THE RHESUS FACTOR IN DEAFNESS

By FLORENCE CAVANAGH (Manchester)

My subject in this symposium is the association of the Rhesus factor with severe deafness in children.

I should like to state here that the use of the word "congenital" in this instance is quite wrong. These Rhesus babies are not born deaf—though they may become deaf from pathological processes occurring in the first two weeks of life.

In order to trace the course of events I must ask your indulgence whilst I travel outside the field of Otology into the realms of Pædiatrics, blood grouping and Pathology.

Introduction

The Rhesus factor was discovered in 1940.

The next year it was found to be the cause of hæmolytic disease and icterus gravis of the newborn.

As far back as 1875 Orth noted the association of severe jaundice in newborn infants with yellow pigmentation of the basal ganglia and the term "Kernicterus" was applied to this staining by Schmorl in 1904.

It was not, however, until 1944 that the first case of severe deafness following Kernicterus was reported by Coquet.

The Rhesus Factor

The Rhesus factor was discovered by Landsteiner and Wiener (1940). This Rhesus factor is an antigen (a protein) on the surface of the red cells of 85 per cent. of the white population. (Landsteiner and Wiener had been injecting blood from the Macacus Rhesus monkey into rabbits to promote the development of immune bodies in the rabbit serum. They found later that this rabbit serum reacted with the blood of many humans as well as the Rhesus monkey—hence the name Rhesus.) People who possess the Rhesus factor on their erythrocytes are called Rhesus positive—those who are without it are Rhesus negative. The Rhesus negative (Rh—ve) person will develop antibodies to the Rhesus factor if Rh+ve red cells are introduced into the circulation. We all know now that this Rhesus incompatibility has in the past accounted for fatal blood transfusion reactions when the blood had been satisfactorily grouped for the A.B.O. compatibility.

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The Rhesus Factor in Deafness

The Rhesus Factor and Erythroblastosis Fœtalis

In 1941, Levine, Katzin and Burnham pointed out that Rhesus sensitization was the cause of the various neonatal conditions grouped together under the name of erythroblastosis fœtalis. This group includes:

(*a*) *Hydrops fœtalis* where the infant usually dies in utero or at birth.

(*b*) *Icterus gravis* where the child is severely jaundiced immediately after birth and frequently develops neurological complications.

(*c*) *Congenital hæmolytic anæmia* where the hæmoglobin falls at an alarming rate and repeated transfusions are necessary to save life. (One baby in my series had 10 per cent. Hb on the fifth day, when admitted to hospital—and he survived!)

Erythroblastosis fœtalis occurs when a Rh—ve woman marries a Rh+ve husband and bears Rh+ve children. The Rhesus factor is inherited according to Mendelian law as a dominant characteristic.

The Rh+ve husband may be homozygous (RH : RH) or heterozygous (RH : rh). The Rh—ve wife is always homozygous (rh : rh).

When a Rh+ve homozygous male marries a Rh—ve wife all the children will be Rh+ve (RH : rh) heterozygous. When the Rh+ve husband is heterozygous some of the children will be Rh+ve and others Rh—ve. The Rh—ve babies are of course, unaffected. The manner in which the Rh+ve babies are affected is probably as follows:

It is thought that some of the fœtal erythrocytes pass through the placental barrier into the maternal blood and so provoke the development of antibodies. These antibodies in turn also cross the placental barrier and enter the fœtal blood. The concentration of antibodies in the mother's blood undoubtedly increases with successive pregnancies and it is generally stated to be insufficient to affect the first baby and seldom sufficient to affect seriously the second. The rate of development of antibodies, in fact, varies enormously—some mothers having five or six normal children before producing a case of erythroblastosis.

The Pathology of Erythroblastosis

It is necessary to have some knowledge of the pathology of this interesting condition in order to understand the associated deafness. When the Rhesus baby is born he is manufacturing his own Rh+ve red cells. He has, in his serum, however, certain Rhesus antibodies from his mother. These antibodies combine with his Rh+ve erythrocytes and cause hæmolysis. This has two obvious effects—firstly he becomes anæmic and secondly the pigment freed by hæmolysis causes jaundice. This jaundice comes on within a few hours of birth, may become orange coloured and may last for many weeks—unlike the so-called physiological jaundice which comes on after the third day and only lasts for a few days. The pigmentation of structures is of special interest to us because certain areas of

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the brain are stained yellow. Stillborn babies do not show these lesions which are only found in babies who have survived a few days and then come to post-mortem.

This pigmentation disappears if the child survives, but if he dies later and his brain is examined the areas which are the usual sites of pigmentation in the neonatal period are found to show degeneration and necrosis of cells with subsequent shrinkage of the area. The common sites of pigmentation are the Dura, Cerebral Cortex, Basal Ganglia, Thalamus, Hippocampus, Dentate nucleus, cranial nerve nuclei (especially 3, 4, 6 and 8),

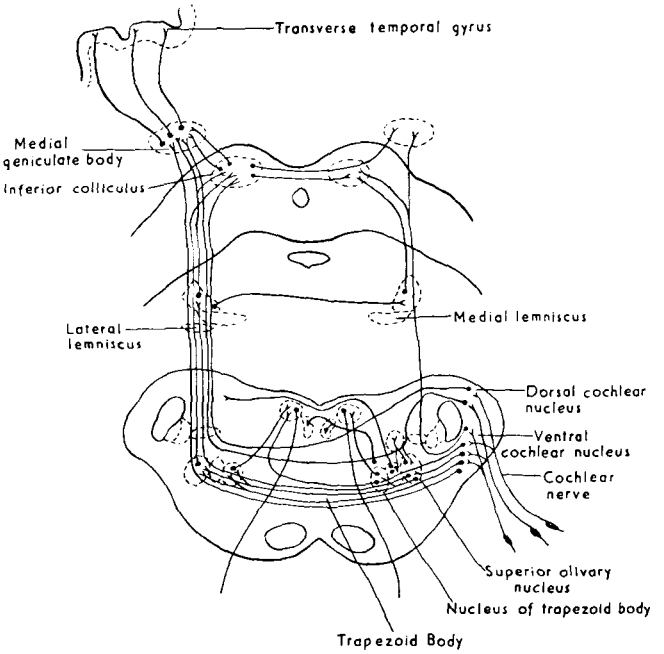


FIG. 1.
(From Larsell, O. *Anatomy of the Nervous System*, 2nd ed. Courtesy Appleton-Century-Crofts, Inc., New York)

Inferior Olive, Quadrigeminal bodies and grey matter of spinal cord. These are findings in a case of Kernicterus.

In 1951 Dublin published a paper in the *American Journal of Clinical Pathology* which is of special interest to members of this section. He examined the brains of seven newborn babies affected with erythroblastosis and paid particular attention to the auditory pathway.

Fig. 1 is a diagram of the auditory pathway taken from Larsell's book *The Anatomy of the Nervous System*. The central fibres of Corti's ganglion are seen reaching the medulla. Each fibre divides into anterior and posterior branches—going to the ventral and dorsal cochlear nuclei.

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Those fibres from the apical coil of the cochlea which carry the low frequencies are said to end in the anterior parts of the nuclei—those from the inferior coil (carrying the high frequencies) terminate further dorsally according to Lewy and Kobrak (1936). Secondary fibres from the ventral cochlear nuclei cross the midline in the trapezoid body and turn upwards to form the lateral fillet. Secondary fibres from the dorsal cochlear nucleus cross the midline near the dorsal surface as the striae acousticae and then join the lateral fillet. Some fibres from the dorsal cochlear nuclei pass ventrally to join the trapezoid body before turning upwards as the lateral fillet.

Again some fibres ascend in the lateral fillet of the same side.

It is probable that there are relay stations with the nucleus of the trapezoid body, the superior olivary nuclei and the nuclei of the lateral fillet.

The lateral fillet ends in the inferior quadrigeminal body and from here some fibres cross the midline to the opposite inferior quadrigeminal body—others pass to the medial geniculate ganglion. Subsequent fibres pass from here through the internal capsule to the auditory cortex. Now Dublin traced this pathway in his specimens. He found the cochlear nerves showed little change.

The dorsal and ventral cochlear nuclei both showed cell injury. In one severe case very few cells were left.

The trapezoid body and lateral fillets showed reduction in the number of fibres as would be expected since they are the processes from the cochlear nuclei.

The superior olivary nuclei showed moderate alteration.

The nuclei of the inferior quadrigeminal body showed mild degeneration, but the medial geniculate body, which is the relay station, showed more severe damage.

There was general lack of myelin in the auditory radiation which Dublin could not evaluate—since little is known about the rate of myelin development in the newborn.

The auditory cortex showed mild changes.

The auditory pathway is, therefore, widely involved and this involvement is usually symmetrical—which is in keeping with the reported findings on audiometric examination.

Whether this damage is due to anoxia or to the presence of pigment need not concern us.

The Clinical Picture of Erythroblastosis Fœtalis

An affected Rhesus baby can appear perfectly normal at birth and yet in 12-24 hours he may be so ill that his only hope of survival is by admission to a special unit where transfusions of Rhesus negative blood can be given at once.

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These babies may be œdematous at birth.

They may have areas of spontaneous bruising.

Jaundice may appear within an hour of birth and deepen very rapidly.

There may be increasing pallor (but if the baby is deeply jaundiced it may be difficult to assess this).

(One baby in my series was described by the resident on admission as "pale as marble".)

The liver and spleen may be enlarged.

Neurological signs may develop after a few days—they may be mild or dramatic and they may pass from mild to gross in the space of an hour or two.

The baby may be drowsy.

He may be reluctant to feed.

He may be slightly stiff or have gross opisthotonus.

He may be hypotonic and "floppy".

He may show unusual eye movements.

He may twitch or have convulsions.

He may develop athetoid movements.

He may have periods of apnœa and cyanosis.

His cry may become high pitched—"the cerebral cry".

He may show spasticity of one or more limbs.

These are the clinical signs of kernicterus in the neonatal period.

With treatment—and sometimes without—the cases may recover—but some will show permanent sequelae. The intensity of the symptoms in the first week is no true guide to the later handicap. Some of the severely affected babies have grown into apparently normal children whilst others more slightly affected at first have been grossly handicapped later.

It is impossible from a study of the neonatal history to predict the degree of deafness.

The Treatment of Erythroblastosis

Nowadays the Rhesus baby is treated by exchange transfusion—using the umbilical vein about 3 hours after birth. At the beginning 30 c.c. of blood is withdrawn. Then 10 c.c. of Rh—ve blood is injected and in a minute or two 10 c.c. of blood is withdrawn—this is repeated about 20 to 30 times taking perhaps two hours.

In this way most of the baby's serum, which contains the maternal antibodies, is removed and Rh—ve blood is injected. The whole procedure may have to be repeated on a few occasions—depending on the degree of sensitization in the particular baby. It is important to realize that although the baby is Rh+ve he is given Rh—ve blood. This is because any maternal antibodies still present would combine with Rh+ve cells—cause hæmolysis, increasing jaundice and further cerebral damage.

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The Rhesus Factor in Deafness

Review of the Literature on the asssociation of Deafness and Rhesus Sensitization

The association between erythroblastosis and the Rhesus factor was discovered in 1941 so that all the literature is recent.

The occurrence of deafness as a sequel is surprisingly little known—and I mean—surprisingly. For although there exists an extensive literature many otologists have not heard of it and several experienced pædiatricians to whom I have spoken were equally ignorant.

In 1944 Coquet reported on the late sequelae of kernicterus in 5 cases and one of these was a deaf mute of 28 years.

In 1948 Lande reported on 8 survivors of kernicterus—and 4 were probably deaf—50 per cent.

In 1950 many papers on the subject appeared.

Evans and Polani report on 16 patients with neurological sequelae of Rhesus sensitization and state that 5 are deaf—30 per cent.

Crabtree and Gerrard report 16 cases of perceptive deafness in 20 cases of kernicterus—i.e. 80 per cent.

Perlstein discusses 3 cases with neurological sequelae. Two were very young and may well be deaf. The third was certainly deaf with a bilateral loss of 80 D.B. for the higher frequencies.

Hazell reports 1 deaf case probably due to kernicterus.

Richards describes 5 mental defectives with athetosis who are also deaf mutes.

All these authors are reporting on deafness in cases of kernicterus.

Goodhill in the same year investigated two groups of children.

The parents of 904 inhabitants of a deaf school were questioned:

27 were probably Rhesus babies

4 were possibly Rhesus babies

Now the normal occurrence of erythroblastosis is 1 in 250 births and, therefore, for this school one would expect about 4 children (though this would be high as some of these babies would have died).

Therefore 27 or 30 is significantly high (about 30 per cent. of the inhabitants of a large deaf school).

One hundred and one cerebral palsy children were similarly investigated because Goodhill had noticed that the children in this group who had athetosis (a well-known sequel of kernicterus) also seemed deaf or had speech defects.

Of the 41 athetoid children:

13 had significant deafness and of these 11 had a history suggestive of Rhesus sensitization.

In 1951 Johnsen reported 1 case from Denmark. This child had been jaundiced for 5 weeks, but had no apparent neurological symptoms. The deafness which is severe for the high frequencies is the only sequel of Rhesus incompatibility.

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In 1952 Johnsen surveyed the school population between the ages of 6 and 16.

He found 50 cases of perceptive deafness. Of these 11 were Rhesus positive children with Rhesus negative mothers, but in only 6 were there any maternal antibodies (6 out of 50).

Gerrard (1952) published in *Brain* an excellent account of the whole subject of kernicterus and he points out the frequency of deafness as a sequel.

Present Investigation

This has been based on a study of 3 groups of children.

The first consists of a group of Rhesus babies born at St. Mary's Hospital, Manchester. This is the main Maternity Teaching Hospital of the Region, it is close to the Blood Transfusion Centre and the newborn babies are under the care of the Professor of Child Health. It may, therefore, be claimed that such babies will have the most up-to-date treatment—given at the earliest period.

Eighty-two of these children were examined for deafness.

The second group examined at the Duchess of York Hospital for Babies consists of children whose Rhesus sensitization was not diagnosed until after birth—sometimes days or even weeks later. These Rhesus babies have suffered more extensive damage, and figures for the occurrence of deafness here may be expected to differ from the first group. Forty-two such children were examined.

The third group consists of known deaf children who were invited to attend with their mothers. Details of the first two weeks of life were obtained and samples of blood from the mother and child were sent to the Regional Transfusion Centre to determine whether there was evidence of Rhesus incompatibility. One hundred and eighteen deaf children were seen.

Group I

Through the kindness of Professor Gaisford I have been able to examine the Rhesus babies born at St. Mary's Hospital after 1948. All known Rhesus negative mothers were delivered in hospital. Many of the babies gave no evidence of Rhesus sensitization and they have not been included in this survey.

Eighty-two *affected* children have been examined. Their ages were as follows:

4/5 years	22 patients
3/4 ,,	23 ,,
2/3 ,,	27 ,,
1/2 ,,	8 ,,

Two children aged between 5 and 7 years—brothers of 2 of the above cases were also seen.

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I mention these ages particularly. First because the youthfulness of the children adds to the difficulty of the investigation. Secondly because babies born as late as 9 years after the discovery of the Rhesus factor are able to benefit from the improved treatment which has evolved. In this respect they are in a different category from other patients reported in the literature—some of whom were born before the Rhesus factor was discovered and most of the others were born in the early 1940s when treatment was inadequate.

Of the 82 affected children 64 needed transfusions. Many of these transfusions were given within a few hours of birth and several children had transfusions repeated over a period of weeks.

Of the 64 transfused children 28 developed neurological signs.

Of those not transfused—the less seriously affected—only 4 developed neurological signs, and these were all mild symptoms—drowsiness, limpness or cyanosis, but strangely enough one of these children shows the greatest degree of deafness in this group.

These 82 children had attended the usual Pædiatric follow-up clinic and none had been suspected of deafness. However, we, as Otologists, know only too well how easy it is for the child suffering from high tone deafness to be overlooked.

I decided to see the children first in the surroundings they knew at St. Mary's Hospital and to have sufficient toys for play and as a basis for testing speech development.

During the last 18 years I have learnt to form a rough estimate of young children's hearing by their speech development though I have always referred doubtful cases to Professor Ewing for further investigation. We all know that the deaf child comes to us because he is not talking—only rarely because his parents suspect deafness. Again the child with severe high tone loss comes to us because he has a speech defect—deafness has not usually been considered. High tone loss as a cause of speech defects has been pointed out by many workers.

In the reported cases of deafness due to Rhesus sensitization the high frequencies have been the most severely affected and so in examining these children their use of the following consonants was noted:

f k p s t ch sh th

In co-operative youngsters a whisper test was also carried out.

Using this method I was able to assure myself that 47 of the 80 were certainly not deaf.

Ten others are probably not deaf—some of these are in the younger age groups, 1-3 years, where it is not reasonable to expect a difficult sound like "th" to be said perfectly.

Ten children would not talk enough for me to have any opinion, but their parents assured me that they talked freely at home and were understood easily by the neighbours. When asked if these children could be

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brought to Professor Ewing's Department the parents refused to attend because the idea of there being any deafness seemed quite ludicrous to them.

In 13 children the speech was slightly suggestive of high tone deafness. One of these, grossly retarded physically and mentally, was unmanageable. The remaining 12 were referred to Professor Ewing for detailed investigation with the following results:

5 have normal Audiograms.
2 have a loss of less than 20 decibels.
1 has a loss of 25-30 decibels.

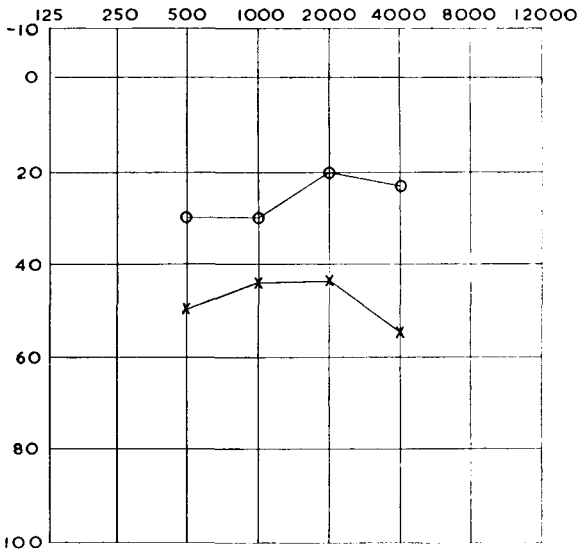


FIG. 2.
Richard B.

1 has a loss of 40-50 decibels on the left and a loss of 20-30 decibels on the right.
3 failed to attend in spite of every effort.

One of these three responded readily to my commands, but her speech was rather slurred. She was under 3 years of age. The other two said a number of words satisfactorily, but would not repeat the actual Test Words—they were both 2½ years old.

My own feeling is that none of the three is deaf, but I would certainly have liked Professor Ewing's report on them (as in all the other cases where there appeared to be any doubt).

There is, thus, one patient with a serious hearing defect—though on one side only (Fig. 2, Richard B.). The unmanageable one may, of course, be deaf and, if so, this would give us 2 cases in 82 affected Rhesus babies—

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an incidence of less than 2½ per cent. Of these two the retarded one was a hypotonic infant who developed athetosis and head retraction in the first week and could not sit up alone at 2 years.

The other was limp, drowsy and slightly cyanosed in the neonatal period but had none of the more dramatic signs of kernicterus.

Group II

Let us now consider the less fortunate group of children. The records of the Duchess of York Hospital for Babies were consulted and also three case

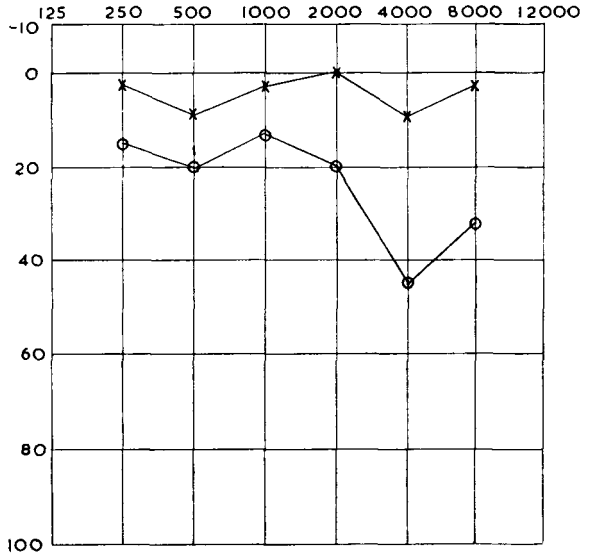


FIG. 3.
Carole T.

records at the Royal Manchester Children's Hospital. Out of 66 recorded cases admitted with symptoms of Rhesus incompatibility 30 were eventually traced and examined. In addition 47 siblings of these children were seen, and among these 47 I found 12 unsuspected cases of Rhesus sensitization—making a total of 42 affected babies.

Seven of these were first children. This is a surprisingly high figure since it is usually stated that maternal antibodies do not develop to a level which will injure the fœtus until later pregnancies. One of these babies (Steven C.) is in fact deaf with a loss of 45-50 decibels over the speech range and he is a grossly incapacitated spastic child. But he is a rather special case since his mother had been transfused in childhood—probably with Rh+ve blood. The other 6 mothers, by their own accounts, had never been transfused. Nevertheless, several of their first babies were very seriously and even permanently affected.

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Thirteen of the patients were second children—again a higher figure than one would hitherto have expected. One of these (Carole T.) is deaf. She was born at home and had no treatment, was jaundiced, drowsy and slow to feed in the first week or so. When I examined her at the age of 7 she had a marked speech defect, was slow to respond to the spoken command and backward in her reading. Her audiogram shows a loss of 50 decibels for the higher frequencies—but on the right side only (Fig. 3, Carole T.).

Four of the 42 cases were third children. One of these (Marilyn T.), sister of Carole T. just mentioned, died of kernicterus on the eighth day. The post-mortem report is as follows:

> "There was symmetrical yellow staining of the basal nuclei and grey matter of mid-brain and spinal cord, also the olives. Slight staining of the membranes. The vestibular nuclei and the dorsal cochlear nuclei were intensely pigmented. The ventral cochlear nuclei were only slightly stained."

Careful sections were made, but unfortunately no characteristic histological picture was found.

Another of these third children (Brian E.) was not admitted till he was 4 weeks old. His hæmoglobin was only 35 per cent. and he had opisthotonus. He did not sit up till he was 13 months, and now at $2\frac{1}{2}$ years he cannot stand alone. He says only mama and baba. Professor Ewing reports that Brian responds to pitch pipes and voice at an intensity of 50-60 decibels, but can localize sounds accurately. He is of the opinion that deafness may in fact be only slight.

There was one fourth child. This baby had an exchange transfusion and developed no symptoms.

One family of five lost the fifth child with kernicterus.

Another family of five is interesting. Four (all except the firstborn) were severely jaundiced immediately after birth, but all their audiograms are virtually normal.

In one family of six only the last child was affected. Potentially a severe case she was transfused two hours after birth and on four further occasions. She is now a lovely normal child of 3.

In a family of seven Rhesus incompatibility was only discovered when the last child (Denise L.) was brought to Hospital at $2\frac{1}{2}$ years because she was unable to stand. She seemed to be a case of kernicterus and Rhesus antibodies were then found in the mother's blood. This child started to walk at $3\frac{1}{4}$ and now at $4\frac{1}{4}$ walks quite well—but she is still only saying odd words. Professor Ewing saw her and thinks she may have slight impairment of hearing but not more than 20 db.

It was interesting on seeing this family to discover another affected child whose condition had not been suspected (Trevor L.). He is now 7 years old and on testing his hearing I noticed that he only repeated what I

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said after his mother had also said the words—because he was watching her lips. He had a speech defect—to which no one had ever paid any attention.

On further questioning, the mother said his gait had been peculiar at first for a long time—and he was still clumsy with his hands. He has some spasticity on the left and is almost certainly a case of kernicterus. His audiogram is similar to those of previously reported cases (Fig. 4, Trevor L.).

In another family of seven children the two youngest ones had been affected, but neither was deaf.

In this whole group of 42 patients:

5 babies died of Rhesus sensitization.

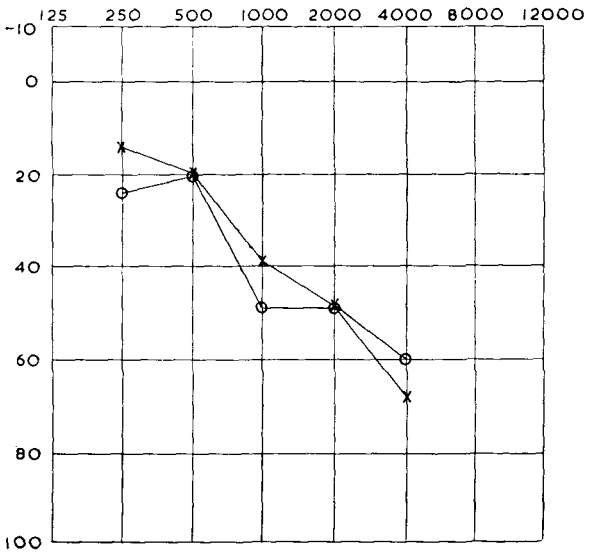


FIG. 4.
Trevor L.

10 developed neurological signs and 5 of these were suspected of deafness.

11 doubtful cases altogether were referred for detailed tests of hearing.

4 are deaf.

1 (Trevor L.) has the typical chart of the literature.

1 (Steven C.) has a uniform loss of 45-50 db.

1 (Carole T.) has a loss up to 50 db. for the high frequencies—but only on one side.

1 (Brian E.) has a slight to moderate loss. (No audiogram was obtained in this $2\frac{1}{2}$ year old retarded child.)

Four cases amongst 42 patients is just under 10 per cent.

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There is thus a significant difference in the frequency of deafness in these two groups which I feel sure is accounted for by the earlier treatment of the first group—in which it will be remembered the incidence amounted at the outside to $2\frac{1}{2}$ per cent. Even in my less favoured group the children have had better treatment than those Rhesus babies born 8-10 years ago.

Now taking Groups I and II together we find among 124 affected Rhesus babies 6 who are deaf (nearly 5 per cent.).

Four of these had severe symptoms in the neonatal period and are now handicapped mentally and physically. Two had only mild symptoms after birth, but both are rather slow mentally and this is certainly not due to deafness for in each of these patients the loss is unilateral and moderate in degree.

I should like to point out that in the literature almost all the reported cases have audiograms showing severe deafness for the high tones which is bilaterally symmetrical. This is not so in my cases and I take this to mean that there are probably many of these less deafened children up and down the country who have not been suspected of any abnormality of hearing. Further reviews of groups of known Rhesus babies might, therefore, be rewarding.

We have, up to now, been considering known Rhesus babies—and searching for any deaf cases. I want now to turn to the opposite problem perhaps the more interesting to us as Otologists—that of the known deaf children in whom Rhesus sensitization may be a causal factor, and this brings us to:

Group III

The case notes of all deaf children seen by me at the Royal Manchester Children's Hospital were consulted.

Unfortunately most of the notes prior to 1948 had been destroyed.

However, 118 children were re-examined with the Rhesus factor in mind. All these patients are deaf enough for admission to a School for the Deaf or Partially Deaf, or need hearing aids and lip-reading instruction.

The histories in 51 of these cases reveal the following apparent causes for their deafness:

1. Meningitis (C.S.)	16
Meningitis (B.coli)	1
2. Meningitis (T.B.)	6
3. Heredity (family history of deaf mutes)	5
4. Congenital Atresia of External Auditory Meati	4
5. Rubella in Pregnancy	3
6. Head Injury (fall)	3
7. Measles (only if associated with pneumonia or encephalitis)	3

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8. ?Congenital Abnormality (associated with other congenital abnormalities lips, palates, heart, etc.)	3
9. Unknown (associated with mental deficiency)	2
10. Mumps	1
11. Diphtheria	1
12. Pneumonia	1
13. German Measles (a very definite history. Child talking well at $2\frac{1}{2}$ and ceased talking after this illness).	1
14. Chronic suppurative otitis media	1
	51

In one case the mother was dead and no Rhesus investigation could be carried out.

Eleven children had suggestive histories—drowsiness, reluctance to feed, jaundice. None had any of the dramatic symptoms. One was given a transfusion on the tenth day. Samples of blood from these 11 children and their mothers were sent to the Regional Blood Transfusion Centre. In addition, at the request of the Director of the Transfusion Service, samples were also sent from 26 unselected cases who had no suspicious symptoms.

The combination of Rh—ve mother with Rh+ve child was found in 4 cases, but in one of these the mother had no antibodies.

In the 3 cases where antibodies were found the children had suspicious histories.

We have, therefore, 3 cases (out of 118) in which Rhesus incompatibility is the probable cause of deafness.

One (David H.) is a firstborn (the eldest of four). He was very delicate at birth, was jaundiced from the fifth to twenty-first day. I saw him when he was 18 months old and suspected deafness which was confirmed by Professor Ewing.

None of the subsequent children in this family had any neonatal symptoms and they are probably all Rhesus negative.

The second of these three cases (Audrey R.) is the middle child of five. She was extremely ill on the third day and was given an injection—probably of blood.

The first child of this family was born with bilateral cataract, the second was jaundiced. The two born after Audrey gave no trouble.

The third patient (Margaret B.) is the second child in a family of four. The first baby died on the fifth day from birth injuries.

Margaret was born jaundiced and remained so for 2 to 3 months. She was slow to feed and was also anæmic. She sat up at 10 months and did not walk until she was 4 years old. At 8—when I saw her—she had a gross speech defect.

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The other two siblings had no neonatal symptoms and are normal children.

The antibodies which have been found in the sera of these three mothers are not likely to have developed in the later pregnancies in view of the absence of symptoms in the later children. The Director of the Regional Transfusion Service regards these patients as cases of Rhesus sensitization. Three cases in 118 children is not, of course, a very high proportion, but it is, after all, exactly the same as the incidence of Rubella in pregnancy in this series of cases.

The Diagnosis of Rhesus Incompatibility in Cases of Deafness

When such cases reach the Otologist it is, of course, too late for remedial measures. It is, nevertheless, of interest to detect this causal factor and a résumé of the points to be noted may not be out of place.

It is obvious that we must ask for details of the child's first week of life.

Was he jaundiced? If so, when did he first become jaundiced and how long did this last?

Was he anæmic? Was there any bruising or œdema? Was he drowsy?—reluctant to feed?

Did he have any "blue attacks"? Did he twitch or convulse? Was he stiff and rigid to hold?—or was he unduly "floppy"?

If we discover that the baby was transfused it is probable that there is Rhesus incompatibility. We require also details of the obstetrical history and the causes of death of earlier siblings. If the patient is a late arrival and earlier children have had suggestive, but milder, neonatal symptoms, the diagnosis is a likely one. We need to know, too, whether the mother has ever had a transfusion.

If, from the answers, we suspect Rhesus sensitization we have to send blood samples from mother and baby for investigation. If the child is Rh+ve and the mother Rh−ve—*and* if antibodies are found in the mother's serum, the diagnosis is confirmed—provided, of course, that there have been no subsequent Rh+ve pregnancies or transfusions which might have been responsible for the high level of the antibodies.

I should like to mention here something about the teeth of these Rhesus children since their appearance may be a help in the diagnosis. Only the milk teeth are affected. These are often green or yellowish green in colour and this unusual appearance is found in no other condition. Another type of tooth is occasionally seen—a black eroded stump with a yellow or greenish core. At present in Manchester Dr. R. M. Forrester and Mr. J. Miller are investigating this pigmentation of teeth in cases of severe neonatal jaundice. They do not yet know whether this second type of tooth is pathognomonic.

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The Rhesus Factor in Deafness

Conclusions from this Investigation

Among 118 deaf children 3 cases of Rhesus sensitization have been found. Among 124 Rhesus babies 6 cases of deafness have been found, none of which had been suspected, although most of the children had been well cared for domestically and medically. It would seem, therefore, that the attention of Otologists and Pædiatricians ought to be drawn to this possible sequel of Rhesus incompatibility. Eventually, no doubt, there will be very few such cases—at any rate in the vicinity of the larger centres.

For if every Rh—ve woman is delivered where there are facilities for testing the cord blood and for an early exchange transfusion (repeated as necessary)—then Rhesus children should cease to be crippled by kernicterus or deafness. In the meantime, however, Rhesus sensitization must be considered among the possible causes of deafness.

Another important point which I feel cannot be stressed too heavily is that the giving of Rhesus incompatible blood is doubly dangerous to the female. In an emergency transfusion if it is not possible to determine the Rhesus group of the patient we should use Rh—ve blood. The child (Steven C.) already mentioned is a tragic result of failure to observe this precaution, and furthermore his mother has now such high antibodies that any subsequent children of this marriage would almost certainly be seriously handicapped—if indeed viable.

I wish to record here the help I have received from workers in other fields:

Professor W. Gaisford of the Department of Child Health, Manchester University, Professor A. W. G. Ewing of the Department for the Education of the Deaf, Manchester University, Dr. F. S. Stratton, Director of the Manchester Regional Blood Transfusion Service. Dr. R. M. Forrester, Senior Registrar in Pædiatrics, Manchester Region, Dr. W. Jackson, Pathologist at Ashton-under-Lyne.

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