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THE PROBLEM OF HEMOLYTIC DISEASE OF THE NEWBORN AND ITS MANAGEMENT IN A GENERAL HOSPITAL

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EDITOR'S NOTE: Since The Lincacre Quarterly professes to be a journal of the philosophy and ethics of medical practice, it is not our policy to publish articles whose content is exclusively medical. To do so, we feel, would be to compete needlessly and ineffectually in an area already adequately covered by the scores of excellent medical journals available to any doctor. The distinctive service which we hope to provide for our readers lies rather in the sphere of medico-morality.

Dr. Sacks' article, because of its immediate and obvious implications, qualifies in an eminent degree for this latter category. The first duty of every physician is to provide his patients with optimum medical care. Specifically in the field of hemolytic disease of the newborn, where infant life and health hang so precariously in the balance, techniques which substantially improve the likelihood of a live and healthy baby are as morally imperative as they are medically superior.

As explained in the final section of this article, The Catholic Hospital Association has already undertaken a unique project in the form of a cooperative immunoserological laboratory program. To the extent that the interest and cooperation of hospital staff members may be necessary to implement this program, it is to be hoped that our doctors will not be found wanting.

In any hospital where an obstetrical population exists the problem of hemolytic disease of the newborn is present. This is especially true where a significant percentage of this population consists of multiparous women. The following data from this hospital help to emphasize the importance of this problem. The figures are approximate to the nearest round number.

In a two year period, slightly more than 10,000 infants were delivered. Of these, 13% had Rho negative mothers. The 1,300 mothers in this group had 900 Rho positive children; 100 of these children had hemolytic disease of the newborn as evinced by a positive Coombs test. About half of these affected children required replacement transfusion. In other words, a case of hemolytic disease of the newborn may be expected about one in every 200 deliveries, and half of these will require replacement transfusion.

In this summary discussion of hemolytic disease of the newborn, it has been necessary to leave out much significant detailed information which belongs more properly in a textbook. For the salient information to help put in practice the discussion enclosed herein, the author recommends the following excellent reference books:


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A survey done elsewhere shows that by the 7th pregnancy at least one out of every four Rh negative women will be sensitized to the RH factor. This indicates that the greater the degree of multiparity in a given hospital population, the more cases of hemolytic disease of the newborn are to be expected.

If an adequate organization for the care of these patients is in existence in a hospital, and this organization can be set into motion with celerity, the mortality from this disease (or its terrible sequelae) can be reduced to 5% of cases. If the disease is not recognized early, or transportation to another hospital is necessary before treatment can be instituted, the mortality will rise sharply.

The fact that a mother has had an infant with severe hemolytic disease of the newborn does not prevent her from having subsequent children who may survive and be normal if adequate therapy is instituted in time. This is especially true if the husband is heterozygous for the offending antigen. We have in our records cases which fully substantiate this. One Rh-negative mother was sensitized to the RH factor by an intramuscular injection of blood given in childhood for measles prophylaxis. Her husband (we found subsequently) was heterozygous for this factor. Her first three infants were Rh negative. Her next three children, all with severe hemolytic disease of the newborn; all surviving normally after early replacement transfusion (within the first hour of life).

In summary, it may be stated that hemolytic disease of the newborn is a serious problem in a hospital, but if an adequate warning system exists, and if adequate therapy is readily available, the problem is by no means insuperable.

THE MANAGEMENT OF HEMOLYTIC DISEASE OF THE NEWBORN

Much has been written on the treatment of hemolytic disease of the newborn and its serological complexities. The very number of publications tends to retard anyone desiring to set up a system for managing this disease in the absence of a specialized blood bank, obstetrical or pediatric staff.

Our hospital has a very active obstetrical service and consequently employs a large staff. After some years of trial and error, an approximation of the system described below has become routine.

I. Responsibility of the obstetric staff (i.e., all those who deliver babies).

Any pregnant woman is to be typed for Rh(D) factor. This is by the most likely factor (90%) in which incompatibility between mother and child will result in hemolytic disease of the newborn. There are various ways of doing this, but the most essential part of the procedure of replacement transfusion is well. Unfortunately both the mother and her child are typed and a Direct Coombs test (DC) is done. If the DC is positive, there will be no difficulty, but the presence of antibodies is a warning of probable difficulty. In the presence of antibody, blood is drawn for titration may be drawn, subsequently to appraise changes, but these are not essential.

On admission to the hospital a red sticker or some similar attention-drawing mark is attached to the mother's chart. After delivery, a similar sticker is attached to the infant's chart.

II. Responsibility of the pediatric staff (i.e., those who take care of the newborn).

When the baby is born, cord blood is taken directly to the blood bank where it is typed for Rh (D) factor and a Direct Coombs test is done. If the Direct Coombs test is positive, it is the unusual case that the serum is not Rh positive. The Direct Coombs test is positive, other tests are done, since the baby has hemolytic disease of the newborn. It is the unusual case that the baby has no hemolytic disease of the newborn. The Direct Coombs test is positive, other tests are done, since the baby has hemolytic disease of the newborn. The Direct Coombs test is positive, other tests are done, since the baby has hemolytic disease of the newborn.

A. Prematurity — The premature infant is far more susceptible to kernicterus than the full-term infant.

B. A history of a previous sibling with severe hemolytic disease of the newborn.

C. Clinical icterus within the first six hours of life (and most with clinical icterus within the first twelve hours). These infants almost always develop a high serum bilirubin level.

D. Hemoglobin less than 14 gm./100 ml. at birth.

E. Reticulocytosis over 10%, or marked erythroblastosis.

F. Cord bilirubin over 5 mg./100 ml. serum.

G. If spectrophotometric studies are to be had, elevated levels of heme pigments other than bilirubin will give an indication of severity of illness. These are not generally available.

H. High maternal antibody titer (level).

The preceding rules appear to involve a great deal of laboratory work, time consuming and fatiguing to both doctor and patient. However, the entire tabulation may be condensed to the following statement:

In the presence of a positive Direct Coombs test and any other of the factors listed, replacement transfusion is the treatment of choice. It is the unusual case which will require more than one or two tests to classify it. Indeed, the milder the case, the more laboratory work and observation will be required.

If the infant has a positive Direct Coombs test with no other positive findings, the serum bilirubin level must be determined at four to eight hour intervals in order to determine the speed of rise. A rise of serum bilirubin approaching one mg/hr. is an absolute imperative. It is also possible for the Direct Coombs test to be positive in cases where the mother is Rh(D) negative and the blood type of the infant is Rh(D) positive. In such cases the Direct Coombs test is more important.
For example, if the ABO system is involved (and this diagnosis is frequently made with indirect Coombs testing to eliminate the rarer antigen systems as culprits), the direct Coombs test will usually be negative and the maternal blood will have antibody in every case. If no clear-cut serologic evidence of hemolytic disease of the newborn is found, the serum bilirubin level and its speed of rise are the sole criteria for performance of a replacement transfusion, and the critical levels are the same as those aforementioned. In borderline cases, it is safer (if the operator is experienced) to do the replacement transfusion than to withhold therapy. In this way, practical, immediate therapy may proceed without definitive serologic diagnosis.

All sera in every case of hemolytic disease of the newborn (samples from mother and baby) should be sent to a blood center for detailed testing, confirmation of diagnosis, and definition of antigen system. This will check results of the hospital laboratory, add knowledge and experience in the disease, and occasionally supply a rare antisemum from the mother which may be used for research purposes. (It will also protect the mother from incompatible transfusions in the future. She should need any.)

Certain elements of the actual performance of the replacement transfusion remain to be discussed. It is safer not to warm the blood but rather to keep the patient warm. It is essential that the operator have an alternative technique available in case where the umbilical vein cannot be catheterized. If the patient has hepatosplenomegaly, cardiac failure is probably present in some degree, and blood should be withdrawn until the venous pressure is about 7 cm. water; then the exchange of blood should begin. Enough calcium (as 10% calcium gluconate) should be given at intervals (1 to 2 ml. for every 100 ml. blood used) to prevent hypocalcemia, which is manifested by irritability before tetany appears.

Insofar as aftercare is concerned, the child should be kept in a heated bed, and routine nursery feedings may be started after twenty-four hours. Serum bilirubin levels at four to eight hour intervals are done to ascertain whether a repeat replacement transfusion is needed; 20 mg./100 ml. serum is the critical level. As soon as this danger is passed, and the child is otherwise in satisfactory condition, it may be discharged. Thereafter, weekly hemoglobin and microhematocrit levels should be done. This is necessary to follow the progressive anemia which usually occurs in these infants. The faster the weight gain, the more precipitous the drop in hemoglobin. This is due to several factors: the bone marrow is temporarily exhausted and does not begin to form erythrocytes for several weeks after birth; the life of transferred cells is shorter than the infant's own; so that a gradually decreasing number of erythrocytes in an increasing body mass and circulating volume manifests itself as anemia. Any antibodies remain-


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A cooperative immunoserological laboratory program for the Catholic Hospital Association

The Catholic hospital has a moral obligation to seek out the most modern and scientific methods and to apply them to the proper care of its patients. Since there is no substitute for experience in this field of immunoserology, experience can be gained only by properly testing large numbers of blood samples. Small facilities rarely have enough well trained people or equipment to perform certain special tests, and only by cooperating with larger facilities can these tests be done accurately.

A cooperative program now exists which will permit such smaller Catholic hospitals to send laboratory specimens (if they are not at present equipped to examine them) to specially trained and equipped institutions which have been set up to perform these special procedures.

This program is in its first phase. An immunoserological training program to instruct the medical staff agreed in advance to care for these patients when the need arose. Thus, one man would always be available, and the experience needed for the acquisition of technical skill would not be spread too thinly among too many people.

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NOTE: Because most hospitals will have fewer than twenty cases of hemolytic disease of the newborn in a year, it would be better if a few members of the medical staff agreed in advance to care for these patients when the need arose.