HAEMOLYTIC DISEASE OF THE NEWBORN

A REPORT FROM THE NATAL RHESUS UNIT

H. L. WALLACE, M.D., F.R.C.P.

W. E. B. EDGE, M.B., M.R.C.P.

N. M. MANN, M.D., M.R.C.P., D.C.H.

and

PHYLLIS MOORES, B.SC.

Addington Children's Hospital, Durban

In 1951, the Director of the Durban Blood Transfusion Service, Dr. J. C. Thomas, put forward the suggestion that a 'Rhesus Unit' should be established at Addington Hospital, Durban, to serve not only Durban but the whole Province of Natal, and to which all Rhesus-immunized women in the province might be referred for their confinements. The advantages of such a scheme seemed obvious in that adequate facilities, both laboratory and clinical, are much more readily available at a large specially-equipped centre than in outlying country districts or even in private nursing homes. The concept of centralization of these difficult cases was wholeheartedly endorsed by the obstetrical and paediatric staffs of the hospital and, accordingly, an explanatory circular was sent to all medical practitioners in the province inviting their cooperation. In the Durban area the response to this appeal has been excellent and it is probably a true statement that in the past 4 years the vast majority of Rhesus-immunized women in the area have been delivered at Addington Hospital. The use made of the unit by the country districts is more difficult to assess, since the number of cases diagnosed in these districts is problematical. Despite the relatively small number of country cases, however, it is encouraging to note that these have come from all parts of the province, and the majority have done well.

At Addington Hospital there is a close liaison between the obstetrical and paediatric departments, and all infants born there come under the care of the paediatric staff, who are thus responsible for deciding on and carrying out the treatment of the newborn infant with haemolytic disease.

The procedure adopted by the Rhesus unit has been standardized as far as possible. The prospective mother's blood group is determined during early pregnancy. If she is Rh-negative antibody tests are carried out and repeated at 24, 32 and 36 weeks if practicable. Should Rhesus antibodies develop admission to hospital is advised in the 38th week.

Immediately after delivery clotted and unclotted samples of cord blood are sent to the special Rhesus laboratory, where the following tests are carried out:

1. The direct Coombs anti-human-globulin test
2. Haemoglobin estimation
3. Blood and Rhesus grouping
4. Serum bilirubin estimation
5. Normoblast count.

Whilst the above tests are being carried out in the laboratory the newborn infant is subjected to a careful clinical examination, during which particular attention is paid to the weight, the state of the general health, the presence or absence of jaundice, and the size of the liver and spleen. Details of the mother's obstetrical history are also carefully assessed. Essential laboratory and clinical investigations are usually complete within an

hour of birth and it is possible, therefore, to institute the required treatment with the minimum of delay.

Town and Country Cases

The series under consideration comprises a total of 112 cases admitted to Addington Hospital during the 4 years 1951-55. Of these, 84 were admitted from the Durban area, the remaining 28 being referred from various country towns throughout the province of Natal.

Stillbirths etc.

The total of 112 cases includes 12 pregnancies which terminated in hydrops foetalis, stillbirth or abortion. For the purpose of this paper these regrettable cases will be excluded from our analysis, which is concerned primarily with the mangement of the affected live-born infant. Suffice it to observe that, where there is a history of one or more stillbirths and where the husband is homozygous, early induction of labour or Caesarean section might possibly increase the chances of procuring a live infant. Such a policy was not generally adopted in this series but will be carefully considered in future cases, bearing in mind the apparent advantages of early induction in selected cases as reported by Kelsall and Vos.[1]

Live-born Infants

During the 4 years 100 live-born infants were born of Rh-sensitized mothers. Although antibodies were detected in the maternal blood, 20 of these infants proved to be Rh-negative and, being unaffected, did not require any treatment. The remaining 80 Rh-positive infants were all affected to a greater or less degree and their treatment will be discussed in some detail with particular reference to the indications for exchange transfusion.

The total number of cases presenting in the 4 years may be tabulated as follows:

Stillbirths and abortions ..	12 cases
Infant Rh. —, Coombs test — ..	20 cases
Infant Rh. +, Coombs test + ..	80 cases
Total	112 cases

Indications for Exchange Transfusion

In the treatment of haemolytic disease of the newborn the merits of exchange transfusion have been proved by a number of investigators.[2,4] Compared with other forms of treatment not only is the survival rate higher, irrespective of the birth weight or of the severity of the disease,[4] but the incidence of kernicterus is reduced by at least two-thirds. Impressed by these undoubted virtues, some units still perform exchange transfusion in all cases where the cord blood gives a positive Coombs anti-human-globulin test. Not only is this a waste of precious Rh-negative blood, but it exposes unnecessarily a considerable proportion of infants (estimated at 30-40% of those affected) to the risks of the operation, viz. shock, air-embolism, infection, incompatible transfusion, portal-vein thrombosis and perforation. Apart from the first we have as yet encountered none of these mishaps, but they are too real to be ignored.

In an attempt to define the indications for exchange transfusion Mollison and Cutbush[5,6] first drew attention to the value of the cord haemoglobin as an index of severity, taking 14·8 g.% as the critical value. Subsequent studies[3,4] on their untreated infants revealed an incidence of kernicterus of 7% in the mature and 14% in the immature groups, and these workers have, therefore, revised their criteria and now regard as indications for immediate exchange tranfusion (in the presence of a positive Coombs test):[7]

1. A birth weight of 6 lb. or less, or an infant born 3 weeks or more before the expected date of delivery (irrespective of other findings)
2. A history of the mother having previously given birth to an affected infant (irrespective of other findings)
3. A cord haemoglobin below 15·5 g.%

They point out that in cases where the cord haemoglobin lies between 15·5 and 17·5 g.% there is still a possibility of kernicterus occurring, and in such cases the onset of jaundice within the first 24 hours should be an indication for treatment. Walker and Neligan,[8] discussing this same problem, regard the cord bilirubin level as being of considerable help, and in cases where the cord haemoglobin lies between 14·8 and 17·7 g.% a bilirubin value of 2·8 mg.% or above is taken as an indication for exchange tranfusion. Other factors which are recognised as being of some assistance in assessing border-line cases are: The degree of positivity of the Coombs test, the maternal anti-Rh titre and the nucleated red-cell count on the cord blood. We would also include splenic and hepatic enlargement.

In the Durban unit we have not favoured the practice of routine exchange transfusion in all affected infants but have attempted to differentiate between those requiring immediate treatment and those which could safely be left untreated. Sometimes the selection of cases for treatment presents little difficulty, as in the severely affected infant whose precarious state is apparent from the moment of birth. More often the decision entails the careful appraisal of a variety of factors. Whilst following fairly closely the indications for exchange transfusion suggested by other units, our standards may have been less rigid in that the decision for or against treatment has not always depended on pre-elected laboratory findings. For example, although the cord haemoglobin level has proved a most valuable guide in all cases, we have not necessarily been bound by any arbitrary figure but rather have considered the haemoglobin level in relation to the many other relevant factors. A further point is that the ultimate decision regarding treatment in each case has rested on one individual, a policy which, we believe, makes for uniformity and consistancy of approach.

It is now proposed to discuss the foregoing guiding principles in the treatment of haemolytic disease of the newborn in relation to this series of cases. To simplify description the latter have been divided into 2 main groups, viz.: *Group I*—immediate exchange transfusion performed (50 cases). *Group II*—no immediate treatment given (30 cases).

Birth Weight. There were 14 infants whose weight was less than 6 lb. at birth. Of these, 12 were given immediate exchange tranfusion and 2 were left untreated. One of the treated cases with a birth weight of only

hour of birth and it is possible, therefore, to institute the required treatment with the minimum of delay.

Town and Country Cases

The series under consideration comprises a total of 112 cases admitted to Addington Hospital during the 4 years 1951-55. Of these, 84 were admitted from the Durban area, the remaining 28 being referred from various country towns throughout the province of Natal.

Stillbirths etc.

The total of 112 cases includes 12 pregnancies which terminated in hydrops foetalis, stillbirth or abortion. For the purpose of this paper these regrettable cases will be excluded from our analysis, which is concerned primarily with the mangement of the affected live-born infant. Suffice it to observe that, where there is a history of one or more stillbirths and where the husband is homozygous, early induction of labour or Caesarean section might possibly increase the chances of procuring a live infant. Such a policy was not generally adopted in this series but will be carefully considered in future cases, bearing in mind the apparent advantages of early induction in selected cases as reported by Kelsall and Vos.[1]

Live-born Infants

During the 4 years 100 live-born infants were born of Rh-sensitized mothers. Although antibodies were detected in the maternal blood, 20 of these infants proved to be Rh-negative and, being unaffected, did not require any treatment. The remaining 80 Rh-positive infants were all affected to a greater or less degree and their treatment will be discussed in some detail with particular reference to the indications for exchange transfusion.

The total number of cases presenting in the 4 years may be tabulated as follows:

Stillbirths and abortions ..	12 cases
Infant Rh. —, Coombs test — ..	20 cases
Infant Rh. +, Coombs test + ..	80 cases
Total	112 cases

Indications for Exchange Transfusion

In the treatment of haemolytic disease of the newborn the merits of exchange transfusion have been proved by a number of investigators.[2,4] Compared with other forms of treatment not only is the survival rate higher, irrespective of the birth weight or of the severity of the disease,[4] but the incidence of kernicterus is reduced by at least two-thirds. Impressed by these undoubted virtues, some units still perform exchange transfusion in all cases where the cord blood gives a positive Coombs anti-human-globulin test. Not only is this a waste of precious Rh-negative blood, but it exposes unnecessarily a considerable proportion of infants (estimated at 30-40% of those affected) to the risks of the operation, viz. shock, air-embolism, infection, incompatible transfusion, portal-vein thrombosis and perforation. Apart from the first we have as yet encountered none of these mishaps, but they are too real to be ignored.

In an attempt to define the indications for exchange transfusion Mollison and Cutbush[5,6] first drew attention to the value of the cord haemoglobin as an index of severity, taking 14·8 g.% as the critical value. Subsequent studies[3,4] on their untreated infants revealed an incidence of kernicterus of 7% in the mature and 14% in the immature groups, and these workers have, therefore, revised their criteria and now regard as indications for immediate exchange tranfusion (in the presence of a positive Coombs test):[7]

1. A birth weight of 6 lb. or less, or an infant born 3 weeks or more before the expected date of delivery (irrespective of other findings)
2. A history of the mother having previously given birth to an affected infant (irrespective of other findings)
3. A cord haemoglobin below 15·5 g.%

They point out that in cases where the cord haemoglobin lies between 15·5 and 17·5 g.% there is still a possibility of kernicterus occurring, and in such cases the onset of jaundice within the first 24 hours should be an indication for treatment. Walker and Neligan,[8] discussing this same problem, regard the cord bilirubin level as being of considerable help, and in cases where the cord haemoglobin lies between 14·8 and 17·7 g.% a bilirubin value of 2·8 mg.% or above is taken as an indication for exchange tranfusion. Other factors which are recognised as being of some assistance in assessing border-line cases are: The degree of positivity of the Coombs test, the maternal anti-Rh titre and the nucleated red-cell count on the cord blood. We would also include splenic and hepatic enlargement.

In the Durban unit we have not favoured the practice of routine exchange transfusion in all affected infants but have attempted to differentiate between those requiring immediate treatment and those which could safely be left untreated. Sometimes the selection of cases for treatment presents little difficulty, as in the severely affected infant whose precarious state is apparent from the moment of birth. More often the decision entails the careful appraisal of a variety of factors. Whilst following fairly closely the indications for exchange transfusion suggested by other units, our standards may have been less rigid in that the decision for or against treatment has not always depended on pre-elected laboratory findings. For example, although the cord haemoglobin level has proved a most valuable guide in all cases, we have not necessarily been bound by any arbitrary figure but rather have considered the haemoglobin level in relation to the many other relevant factors. A further point is that the ultimate decision regarding treatment in each case has rested on one individual, a policy which, we believe, makes for uniformity and consistancy of approach.

It is now proposed to discuss the foregoing guiding principles in the treatment of haemolytic disease of the newborn in relation to this series of cases. To simplify description the latter have been divided into 2 main groups, viz.: *Group I*—immediate exchange transfusion performed (50 cases). *Group II*—no immediate treatment given (30 cases).

Birth Weight. There were 14 infants whose weight was less than 6 lb. at birth. Of these, 12 were given immediate exchange tranfusion and 2 were left untreated. One of the treated cases with a birth weight of only

4 lb. 14 oz. died, and the remainder made a good recovery. We do not feel convinced, provided the other factors are satisfactory, that all infants weighing 6 lb. or less at birth require immediate treatment.

Mother's Obstetrical History. As already mentioned, the previous obstetric history of the mother must influence the decision whether her infant should receive immediate treatment. In this series 16 mothers gave a history of having had one previous infant affected and in 4 of these the new infants were left untreated and made an uneventful recovery. A further 11 mothers had had more than one affected infant and in all these cases immediate exchange transfusion was carried out. It is suggested that a history of only one previous infant affected is not an absolute indication for immediate treatment, but that where there have been 2 or more infants affected exchange transfusion should usually be carried out.

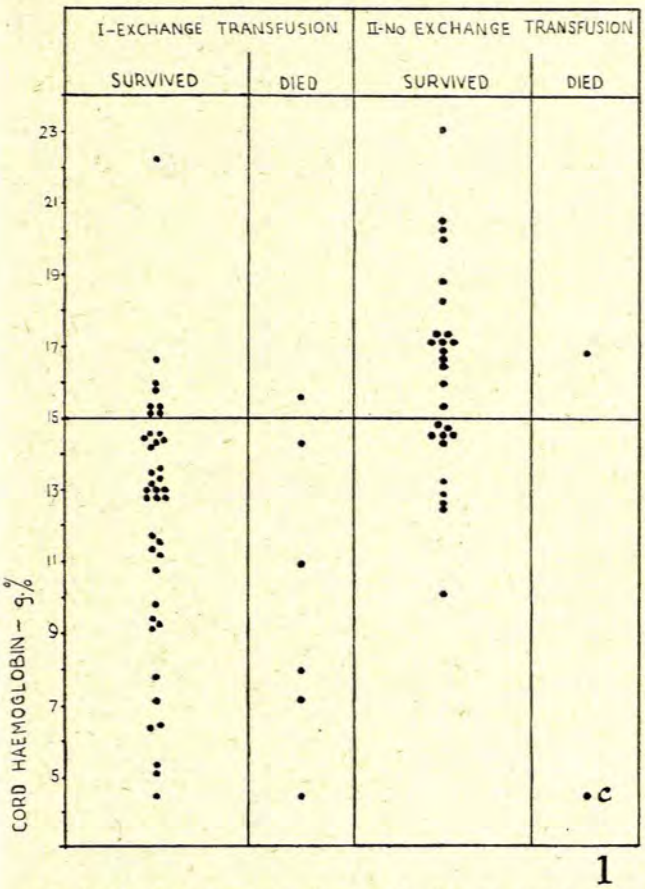

Fig. 1. Cord haemoglobin levels. C=due to anti-c, undetected antenatally.

Cord Haemoglobin. Fig. 1 shows that the majority of cases having exchange transfusion had cord haemoglobin levels below 15 g.%. Those above this level had other indications for treatment. It will be noted that 11 cases with haemoglobin levels below 15 g.% were left untreated and made a good recovery, and it is probable that a considerably higher proportion of cases in this category could be spared unnecessary operation by careful assessment of other factors. It is of interest to note that one case which was left untreated and died of kernicterus had a cord haemoglobin of 16·9 g.%.

Serum Bilirubin. Fig. 2 illustrates the serum-bilirubin values of the cord blood which was estimated in the majority of cases. Though all the fatal cases had values above 3 mg.%, it will be noted that over 50% of the non-fatal cases also had values above this figure. A serum bilirubin of 4 mg.% or over would, however, appear to have some prognostic importance, since 28% of our cases in this category proved fatal.

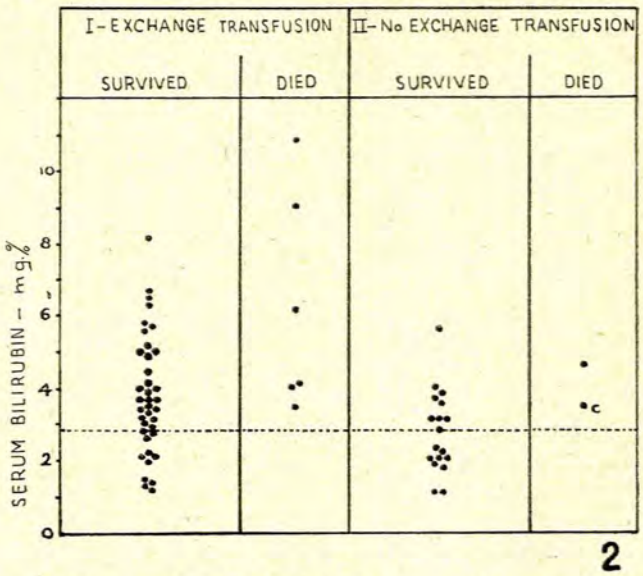

Fig. 2. Serum bilirubin levels. C=due to anti-c, undetected antenatally.

The association between very high serum-bilirubin levels and kernicterus is well-established,[9] and it would therefore appear advisable to perform exchange transfusion and, if necessary, to repeat this procedure whenever the serum bilirubin rises to 20 mg.%, and perhaps less in premature infants. We have had occasion to repeat the exchange transfusion in one instance, with a successful outcome.

Degree of Positivity of the Coombs Test. This has been estimated in 4 degrees (in nearly all cases by the same technician), and the distribution in the 2 groups is shown in the following table:

Coombs Test	*Group I*		*Group II*	
	Successful	*Fatal*	*Successful*	*Fatal*
++++	26	5	9	1
+++	8	1	4	—
++	3	—	5	1
+	7	—	10	—

The association of a strongly positive Coombstest with the need for exchange transfusion, and particularly with the fatal cases, is evident. No further conclusions can be drawn from this small series, but it is felt that in doubtful cases a strongly positive Coombs test should swing the balance in favour of exchange transfusion.

The Maternal Antibody Titre. Weiner[10, 11] has for long fought rather a lone battle in defence of the maternal

anti-Rh titre as an index of the severity of the disease in the infant, although Mollison[7] has recently observed that a titre of over 64 can be correlated with an increased risk of kernicterus. Our own figures lend considerable support to Weiner's view as will be seen from the table.

Maximum Maternal Anti-Rh Titre (Albumin)	*Group I*		*Group II*	
	Successful	*Fatal*	*Successful*	*Fatal*
8,192	2	1	1	—
4,096	6	—	2	—
2,048	8	1	2	1
1,024	4	1	2	—
512	5	1	2	—
256	6	1	4	—
128	8	1	2	—
64	1	—	7	1
32	1	—	1	—
16	1	—	4	—
8	1	—	—	—
4	1	—	—	—
2	—	—	—	—

It will be noted that 45 of the 50 cases requiring exchange transfusion had a maternal antibody titre of over 64, and all the fatal cases, with one exception, belonged to this group. In view of these findings we feel that in doubtful cases a maximum maternal antibody titre of more than 64 is a definite pointer in favour of exchange transfusion.

The Normoblast Count. This we have found to be a very variable and somewhat unreliable test, but a count of 10 or more per 100 white cells has usually been associated with severe disease. Our results show that, of the cases requiring exchange transfusion, 93% had a normoblast count of 10 or more, whereas in those cases which were left untreated only 62% had a count in this range. From a practical point of view, however, we consider the normoblast count to be of little value.

Splenomegaly. The degree of splenomegaly, where it was accurately recorded, may be depicted as follows:

Splenomegaly	*Group I*		*Group II*	
	Successful	*Fatal*	*Successful*	*Fatal*
++	8	4	—	—
+	19	2	5	—
0	12	—	20	1

It will be noted that 33 of the cases in group I, or 73%, had splenomegaly, as compared with only 20% in group II. Moreover, in the latter group there were no cases which exhibited gross splenic enlargement. We are well aware of the difficulty in assessing splenic enlargement in the newborn, but experience leads us to believe that a readily palpable spleen is usually indicative of severe disease.

To summarize this section concerning the various factors which influence the decision whether or not immediate treatment of the affected infant is indicated, it is suggested that there is a considerable group of cases with cord haemoglobin levels below 15 g.%, in which fine judgement can lead to a decrease in the number of exchange transfusions performed. In such cases knowledge of the birth weight and of the mother's obstetric history is of prime importance, and valuable guidance is obtained from the serum-bilirubin level, the maternal antibody titre, the positivity of the Coombs test, and the size of the spleen.

TECHNIQUE OF EXCHANGE TRANSFUSION

In the majority of our cases exchange transfusion was carried out by way of the umbilical vein in accordance with the technique originally advocated by Diamond in 1947.[12] It must be recorded, however, that in 5 cases where exchange transfusion was considered advisable it was found impossible to establish a satisfactory flow from the umbilical vein. In 2 of these a polythene catheter of 0·5 mm. bore was passed into an umbilical artery and a successful exchange performed by this route. We suggest that this technique is well worth attempting when difficulty is encountered with the umbilical vein. Approximately 70-80 c.c. per lb. body-weight of group-O Rh-negative blood were given and the same amount withdrawn. Immediately before the operation the donor blood was concentrated by decanting about 15% of the plasma. Latterly, after every 100 c.c. exchanged, 1 c.c. of 10% calcium gluconate has been injected into the vein.[13] Warming of the blood was not a routine precaution but it is probably advisable. Marting *et al.*[14] quote Wheeler's interesting suggestion that the transfusion of cold blood may precipitate cardiac arrhythmias. Although in this series no obvious cardiac irregularities developed, 2 infants showed signs of collapse towards the end of the transfusion but quickly revived when warmed up in an incubator. In fact, one of the difficulties has been to maintain body heat during a somewhat lengthy procedure, and the giving of warmed blood might help to resolve this difficulty.

A repeat exchange transfusion was given on the second day in one case when the serum bilirubin rose to 21 mg.% and jaundice became intense. Since the umbilical vein was no longer patent the exchange was successfully carried out through the saphenous vein in the right thigh,[15] and the infant made an excellent recovery.

RESULTS

The results obtained in this series of 80 infants affected with haemolytic disease of the newborn may be described briefly as follows:

Group I. In this group, comprising 50 cases, immediate exchange transfusion was performed. Complete recovery occurred in 43 cases, or 86%. One further case survived but is suffering from the effects of kernicterus, and the remaining 6 cases died. Four of the cases in this group required subsequent direct transfusions.

Group II. In this group of 30 cases no immediate treatment was given, although 7 were given subsequent direct transfusions during the neonatal period, when the haemoglobin showed signs of falling rapidly. This was a precautionary measure and possibly was not necessary in all cases. In this group, 28 infants recovered completely and 2 died.

The total results are shown in the following table:

Group	*Cases*	*Deaths*	*Mortality %*	*Kernicterus (surviving)*
I. (exchange transfusion)	50	6	12·0	1
II. (no exchange)	30	2	6·6	—
Totals	80	8	10·0	1

The over-all mortality of 10% is reasonably satisfactory and compares favourably with results from many other centres. The mortality figures include one case where death may not have resulted from haemolytic disease since autopsy revealed gross congenital defect of the left kidney and ureter. Another fatal case was due to anti-c and was undetected before death (see below). These 2 somewhat doubtful cases have been included in the over-all mortality rate of 10%.

Short summaries of the fatal cases are shown at the end of this article; these reveal some interesting facts which may serve as a guide to reducing mortality in future cases.

For those babies who died after exchange transfusion perhaps little could have been done, but in the light of more recent knowledge they might have been given the benefit of a second or third exchange if and when the serum bilirubin rose to 20 mg.%[9, 16, 17], even though signs of kernicterus had already appeared. Moreover, it is just possible that those deaths that occurred within 24 hours of transfusion (cases D and F) might have been associated with electrolytic disturbances,[18] though the blood used was not old. The injection of calcium gluconate now forms part of our routine.

There remain the two cases (G and H) in which the patients died without exchange transfusion. Case G was the first affected child, was not premature, and had a cord haemoglobin of 16·9 g.%. Jaundice was first noticed 36 hours after birth. On Mollison's criteria, therefore, there was no indication for exchange transfusion, but Walker would have been influenced in its favour by the serum bilirubin of 4·4 mg.%. In retrospect we consider that the very strongly positive Coombs test and the high maternal antibody titre of 2,048 were additional factors which should have influenced us in favour of performing exchange transfusion in this case.

Case H was due to anti-c and occurred in an Rh-positive (D) woman who had received a blood transfusion 6 years previously. We feel that death in this instance was inevitable, since the incompatibility was unsuspected and the infant died 20 minutes after birth. Nevertheless, this unfortunate case must surely underline the danger of indiscriminate blood-transfusion in female children and young adults, and illustrates the necessity of searching for unusual antibodies in Rh-positive women who give a history of previous blood-transfusion.

KERNICTERUS

It will be noted in the summaries of the 8 fatal cases that signs of kernicterus were evident before death or at autopsy in 4. The majority of the surviving cases have been followed up for at least 6 months and, so far as it has been possible to ascertain, only one of these exhibits signs attributable to kernicterus. This infant was quite severly affected at birth with a cord haemoglobin of 12·0g.% and serum bilirubin of 5·8 mg.%, although there was no obvious jaundice. The Coombs test was strongly positive. Immediate exchange transfusion was performed and the infant was discharged from hospital apparently vigorous and well. Subsequently convulsive attacks became frequent and there is now gross mental defect and blindness. A happy sequel for the mother of this tragic case has been the recent birth of a healthy unaffected infant.

FOLLOW-UP

We are fortunate in being able to follow-up these cases in the clinic at Addington Hospital for babies born in the maternity section. Weekly haemoglobin estimations are carried out in all cases of haemolytic disease, and it is thus possible to observe their progress during the first few months of life. The majority of infants in this series have been followed up for at least 6 months.

The usual haemoglobin pattern has been a fairly steady fall until the 6th or 7th week, followed by a spontaneous and sustained rise. Provided the infant is thriving satisfactorily, our practice has been to withhold blood transfusion unless the haemoglobin level falls below 6 g.% (40% Haldane).

SUMMARIES OF FATAL CASES

Case A

First child normal; second, third and fourth children died of congenital haemolytic disease; fifth child unaffected.

Sixth child. Caesarean section. B.W. 10 lb. Cord Hb. 14·2 g.%. Cord bilirubin 4·0 mg.%. Coombs ++++. Hepato-splenomegaly ++. E.T. 825/800 c.c. Well, but slight jaundice on the following day. Signs of kernicterus on 3rd day. Increasing jaundice and death on 4th day. P.M. refused.

Case B

First child normal. Second child jaundiced and died on 3rd day.

Third child. B.W. 7 lb. 1 oz. Cord Hb. 4·4 g.%. Cord bilirubin 4·4 mg.%. Coombs ++++. Slight jaundice with mottling of skin. Hepato-splenomegaly +. E.T. 850/800 c.c. Condition poor at end of exchange transfusion, but improved. On 3rd day respiratory difficulty, and oliguria and haematuria and oedema of legs developed; still jaundiced. On 4th day skin petechiae, haemoptysis and death. P.M.—Pulmonary and bladder haemorrhage; kernicterus.

Case C

Second child. B.W. 8 lb. Cord Hb. 15·7 g.%. Serum bilirubin 3·6 mg.%. Coombs ++++. Splenomegaly ++. E.T. 700/700 c.c. Increasing jaundice from 2nd day. Kernicterus and death on 4th day. P.M.—Kernicterus and pulmonary haemorrhage.

Case D

First 2 children normal. Third child given exchange transfusion.

Fourth child. B.W. 7 lb. Cord Hb. 7·2 g.%. Cord bilirubin 6·2 mg.%. Coombs ++++. Jaundiced with ecchymoses on face and back. General condition poor. E.T. 700/700 c.c. Deteriorated during transfusion. Died 18 hours after birth. P.M.—Hepato-splenomegaly; scattered pulmonary haemorrhages; no kernicterus.

Case E

First two children normal. Third and fourth children stillborn.

Fifth child. B.W. 7 lb. 10½ oz. Capillary Hb. 10·9 g.%. Cord bilirubin 10·8 mg.%. Coombs ++++. Deeply jaundiced. Splenomegaly ++. General condition poor. E.T. 730/730 c.c. Deterioration during procedure, with temporary improvement later. Died 20 hours after birth. P.M.—Cerebral haemorrhage right ventricle; left hydronephrosis with grossly dilated ureter.

Case F

First, third and fourth children alive. Three stillbirths and 2 miscarriages.

Seventh child. Elective Caesarean section at 39 weeks. B.W. 4 lb. 14 oz. Cord Hb. 8·0 g.%. Cord bilirubin 9·1 mg.%. Coombs +++. Jaundiced. Hepato-splenomegaly ++. E.T. 425/405. Condition improved after transfusion. Grunting respira-

tion with blood-stained mucus oozing from mouth 7 hours afterwards. Fine crepitations heard at left lung base. Died 12 hours after transfusion. P.M. refused.

Case G

Maternal antibody titre—2,048 (incomplete).

Second child. B.W. 6 lb. 11¾ oz. Cord Hb. 16·9 g.%. Cord bilirubin 4·4 mg.%. Coombs ++++. No jaundice or hepatosplenomegaly. Exchange transfusion not done. Slight jaundice first noticed 36 hours after birth, which then increased. Signs of kernicterus on 4th day. Died on 6th day. P.M.—kernicterus and pulmonary haemorrhage.

Case H.

Maternal blood-transfusion 6 years previously.

Second child. Antibodies not detected antenatally. B.W. 7 lb. 12½ oz. Cord Hb. 4·4 g.%. Cord bilirubin 3·5 mg.%. Coombs ++. Antibodies type anti-c detected—titre 64 (incomplete). Died 20 minutes after birth. P.M.—intracranial haemorrhage; liver and spleen +; scattered haemorrhages, especially retroperitoneal; jaundice; no kernicterus.

SUMMARY

The procedure adopted at the Natal Rhesus Unit, centred at Addington Hospital, Durban, is described from its inception in 1951 to 1955.

The number of cases of haemolytic disease of the newborn encountered during this 4-year period is shown, and the indications for exchange transfusion are discussed.

Results obtained in infants subjected to immediate treatment and in those left untreated are shown, the over-all mortality for the series being 10%.

The incidence of kernicterus is described.

Reference is made to the progress of affected infants after leaving the hospital, the majority having been followed up for at least 6 months.

Short summaries of the fatal cases are included.

We wish to record our thanks to Dr. J. V. Tanchel, Medical Superintendent of Addington Hospital, for permission to publish this report; to Mr. Harold Renton, Senior Visiting Obstetrician to the hospital, for maintaining faith in our judgement of these cases; and to Dr. J. C. Thomas who, as Director of the Durban Blood Transfusion Service, organized the Rhesus Laboratory Service.

REFERENCES

1. Kelsall, G. A. and Vos, G. H. (1955): Lancet, **2,** 161.
2. Allen, F. H., Diamond, L. K. and Vaughan, V. C. (1950): Amer. J. Dis. Child., **80,** 779.
3. Mollison, P. L. and Walker, W. (1952): Lancet, **1,** 429.
4. Armitage, P. and Mollison, P. L. (1953): J. Obstet. Gynaec. Brit. Emp., **60,** 605.
5. Mollison, P. L. and Cutbush, M. (1948): Lancet, **2,** 522.
6. *Idem* (1949): Brit. Med. J., **1,** 123.
7. *Idem* (1954): *Recent Advances in Paediatrics*, p. 110. London: Churchill.
8. Walker, W. and Neligan, G. A. (1955): Brit. Med. J., **1,** 682.
9. Lath, S. H. (1955): Brit. Med. J., **1,** 192.
10. Weiner, A. S. *et al.* (1952): Amer. J. Obstet. Gynec., **63,** 6.
11. Weiner, A. S. *et al.* (1954): J. Pediat., **45,** 546.
12. Diamond, L. K. (1947): Proc. Roy. Soc. Med., **40,** 546.
13. Gustafson, J. E. (1951): J. Pediat., **39,** 593.
14. Marting, F. L., Wagoner, S. C. and Wilson, V. C. (1955): Amer. J. Dis. Child., **89,** 289.
15. Arnold, D. P. and Alford, K. M. (1948): J. Pediat., **32,** 113.
16. Editorial (1954): Brit. Med. J., **1,** 692.
17. Hsia, D. Y. Y. (1953): Amer. J. Dis. Child., **86,** 484.
18. Smith, H. (1955): Brit. Med. J., **1,** 1089.