1951

Rh anamnestic reaction and its significance to the newborn

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THE RH ANAMNESTIC REACTION
AND
ITS SIGNIFICANCE TO THE NEWBORN

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Submitted in Partial Fulfillment
for the
Degree of Doctor of Medicine

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Omaha, Nebraska

February 12, 1951

The discovery of the Rh factor[1] and its relationship to congenital hemolytic disease and intra-group transfusion reactions[2] have attracted much attention in a relatively short period of time. The interest has not been confined to the medical practitioner nor the written discussions to scientific publications. In many periodicals intended for the general public, papers with varying degrees of scientific accuracy have appeared. These often have been responsible for considerable distress on the part of many women who have read them[3]. Because of this, hemolytic disease of the new-born has assumed an importance altogether out of proportion to its low incidence.[4]

Although the discovery of the Rh factor has answered a few questions, it has in turn brought forth many new problems which are still unsolved[3,5]. One of these problems concerns antibody production and associated with it, a disturbing phenomenom occasionally encountered, namely, the anamnestic reaction.

The anamnestic reaction, also known as the Hektoen phenomenom, may be defined as "an increase or reappearance of immune antibodies already produced in the system on the injection of a non-specific antigen."[6] This reaction is not a new discovery, nor is it limited to the Rh system. Dieudonne in 1906 showed that the injection of sodium cinnamic acid into typhoid-immunized

rabbits caused a renewed formation of agglutinins.[7] It was not until World War I and the problem of arriving at the diagnosis of typhoid fever that much attention was paid to this demonstration. The name "anamnestische serum reaktion" resulted from observation by Conradi and Bieling in 1916 who noted that soldiers previously vaccinated against typhoid fever had a sharp rise in titers to the Gruber-Widal reaction during the course of febrile diseases simulating typhoid fever but which later proved to be something else.[7] . Subsequent experiments confirmed the observations of Dieudonne and of Conradi and Bieling and in addition demonstrated that other antigen-antibody reactions were similarly affected.[7,8,9,10].

The anamnestic reaction is of interest because of: 1) the bearing it has on the understanding of the mechanism of immunization and 2) the diagnostic implications involved.[11].

Although the anamnestic reaction has been recognized generally, little is known as to why it occurs.[7]. Hektoen suggested that it is possibly an allergic response.[8]. The anamnestic reaction certainly has been an important obstacle to the theories of antibody production.[12].

Diagnostically, it poses quite a problem. Since the course of antibody levels resembles that of incompatible pregnancies, it is impossible to distinguish, by means of antibody behavior alone, between a benign anamnestic re-

action and one which may lead to erythroblastosis.[11].

INCIDENCE OF THE RH-ANAMNESTIC REACTION

In a random white population, including both males and females, approximately 85% are Rh positive and 15% are Rh negative.[3,13]. By application of the binomial theorem, Levine has calculated gene frequencies. For the D-d system the results were as follows: D/D (homozygous) equals 37%, D/d (heterozygous) equals 48% and d/d (homozygous) equals 15%.[14].

For purposes of estimation assume, now, that every sensitized mother will actually develop an anamnestic reaction and that all d/d conceptus are not susceptible to erythroblastosis and have no other genetic handicap associated with the Rh status. The calculated incidence of the anamnestic reaction would be, then, the frequency with which an already sensitized mother would be expected to carry a d/d (Rh negative) fetus.[15].

With monogamous and random matings the upper limit for the anamnestic reaction would be approximately 33% of the total reactions of pregnancy in which the antibody is produced. This gives an over-all upper limiting ratio of anamnestic reactions to incompatible reactions of approximately 1:2 or approximately one anamnestic reaction in 800 births.[15].

The above calculations were based on the D-d system since anti-D serum is the type most readily available and because D-incompatibilities include approximately

93% of all cases of erythroblastosis. [3,14] Similar calculations could be applied to each of the other Rh-Hr antigens, if sufficient data were available, but probably they would not alter the figures.[15] Group ABO anamnestic reactions, whether frequent or infrequent, in pregnancies, are probably of little significance since A and B antibodies rarely lead to erythroblastosis.[17]

In clinical practice the incidence of the anamnestic reactions is much lower. This is not surprising when one considers the factors involved. Several pregnancies are usually necessary to adequately sensitize an Rh negative mother.[15] However, with previous Rh-incompatible blood transfusions, an Rh negative mother may be sufficiently sensitized to have an incompatible or an anamnestic reaction with the first pregnancy--this would tend to increase the incidence of anamnestic reaction slightly. On the other hand, the trend toward small families, and the failure of many Rh negative women to produce anti-Rh antibodies[4] would help to explain the low incidence. There is a scarcity of available series which would be of value in calculating the incidence of the anamnestic reaction as seen in obstetrical practice. Page, Hunt, and Lucia observed five anamnestic and twenty-five incompatible reactions in over four thousand patients or the ratio of 1:5 or one anamnestic reaction in approximately 800 births.[18] Schneider et. al. observed three anamnestic re-

actions and sixteen incompatible reactions in six thousand, one hundred eighty-five pregnancies--a ratio of 1:5 or one anamnestic reaction per two thousand births.

It might be well to emphasize, however, that even an incidence of one benign anamnestic reaction in every five Rh antibody reactions of pregnancy is of significance in practice.

ANAMNESTIC REACTIONS REPORTED IN THE LITERATURE

Case 1.--The mother, gravida vi, had had three normal children by her first husband. She had had one normal child by her second husband who was Rh positive (heterozygous). Her fifth pregnancy ended in the delivery of a stillborn fetus (hydrops). The mother's blood was Rh negative and had a high titer of anti-Rh agglutinins six weeks after the fifth delivery. The blood of the mother six months after the sixth delivery still had a high titer of anti-Rh agglutinins.[16.]

The high titer present after the sixth delivery may represent residual antibodies resulting from the fifth pregnancy but more likely represents an anamnestic reaction.

Case 2.--The mother, gravida iv, was group AB, Rh negative; the husband was group A, Rh positive. In 1936 her first pregnancy resulted in a stillborn infant at six months. Later the same year, she delivered a normal

male infant (type A, Rh positive). In 1943 she delivered a stillborn infant with typical findings of erythroblastosis (hydrops). After artificial insemination (Donor, was Rh negative, group A, MN), the mother became pregnant in November, 1945. Saline agglutinins could not be found at any time during the course of her pregnancy. Blocking antibodies were observed from the fourth month on, reached a peak at the seventh month (1:20), remained at that level except for a brief drop two weeks prior to the delivery of a normal infant (type B, Rh negative).[19]

The possibility of the A factor acting as a non-specific antigenic stimulus is very unlikely since the baby did not inherit the A factor.[19]

Case 3.--Mrs. M. J., age 28, gravida vi, was type O, cde/cde. The present mate, type O, cDe/cde, is her third husband. Her past obstetrical history is as follows: In 1938 and 1939 she gave birth to normal, term infants. Her third pregnancy in 1942 terminated at eight and one-half months with the birth of an erythroblastotic baby who died of pneumonia on the 38th day after birth. In 1946 she miscarried at six weeks. A seven months infant (hydrops) was delivered in 1947. The first and fifth pregnancies were complicated by severe pre-eclampsia.

The expected date of confinement for the sixth

pregnancy was July 8, 1949. The patient was first seen on January 24, 1949. Blocking antibodies were present in a titer of 1:256. Weekly titers varied considerably but the general trend was from 1:256 at the outset to 1:1024 at delivery. The patient received 600 mg. Rh hapten weekly with little affect on the titer.

The baby was type O, cde/cde. Coombs test on the baby's red blood cells at birth was negative and the baby was normal in every respect. The typing was verified at two days, six, eight and thirty-two weeks.[20]

Case 4--Mrs. M. B., a 26 year old, gravida iv, was Rh negative. Her first pregnancy was complicated by toxemia, but she delivered normal twins. Her second pregnancy resulted in a miscarriage at six months. With the third pregnancy she was induced early; the infant had mild hemolytic disease but survived without transfusions.

The expected date of confinement for her fourth pregnancy was February 12, 1948. At 16 weeks gestation, the antibody titer was 1:16. The titer rose to 1:64 at the 25th week and dropped to 1:32 by the 34th week. Because of the rising titer, she was placed on ethylene disulfonate without an appreciable effect on the antibody titers. She was induced at 38 weeks and delivered spontaneously a normal, Rh negative infant.[21]

Case 5.--Mrs. N. K., age 37, gravida iv, estimated date of confinement, July, 1948. The first pregnancy resulted in the birth of an infant with moderately severe hemolytic disease but the child recovered after several small transfusions.

The patient was first seen in the fourth pregnancy on March 12, 1948. The antibody titer at that time was 1:8 in albumin. On April 27, 1948 the titer had risen to 1:32. The patient was induced and delivered on July 11, 1948. The infant was Rh negative and normal in every respect.[21]

Case 6.--Mrs. A. B., age 35, gravida iv, estimated date of confinement, October 30, 1948. The first child was normal Rh negative. In 1945 she delivered a term infant who expired soon after birth of erythroblastosis. With the third pregnancy in 1946, she was injected with pertussis vaccine in a study of the competition of antigens. The antibody production continued unabated. Labor was induced and a normal Rh negative baby was delivered.

The fourth pregnancy was treated with ethylene disulfonate but the titers rose from 1:64 at eleven weeks to 1:1024 at thirty-two weeks. She again delivered a normal Rh negative baby. This case epitomizes some of the difficulties in the problem of Rh iso-immunization.[21]

Case 7.--The patient was a 23 year old, unmarried, gravida iv, type A, Rh negative (cde/cde) mother. Her first pregnancy in 1940 resulted in a normal baby but the home delivery was complicated by hemorrhagic shock. She was treated by two transfusions at a hospital. The second transfusion (type A, from her mother) was followed by "shaking chills". In 1945 her second baby was type A, Rh positive and had mild erythroblastosis. Because of profuse uterine bleeding, the patient was again transfused with type A blood which was discontinued because of chills and fever.

The third pregnancy was induced four days before the calculated expected date of confinement and a normal type A, Rh negative (cde/cde) female was delivered. Saline antibody titers were negative at all times. Second order albumin antibodies rose from a titer of 1:128 at the seventh month to a titer of 1:512 by the thirty-eighth week of pregnancy. Blocking antibodies (1:128) were present six months postpartum. The father was type A, Rh positive (CDe/cde).[11]

Case 8.--Mrs. B. M. a 27 year old white female was followed closely during her third pregnancy because of a history of erythroblastosis. From her first pregnancy, delivered at term in 1943, she obtained a normal living boy. The second child, delivered at term in 1945, died of erythroblastosis at two days of age despite trans-

fusions with Rh negative blood.

The third pregnancy was interrupted prematurely at thirty-six weeks because of a rising titer of the mother's blood similar to those seen which lead to erythroblastosis. The saline antibody titer had increased to 1:256; the albumin antibodies to 1:1024. The baby was a normal type O, Rh negative (cde/cde) infant who expired at 53 hours because of complications due to prematurity. At autopsy, there was no evidence of erythroblastosis. Coomb's test on cord erythrocytes was negative. The mother was type O, Rh negative (Cde/cde); the father type O, Rh positive (CDe/cde).[11]

Case 9.--Mrs. R. J., a 28 year old, white, housewife, type O, Rh negative, (cde/cde), was electively delivered of her third pregnancy at thirty-six weeks by Caesarian section in 1947. Her first baby, an Rh positive girl, born in 1941, was normal. Her second baby, a boy, was stillborn in 1946, three days after the heart sounds failed; the thirty-nine week old fetus was macerated and edematous but not icteric.

During the third pregnancy, the saline antibodies were not found. The albumin antibodies increased from the titer of L:2 at the 28th week to the titer of L:64 at the thirty-sixth week. The baby, typeO, Rh negative (cdE/cde) had no signs of erythroblastosis. Fifteen months postpartum albumin antibodies were present to a

titer of 1:128 against both CDe and cDE cells suggesting a postpartum stimulation of antibody production had occurred. The husband was type A, Rh positive (CDe/cdE).[11]

Case 10.--Mrs. J. K., age 33, gravida iv, para iii, had delivered two normal children. Her third pregnancy late in 1948 resulted in a stillborn baby (erythroblastosis fetalis). Heart sounds had failed approximately one week prior to the onset of labor which was eleven days premature. Blocking antibodies one month postpartum were present to a titer of approximately 1:2000.

She was seen during her present pregnancy by her local doctor who advised an abortion. Because of religious beliefs she changed doctors and was given prenatal care by another physician. Antibody titers were taken repeatedly and about 36 weeks a rapid rise in titer to 1:64 was noted. Because of her past obstetrical history and the possibility of an incompatible Rh reaction, she was referred to an Omaha obstetrician.

An examination on July 3, 1950 revealed the expected date of confinement to be August 1, 1950. The fetus was presented vertex. Fetal heart tones were 132 in the left lower quandrant. Height of the fundus was 33 cm. with no engagement. The fetal movements were palpable but no uterine contractions were present. Her blood pressure was 136/92.

On July 3, 1950 an elective Caesarian section was performed and a 5 lb. 4 oz. type O, Rh negative baby girl was delivered. The baby cried spontaneously. Her color was good and there was no evidence of jaundice or edema. The spleen was not palpabable. The liver was normal size.

The laboratory findings on July 3, 1950 were: hemoglobin, 18.1 gm. (116%); RBC, 4.4 million; WBC 23,000, with differentials as follows: neutrophils 67, eosinophils 2, basophils 1, lymphocytes 24, monocytes 6 and metamyelocytes 25. There was moderate polychromasia and normoblasts were present in the ratio of 1:100 WBC. A complete blood count on July 6, 1950 was essentially the same except for the presence of only 11,400 WBC.

Case 11.--Mrs. E.J.C., age 34, gravida iii, para ii, group O, Rh negative. Her husband was group A, Rh positive. In 1941, she had received a blood transfusion from her sister who is Rh positive.

Past obstetrical history was as follows: in February, 1946 she delivered a 7 lb. 8 oz. premature stillborn infant with the cord about its neck. Her second pregnancy was induced two weeks early on July 27, 1947 and she delivered a macerated fetus (erythroblastosis). No fetal heart tones were heard after July 3.

The present pregnancy is as follows: she was first examined on November 12, 1949 and the estimated date of confinement was June 30, 1950. Physical examination was

essentially negative.

The prenatal history was uneventful. She had a weight gain of twenty pounds (132# to 152#).

Medications consisted of 1 gram Meonine daily. On December 12, 1949, the dosage was increased to 1½ grams daily. On April 3, 1950 the dosage was further increased to 5 grams daily which was maintained until delivery. On March 6, 1950 vitamin K, 5 grams daily and Praenone 10 mgm. daily were administered.

Blood was sent to Dr. Levine at the Ortho Research Foundation, Raritan, New Jersey for antibody titration. Results were as follows: April 6, 1959, blocking antibody titer was 1:64, May 5, titer was 1:128, and May 19, titer was 1:64.

The patient was delivered on May 23, 1950 by elective Casesarian section and a premature 4 lb. 13 oz. baby boy (Rh negative) was obtained. The baby developed normally.

The placenta showed neither gross nor histologic evidence of erythroblastosis.

Case 12.--Mrs. E.S. was a referred patient because of previous Rh incompatabilities.

In 1941 she miscarried at three months. In February, 1945 she delivered a 7-8 month stillborn which was edematous; the baby had been dead three days in utero. Her third pregnancy in July, 1948 resulted in a live baby

girl who received two blood transfusions.

The present pregancy is normal, the estimated date of confinement being January 27, 1951.

On July 25, 1950 blood was sent to Dr. Levine for typing. Mrs. S. was reported type AB, Rh negative (cde/cde). Mr. S. was reported type A, Rh positive (homozygous, CDe/cDE). Blocking antibodies were present to a titer of 1:16 which undoubtedly represented some residual antibodies from the previous pregnancy. Since Mr. S. was homozygous, the outlook for this pregnancy was not at all favorable.

Blocking antibodies reported on September 6, 23, November 24, and December 22 were 1:128, 1:64, 1:64 and 1:32 respectively.

Therapy consisted of Meonine, 5 grams daily, Vitamin K, 5 mgm. daily and Praenone, 10 mgm. daily.

On January 18, 1951, medical induction was attempted and a 7 lb. 7 oz. baby boy was delivered by low forceps. The baby cried spontaneously. There was no jaundice or evidence of erythroblastosis. Baby was type A, Rh negative (cdE/cde). The direct Coombs test was negative.

Apparently the husband must be heterozygous. The laboratory findings: January 18, 1951--cephalin cholesterol flocculation--24 hours, negative; 48 hours, 3 plus. Hemoglobin and RBC on January 18, 19, and 22 showed no evidence of anemia.

DISCUSSION

A true anamnestic reaction is often difficult to determine, and in many cases it can only be assumed. The lack of knowledge concerning the Rh factor and its manisfestations is a tremendous barrier.

By definition, the anamnestic reaction must demonstrate an increase in immune antibodies and a non-specific antigen must be responsible for the sensitization.

Both the pregnant and nonpregnant sensitized woman may show considerable variation in antibody titers if followed closely.[20] The concentration of antibodies in the blood increases following the termination of pregnancy and usually reaches a maximum seven to twenty-one days after delivery.[22] The titer then falls and within a few months antibodies may be non-demonstrable. They may, however, persist for many years.[3,19,23]

Routinely, antibody titers are often not performed until approximately the fifth to the seventh month of the pregnancy. A positive titer at that time could not be definitely interpreted as being the result of the present pregnancy as the titer could represent a residual antibody.

Only repeated tests make it possible to recognize a trend in antibody production which may permit clinical interpretation.[19] A slight variation in titers may or may not be significant because of the variability of the

agglutination of red cells and of the persons reading the results. Therefore, it is only when a definite rise in titers is noted that one can be sure that the sensitization is the result of the present pregnancy.

One must then decide if the rise in titers is due to an incompatible reaction or a benign anamnestic reaction. If the father is Rh positive (homozygous), the increase in titers would have to be the result of an incompatible reaction. However, the best clinical laboratories make an occasional mistake. In case 12, an Rh positive infant was expected and the prognosis for obtaining a healthy baby was extremely poor yet the father was subsequently proved to be Rh positive (heterozygous).

If the father is Rh positive (heterozygous), it is not possible antepartum, by antibody titers alone, to predict the outcome of the pregnancy.[11]

After delivery, should the baby show clinical evidence of hemolytic disease, it could then be stated positively that the antibody production was due to an incompatible pregnancy. Potter has stated, "When a woman has once been immunized to a degree sufficient to cause hemolytic disease in one infant, all Rh positive children born subsequently will likewise be affected and all Rh negative children will be free of the disease."[3] Rh typing of the baby will verify this fact.

In order to consider antibody stimulation as resulting from an anamnestic reaction, the baby must be Rh negative. Some children appear to be Rh negative when tested at birth but later prove to be Rh positive.[18,24] In such falsely Rh negative babies, the Rh positive erythrocytes are coated with incomplete or blocking antibodies and hence may fail to agglutinate when tested with the standard type saline sera.[11] The Coombs[14] test on the infant's cord blood on repeated typings with C, D, and E sera both in the saline and in the albumin method[11] will correct this error.

The most difficult criterion in the definition of the anamnestic reaction to prove is that the Rh negative factor was the non-specific stimulus. Typing sera generally available is of D specificity. As mentioned previously, the D factor is responsible for sensitization in 90% of the cases in which the antibody is produced. Also, the D factor is believed to be the most strongly antigenic of the Rh-Hr antigens although not to the exclusion of the other Rh-Hr factors. Since a preliminary sensitization is essential and since type D seems to be by far the most likely to provide sensitization, the anamnestic reaction would also be expected to be preponderantly of D specificity.[15]

Schneider et.al. (cases 7,8, and 9) demonstrated that, as far as could be determined, the D factor was

responsible for the sensitization. He stated, however, that it could not be excluded that there may have been an incompatibility of some of the possible Rh sub-groups such as are currently being reported, or blood groups or tissue factors which may be discovered.[11] Davidsohn, in commenting on case 2, said, "there is little doubt that our knowledge of individual antigenic differences is still too limited to exclude the presence of a hitherto unknown antigen in the fetus and its absence in the mother. According to present knowledge such an antigen would be nonspecific with regard to the Rh factor, thus justifying the reference to the observed phenomenon as anamnestic Rh antibody reaction."[19]

Most anamnestic reactions are a complete surprise. Usually the mother has had an incompatible blood transfusion or presents a history of hemolytic disease in a previous pregnancy. An incompatible pregnancy should be expected especially, if during the course of the pregnancy, there should occur a rise in antibody titers. If the father is Rh positive (homozygous), the prognosis for a healthy baby is nil; if heterozygous, there is an even chance that the baby will be Rh negative and free from hemolytic disease. But there is no way to determine prepartum the Rh factor of the fetus. Therefore, every pregnancy with such a history should be considered incompatible andtherapy directed toward the prevention of

fetal injury.[25]

Numerous attempts have been made to minimize the effect of hemolytic disease.[11] Prenatal control of antibody levels with Rh haptens[26] may yet provide the most effective prophylaxis and therapy.

In 1949, Philpott described the use of methionine in amounts sufficient to cross the placental barrier and thus protect the fetal liver. Methionine does not prevent hemolysis or antibody production. It is not too difficult to treat a servere anemia but almost impossible for a baby to survive with a severely damaged liver.[27] Methionine was prescribed therapeutically in cases 10, 11 and 12.

Antibody titers should be repeated regularly throughout the course of the pregnancy, preferably fromthe third month on. The pregnancy should be carried to atleast to the thirty-sixth to the thirty-eighth week. If at this time there should be a rising antibody titer, medical induction might be considered. Caesarian section probably should not be attempted unless other indications are present.[25]

At delivery it is good practice to have a transfusion team standing by ready to transfuse the baby should the necessity arise. The Coombs test on cord blood will demonstrate neonatal sensitization and direct attention toward the sensitized Rh positive baby sparing

those with benign anamnestic readtions from major procedures which, for them, are unnecessary.[25]

SUMMARY

The discovery of the Rh factor has answered a few of the questions concerning immunization but in turn has brought forth many new problems, one of which is the anamnestic reaction.

The anamnestic reaction is defined as "an increase or reappearance of immune antibodies already produced in the system on the injection of a non-specific antigen." Previous sensitization is implied.

Although the incidence is low--the ratio being approximately one anamnestic reaction to five incompatible reactions--it poses a diagnostic problem. Therefore, the importance of the anamnestic reaction centers about the individual case.

Nine anamnestic reactions reported in the literature and three from the private files of a local obstetrician were presented. It was impossible to predict by antibody titers alone the outcome of the pregnancies. Differentiation between incompatible reaction and anamnestic reaction is necessary because of the prognosis for the baby. The incompatible reaction might lead to varying degrees of hemolytic disease whereas the anamnestic reaction is characterized by an Rh negative baby entirely free of the disease. Such was the findings in each case reported.

Observations from the cases reported are as follows: 1) In each case there was evidence of previous maternal sensitization either from an incompatible blood transfusion or from an incompatible pregnancy. 2) Various therapeutic agents were used; for example, ethylene disulfonate (cases 4,5, and 6); pertussis vaccine (case 6, third pregnancy), Rh hapten (case 3), and methionine (cases 10, 11, and 12) without an appreciable affect on antibody production. 3) Case 2, presented a problem because the rising titers were thought to be due to breach of instructions. Artificial insemination from an Rh negative donor had been attempted to prevent fatal erythroblastosis. 4) In case 6, the anamnestic reaction occurred with two successive pregnancies. 5) Case 8, death of the Rh negative infant was due to complications of prematurity rather than to hemolytic disease. 6) Several of the pregnancies showed a tremendous increase in antibody titers, (cases 6,7, and 8) suggesting that some women may be extremely labile with respect to antibody production. 7) All cases presented should serve to stay the hand to those prone to do abortions in such instances.

It can be expected that the D factor is responsible for sensitization in a great majority of the cases in which the Rh antibody is produced but not to the exclusion of the other Rh-Hr factors.

Pregnancies in which there is a history of incompatible reactions should be followed closely with antibody titers. Therapy should be directed toward preventing fetal injury. Termination of pregnancy at thirty-six to thirty-eight weeks by medical induction or Caesarian section might be considered. When there is an incompatible or anamnestic reaction suspected, the baby should be typed after birth to prevent unnecessary procedures.

CONCLUSIONS

1. Although the incidence of the anamnestic reaction is low, the individual case is important.

2. In those pregnancies in which the father is Rh positive (heterozygous) and the mother Rh negative, it is impossible to predict in advance the outcome of the pregnancy.

3. Repeated antibody titers is desirable in those pregnancies in which the mother is Rh negative and in which there is a history of an Rh positive baby or incompatible blood transfusion.

4. In all cases presented above, the rising titer was due to a non-specific stimulus--the baby being Rh negative and free from hemolytic disease.

5. When there is a possibility of an anamnestic reaction, the risks involved with premature termination of the pregnancy should be considered.

6. The typing of infants for the Rh factor will prevent unnecessary procedures on Rh negative infants.

I wish to express appreciation to Dr. L. S. McGoogan and Dr. D. C. Vroman who generously furnished private case histories for presentation in this study.

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