O	4.2	4.7	4.8	4.0	5.1	4.4
B	B	7.9	8.8	11.1	10.3	5.9	7.7
AB	A	3.8	5.1	4.8	5.8	4.8	5.5
AB	B	3.0	2.9	3.5	2.2	3.7	1.6
AB	AB	2.0	2.2	2.9	2.2	2.9	0.5
Compatible, total		7.48	77.8	84.5	80.9	75.2	69.8
O	A	9.3	8.1	4.6	4.5	8.3	14.5
O	B	4.2	3.6	1.9	1.8	5.6	4.9
A	B	2.4	2.6	2.9	1.3	2.1	3.3
A	AB	3.8	3.0	2.5	3.6	3.5	2.7
B	A	2.4	2.8	2.3	3.1	2.9	3.3
B	AB	3,1	2,1	1,2	4,5	2,4	1,6
Incompatible, total		25.2	22.2	15.4	18.8	24.8	30.2

combinations of the mothers and their premature infants.

Next it was analysed whether the maternal and newborn blood group combinations observed differed from those computed on the basis of gene frequencies. The results are presented in Table III. Of the 14 combinations 8 were compatible (transfundophilic combinations), and 6 were incompatible (agglutinophilic combinations). The computed total frequency of the former was 74.77 per cent; of the latter, 25.23 per cent. The expected and observed values agreed well, there were only two categories in which the difference exceeded 1 per cent. Thus, there was no blood group combination which would have occurred significantly more often or less frequently than expected.

In the past few years several authors have claimed the existence of a correlation between the ABO groups and spontaneous miscarriages. Others [9, 25, 21, 19, 14, 17, 11, 18, 23], found no such relationship. Without taking sides in this issue, the above data make the impression that blood group incompatibility has either no role at

all, or plays a very subordinate part, in the genesis of premature delivery.

(iii) *Relationship between blood groups and jaundice.*

The frequency of the single combinations in relation to the incidence of jaundice in the premature infants is shown in Table III. The material has been divided into four groups: *a)* no jaundice, *b)* slight jaundice, *c)* moderate jaundice, and *d)* grave jaundice. (The cases of kernicterus have been included in the last group.) As shown in Table III, the compatible combinations were more frequent in the cases without jaundice or with slight jaundice, and less frequent among the patients with grave jaundice, than calculated. There was a good agreement beween the expected and observed results in the group of moderate jaundice. The increased incidence of O-group mother and A-group child combinations in the group of grave jaundice was remarkable; as opposed to the calculated value of 9.3 per cent it occurred in 14.5 per cent. These results suggest a role of ABO incompatibility in the grave jaundice of the premature infant; since, however, grave jaundice occurred also in the compatible group, the ABO incompatibility cannot be the sole causative factor.

To facilitate comparison, data for an earlier, unselected newborn material [2] are presented in Table IV. Evaluation was based on essentially the same principles as with the premature babies.

The incidence of jaundice among mature newborns was 52.7 per cent,

TABLE IV

Percentage Incidence of Jaundice among Premature Infants and Unselected Newborns

Grade of jaundice	Premature infants 1441 cases	Newborns 784 cases
None	33.24 per cent	47.70 per cent
Slight	15.48 per cent	43.88 per cent
Moderate	26.02 per cent	7.27 per cent
Grave	25.26 per cent	1.15 per cent

a figure closely comparable to the 55 per cent reported by LENART and BIRÓ [16]. Among the premature infants the incidence of jaundice was 66.2 per cent (Table III). Our results agree well with the data in the literature in that an elevated serum bilirubin level is more common in premature infants than in mature newborns [27, 15, 24, 7]. Grouping our data according to the severity of jaundice, it will be found that in the group of unselected newborns the incidence of moderately severe and grave jaundice was markedly lower than in the premature infant material.

In Table V, we present data illustrating the frequency of the expected and observed combinations. In this group (part of the Budapest series II) the gene O occurred more frequently than in the group of premature infants (see columns 5 and 6 in Table II). The frequency of combinations has been computed with regard to that. The calculated and observed values were again in good agreement. The combined total of compatible and incompatible combinations hardly differed from the computed value. In the cases without jaundice and in those

TABLE V

Frequency of ABO Blood Group Combinations among Unselected Newborns

Blood type of		Frequency calculated	Frequency observed				
			total	jaundice			
mother	child			none	light	moderate	grave
O	O	19.2	20.0	20.6	19.5	21.1	11.1
A	O	9.4	9.9	11.2	9.9	3.5	
A	A	25.6	23.8	23.0	27.3	8.8	11.1
B	O	4.7	5.6	3.7	7.0	10.5	
B	B	8.3	7.9	8.8	7.5	5.3	
AB	A	3.4	3.2	2.7	3.5	5.3	
AB	B	2.8	2.3	2.7	2.0	1.7	
AB	AB	1.7	1.7	0.8	2.6	—	11.1
Compatible, total		75.1	74.4	73.5	79.3	56.2	33.3
O	A	9.4	8.7	7.0	7.0	22.8	55.6
O	B	4.7	4.5	3.7	4.4	10.5	
A	B	2.3	3.7	4.0	3.8	1.7	
A	AB	3.4	3.4	3.7	3.2	3.5	
B	A	2.3	3.2	4.6	1.5	3.5	11.1
B	AB	2.8	2.2	3.5	0.9	1.7	
Incompatible, total		24.9	25.7	26.5	20.8	43.7	66.7

with slight jaundice the incidence of compatible combinations was as expected, or even somewhat higher. In contrast, in the groups of moderate jaundice and grave jaundice the incidence of compatible combinations was 56.2 per cent and 33.3 per cent, respectively, *i. e.* significantly lower than the calculated 75.1 per cent value.

In the premature infant material lesions due to D-factor isoimmunisation were observed in 2 cases (0.14 per cent). According to data in the literature, in obstetric material the incidence of such lesions is around 0.3 per cent. This, however, includes the foetuses died *in utero*, whereas we analysed the data exclusively for live births. It is at any rate clear that lesions due to Rh isoimmunisation were not more common among the premature infants than in the mixed, unselected newborn material.

In the group of premature infants grave jaundice occurred in 25.3 per cent (365 cases) (Table IV). Among these 70 cases were considered extremely serious, there having been kernicterus or grave jaundice (or both) and exchange transfusion had to be performed.

TABLE VI

Distribution of Kernicterus Incompatibility, and Complications

Year	Total number of cases	Incompatibility			Complications	
		ABO	Rh(D)	none	present	none
1956	18	5	1	12	12	6
1957	2	1	1	8	7	3
1958	2	1	—	1	1	1
1959	4	—	1	3	3	1
Total	34	7	3	24	23	11

The principal clinical data in these cases associated with grave jaundice were as follows.

Without there having been a change in the number of premature infants treated per year, the incidence of kernicterus became significantly less as a result of the improved clinical treatment [27, 15]. The incidence in 1956 was 18 per cent; in 1957, 10; in 1958, 2; and in 1959, 4 per cent. The condition was associated with haemorrhage in the cerebrum, cerebellum or vertebral canal in 13 cases, with pneumonia in 3, with aspiration in 3 cases and with umbilical septicaemia in 1 case (Table VI). Blood exchange transfusion was performed in 37 cases (Table VII); it had to be performed in 11 cases in 1956, in 11 in 1957, in 10 in 1958, in 5 in 1959. The apparent reduction in 1959 was due to the fact that in the case of 4 premature infants contraindications had prevented us from carrying out the exchange. Three of these babies died; necropsy revealed kernicterus, extensive cerebral haemorrhage and bronchopneumonia.

TABLE VII

Distribution of Exchange Transfusions according to Indications

Year	Total number of cases	Incompatibility		
		ABO	Rh(D)	None
1956	11	6	—	5
1957	11	5	—	6
1958	10	6	1	3
1959	5	3	1	1
Total	37	20	2	15

Except for these few cases the exchange transfusion was performed when the serum bilirubin level was higher than 3 mg per 100 ml in umbilical blood or 18 mg per 100 ml in systemic blood during the next few days. If we discount the two cases of Rh isoimmunisation, of the 68 cases of grave jaundice 41 were compatible from the point of view of the ABO system and 27 (39.8 per cent) were incompatible, a value definitely higher than the calculated one of 25.2 per cent.

In 10 of the 27 incompatible cases the maternal sera showed the serological changes usual with ABO-isoimmunisation: the complete agglutinin titre was 1 : 512 or higher (in three cases 1 : 4096), the incomplete agglutinin titre 1 : 8 or higher (in 2 cases 1 : 128), and the haemolysin titre varied between 1 : 4 and 1 : 16. In these 10 cases the serological and clinical findings pointed clearly to ABO-isoimmunisation. As related to our total material, this represents an incidence of 0.7 per cent. According to data in the literature, the incidence

of perinatal damage due to ABO isoimmunisation is about the same as, or somewhat higher than, that of Rh isoimmunisations [28, 20, 6, 10]. Among premature infants the lesions due to ABO isoimmunisation occur five times more often than those connected with the D factor.

The role of ABO incompatibility in the pathogenesis of jaundice of the newborn is far from being an exclusive one, since jaundice may appear with compatible combinations as well, but its significance must not be underestimated. Grave jaundice occurred in 364 of a total of 1141 premature infants: 254 were born to compatible and 110 to incompatible parents. Had there been no correlation between the incidence of grave jaundice and the ABO blood group system, the number of babies born from incompatible combinations were 92, in accordance with the calculated value of 25.2 per cent. The difference between the calculated and observed number of cases (18 cases) represented 1.3 per cent of the total number of patients studied and seemed to be correlated with ABO incompatibility.

In the group of mature newborns (784 cases) the incidence of grave jaundice was 1.15 per cent (9 cases); in 3 cases (0.38 per cent) Rh incompatibility and in 6 (0.76. per cent) ABO isoimmunisation was responsible for it. Moderate jaundice was observed in 57 newborns (7.4 per cent), 25 of whom had been born to ABO-incompatible parents. Without a correlation between the incompatible combinations and the number of newborns with moderate jaundice, the number should have been 14, according to the computed incidence of 24.9 per cent. The difference between the calculated and the observed number of cases (11 cases) represented 1.4 per cent of the total number examined.

On the basis of the above figures ABO incompatibility was responsible for the development of moderate jaundice in 1.4 per cent of the mature newborns, whereas in the group of premature babies it produced grave jaundice with about the same frequency (1.3 per cent). The combined incidence of moderate and grave jaundice due to ABO incompatibility in the group of mature newborns was 2.2 per cent, more than the 1.3 per cent incidence for the grave jaundice in premature babies. (According to the data in Table III, ABO incompatibility cannot be made responsible for moderate or slight jaundice in premature infants.)

According to our results, both Rh incompatibility and ABO isoimmunisation produce jaundice more frequently among mature newborns than among premature babies. Jaundice due to ABO incompatibility is much slighter in the mature newborn than in the premature infant. The circumstance that the effect of isoimmunisation manifests itself less often in premature infants, tends to point to a decisive role of the immaturity of the liver and of the anoxic lesions in the pathogenesis of jaundice in the premature infant. The more marked effect of isoimmunisation in the mature newborn may be correlated

with the longer duration of pregnancy and the stronger antigenicity of the erythrocytes of the mature newborn.

For the sake of completion let us mention that isoimmunisation against any blood group antigen other than A, B, and D did not occur in our material. In the cases of grave jaundice the direct antiglobulin reaction with the erythrocytes of the newborn was always negative, except the cases of Rh immunisation. Similarly negative were the indirect antiglobulin reactions with maternal serum and newborn erythrocytes.

Summary

A material of 1441 premature infants has been studied for blood groups, together with blood typing of the mothers. The results were compared with those obtained for 784 unselected newborns.

The maternal — foetal blood group and gene frequencies observed in the premature infants did not differ either from the Budapest frequency (determined on the basis of 4007 tests) or from the calculated frequencies.

Blood group combinations (ABO or Rh) substantially different from the computed ones have not occurred in the material. Thus, blood group incompatibility could not be demonstrated to have played a significant role in the premature deliveries.

As to the correlation between blood group incompatibility and jaundice, as well as the severity of the jaundice, in premature infants, ABO compatible combinations were found to occur more frequently among the cases with no or slight jaundice and less often among those with grave jaundice, than the calculated figures. Alongside other factors, ABO incompatibility plays a significant role in the pathogenesis of icterus gravis of the premature infant. According to the calculations, ABO incompatibility causes moderate jaundice in 1.4 per cent of the mature newborns and grave jaundice with about the same frequency in premature infants.

The incidence of Rh isoimmunisation has been found to agree with the data reported in the literature.

References

1. Allen, F. H., Diamond, L. K.: Erythroblastosis foetalis. Little, Brown & Co, Boston (1958)
2. Backhausz, R., Bedő, K.: Anyák és újszülöttek vérének rendszeres vizsgálata inkompatibilitásra kb. 800 eset kapcsán. Meeting of Hungarian Gynaecologists, Budapest (1956)
3. Backhausz, R., Nemeskéri, J.: Häufigkeit der ABO-Blutgruppen und des D-Faktors in Ungarn. Z. Morph. Anthrop. **51,** 103 (1960)
4. Backhausz, R., Nemeskéri, J., Vajda, J.: Rh-Faktor Untersuchungen in Ungarn. Homo, **1,** 192 (1950)
5. Bernstein, F.: Zusammenfassende Betrachtungen über die erblichen Blutstrukturen des Menschen. Z. indukt. Abstamm.-u. Vererblehre **37,** 237 (1925)
6. Biermé, R., Ducos, J., Ruffié, J.:

La maladie hémolytique perinatale due à l'immunisation maternelle par les facteurs A et B. Sangre, **3,** 205 (1958)
7. Dieckhoff, J., Thiele, L.: Zur Pathogenese und Therapie der Hyperbilirubinämie des Neugeborenen. Münch. Med. Wschr. **102,** 209 (1960)
8. Halbrecht, J.: Role of Hemagglutinins anti-A and anti-B in Pathogenesis of Jaundice of the Newborn (icterus neonatorum praecox). Amer. J. Dis. Child. **68,** 248 (1944)
9. Hirszfeld, L., Zborowski, R.: Gruppenspezifische Beziehungen zwischen Mutter und Frucht und elektive Durchlässigkeit der Placenta. Klin. Wschr. **1,** 1152 (1925)
10. Hsia, Y. Y., Gellis, S. S.: Studies on Erythroblastosis due to ABO Incompatibility. Pediatrics **13,** 503 (1954)
11. Hunt, A. L., Plampin, D. W.: High Titre alpha and beta Antibodies as a Cause of Repeated Miscarriages. J. Med. lab. Techn. **13,** 391 (1956)
12. Kaloud, H.: Ikterus gravis, hervorgerufen durch Unverträglichkeit im Rahmen der klassischen Blutgruppen. Wien. klin. Wschr. **72,** 121 (1960)
13. Khérumian, R.: Génétique et anthropologie des groupes sanguins. Vigot Frères, Paris (1951)
14. Kirk, R. L., Shield, J. W., Stenhouse, N. S., Bryce, L. M., Jakobowitz, R.: A Further Study of ABO Blood Groups and Differential Fertility among Women in Two Australian Maternity Hospitals. Brit. J. Prev. soc. Med. **9,** 104 (1955)
15. Kiss, P.: Beiträge zur Behandlung des Icterus gravis von Frühgeborenen. Kinderärztl. Prax. **27,** 290 (1959)
16. Lenart, G., Biró, S.: Die Isoagglutination bei den Neugeborenen und ihre Beziehungen zum Icterus Neonatorum. Jb. Kinderheilk. **124,** 77 (1929)
17. Mataunaga, E.: Selektion durch Unverträglichkeit im ABO-Blutgruppen-System zwischen Mutter und Foetus. Blut **2,** 188 (1956)
18. McNeil, C., Trentelman, E. F., Fullmer, C. D., Kreutzer, V. O., Orlob, B. B.: The Significance of Blood Group Conflicts and Aberrant Salivary Secretion in Spontaneous Abortion. Amer. J. clin. Path. **28,** 469 (1957)
19. McNeil, C., Warenski, L. C., Fullmer, C. D., Trentelman, E. F.: A Study of Blood Groups in Habitual Abortion. Amer. J. clin. Path. **24,** 767 (1954)
20. Moullec, J. Lewi, S.: La maladie hémolytique du nouveau-né causée par l'incompatibilité des groupes ABO. Rev. franç. Ét. Clin. Biol. **2,** 1048 (1957)
21. Sora, P.: Incompatibilita ABO tra i coniugi ed aborto; contributo clinico. Minerva ginec. (Torino) **6,** 80 (1954)
22. Steffan, P.: Handbuch der Blutgruppenkunde. Lehmann, München (1932)
23. Stojanov, S. G.: Rh-Faktor und habituelle Abortus. Zbl. Gynäk. **85,** 585 (1960)
24. Török, I., Szabó, L.: Über die Gelbsucht der Frühgeborenen. Acta paediat. hung. **1,** 55 (1960)
25. Waterhouse, J. A. H., Hogben, L.: Incompatibility of Mother and Foetus with respect to Isoagglutinogen A and its Antibody. Brit. J. soc. Med. **1,** 1 (1947)
26. Wiener, A. S., Wexler, J. B., Hurst, J. G.: The Use of Exchange Transfusion for the Treatment of Severe Erythroblastosis due to A, B Sensitization, with Observations on the Pathogenesis of the Disease. Blood **4,** 1014 (1949)
27. Wohlmuth, G., Kiss, P.: Die medikamentöse Behandlung des Icterus gravis Frühgeborener. Acta paediat. hung. **1,** 41 (1960)
28. Wolf, H. G.: Morbus haemolyticus neonatorum. Eine kritische Übersicht. Wien. Z. inn. Med. **36,** 288 (1955)
29. Wolff, J.: Neue Forschungen über die Bedeutung des Blutgruppensystems ABO. II. Wirkung einer ABO Unverträglichkeit auf das Neugeborene. Kinderärztl. Prax. **25,** 223 (1957)
30. Wöllner, D., Plückthun, H.: Klinische und serologische Untersuchungen zur haemolytischen Neugeborenenerkrankung infolge ABO-Unverträglichkeit. Z. Kinderheilk. **81,** 609 (1958).

Dr. R. Backhausz,
Szállás u. 5.
Budapest X., Hungary