

APPENDIX E

Rh D Hemolytic Disease

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Rh D hemolytic disease of the newborn is a condition that arises because of an incompatibility between a mother's blood and that of her fetus.

The majority of the human population has Rh+ blood, meaning they produce an inherited protein on the surface of their red blood cells. This protein is known as the D antigen. Approximately 15% of Caucasians, and 7% of African Americans lack this protein and so are considered Rh negative. If an Rh negative woman and an Rh positive man conceive a baby who inherits the man's Rh+ blood, there is a danger during the pregnancy, and especially during labor and delivery, that some of the baby's blood will enter the mother's bloodstream via the placenta. This induces an immune response in the woman against the baby's blood. The woman will produce antibodies which will fight against the baby's Rh+ blood, leading to the destruction of the baby's red blood cells. If enough red blood cells are destroyed, this will lead to hemolytic anemia and possibly severe consequences to the fetus. When these red blood cells are hemolyzed quickly, the fetus may develop jaundice, edema (hydrops), brain damage, and heart failure.

Administration of Anti-D Immune Globulin (RhoGAM)

The administration of anti-D immune globulin (RhoGAM) to Rh D negative women is needed to prevent Rh D sensitization. Before the advent of RhoGAM, this sensitization caused severe hemolytic disease in the fetus and newborn and was a major cause of perinatal morbidity and mortality.

Isoimmunization to the D antigen occurs most of the time at delivery from fetomaternal hemorrhage. About 10% of the cases result from spontaneous antenatal fetomaternal hemorrhage, usually in the third trimester. External cephalic version, whether successful or not, can cause this hemorrhage as well. Some events during the first and second trimesters have also been known to cause isoimmunization. These events can be any of the following: therapeutic or spontaneous abortions, ectopic pregnancies, threatened abortions, and clinical procedures such as chorionic villi sampling, amniocentesis, and cordocentesis.

Anti-D immune globulin is collected from volunteer donors who have high titers of circulating anti-D antibodies. The donated plasma is pooled and fractionated by drug manufacturers. Since the manufacture of RhoGAM is dependent upon blood donors, the supply can sometimes be limited. For this reason, recommendations for the administration of RhoGAM have been established that more than 90% of the time will prevent isoimmunization.

For the Rh D negative woman who has not been sensitized, the recommendations are to give RhoGAM at the following times:

- At approximately 28 weeks gestation (unless the father of the baby is known to be Rh negative as well). Draw an antibody screen first before administering the RhoGAM, as women can become sensitized prior to 28 wks. gestation.
- Within 72 hours of delivery
- After a first trimester pregnancy loss (e.g. therapeutic or spontaneous ab, ectopic, etc.)
- After invasive procedures such as CVS (chorionic villi sampling) and amniocentesis

The clinician may also consider giving RhoGAM in the following circumstances:

- Threatened abortion
- Second or third trimester antenatal bleeding
- External cephalic version
- Abdominal trauma

If a woman who is Rh negative presents for prenatal care late in pregnancy (after 28 wks.), she should still be given RhoGAM. If delivery occurs within three weeks of giving the anti-D immune globulin, the postnatal dose may be withheld unless excessive fetomaternal hemorrhage has occurred.

If somehow an Rh D negative woman is discharged from the hospital without receiving anti-D immune globulin, she may still benefit at least partially if she gets the RhoGAM as late as 28 days postpartum. Check with the clinician first if this situation arises.

Interpreting the Lab Results

All pregnant women need blood typing for the blood group and Rh factor. In addition, the blood is tested for antibodies to foreign antigens. These foreign antigens can get into the mother's blood from past blood transfusions or from blood group factors that the fetus has inherited from the father. Any situation where fetal-maternal bleeding occurs can potentially transfer these foreign antigens to the mother and stimulate the production of antibodies.

Rh D negative women who are sensitized will need serial blood tests to titer the number of circulating antibodies. You may need to submit more blood for this titer to be done. The past pregnancy history of a sensitized woman is also important as this may predict the prognosis of the pregnancy. The severity of hemolytic disease will usually be at least equal to or greater than the prior pregnancy. Regardless of the history, though, all pregnant women need blood group and Rh factor testing, plus screening for atypical antibodies at the first prenatal visit.

Other blood incompatibilities can exist, such as an ABO incompatibility; however, this is not usually a serious cause of anemia in the newborn. About 20% of all infants have an ABO incompatibility with only about 5% being clinically affected. Fortunately, this causes only mild hemolytic anemia seen as jaundice or anemia of the newborn and is usually treated with phototherapy.

Other atypical antibodies can also be present in the mother's blood even with Rh+ women. Some of these can cause severe hemolytic anemia while others are insignificant. Contact the blood bank for more information on these antibodies.

Sometimes a report will return with blood typed as Rh negative but Du positive. Once, this was thought to be a variant of the D antigen. Currently, this designation is considered to be a "weak D positive" and therefore Rh+. No RhoGAM should be given to these women. Some centers do not test for this Du antigen and women may inadvertently receive RhoGAM. Antibodies induced from this administration may take up to 12 weeks to dissipate. In the rare instance when a woman arrives for delivery where her Rh status is negative or unknown and the postpartum screen reveals a Du positive result, RhoGAM should be given and the possibility of fetomaternal hemorrhage should be investigated by other tests.

Resources:

ACOG Practice Bulletin, May 1999, Number 4, "Prevention of Rh D Alloimmunization".

ACOG Educational Bulletin, August 1996, Number 227, "Management of Isoimmunization in Pregnancy".

March of Dimes Public Health Education Information Sheet, 1994, "Genetic Series: Rh Disease".

Leveno, J. and Cunningham, F. et. al., Williams Manual of Obstetrics, 21st Edition, Chapter 38, pgs. 268-274.