

PROTOCOL #16 - Maternal Fetal Medicine, University of New Mexico

ISO-IMMUNE DISEASE IN PREGNANCY

General:

Although the use of Rho(D) Immune Globulin (human) has decreased the number of cases due to Rho(D) sensitization, there are still a large number of patients sensitized to the Rho(D) antigen and to other antigens of the Rh system (C, c, E, e). Also, severe hemolytic disease of the newborn may be caused by antibodies to red cell antigens which are NOT of the Rh system (Kell, Duffy, Kidd, etc.).

1. Detection of Patients at Risk

All patients should have an Rh and ABO determination and an antibody screen at the first visit. This is especially important for all patients with a history of transfusion or unexplained fetal loss. If the patient is Rh negative and the antibody screen is negative, the antibody screen is repeated at 28 weeks of gestation.

2. Management of Patients Detected to be at Risk

Once a positive antibody titer is detected, the antibody should be identified and categorized as to whether it is or is not associated with iso-immunization. Those patients with antibody titers associated with erythroblastosis should have antibody titers every four weeks. If the titer remains less than 16, these patients may be delivered at term. If the antibody titer is 16 or more, these patients should be followed per the protocol for patients with significant sensitization.

3. For patients with Kell sensitization, antibody titers are less reliable for disease prediction and a lower threshold should be used to initiate ultrasound.

All patients need an early ultrasound to determine gestational age and need the paternal blood type and phenotype. If the paternal blood type is Rh-, then no further studies are necessary if paternity can be assured.

Inheritance of the D antigen as well as K, C, c, and E antigens can be determined by analyzing cell-free DNA in maternal plasma. This is a non-invasive means to determine the fetal risk from maternal sensitization with clinically significant antibodies. It is currently available in Europe after 16 weeks gestation. This technology is anticipated in the USA in the near future.

First sensitization in pregnancy (low level sensitization):

- Initial ultrasound for dating and anomalies at 16-20 wks
- Obtain the genotype of the fetus's father. If the father does not possess the antigen, the fetus is not at risk. If the father is heterozygous for the antigen, there is only 50% chance that the fetus will be affected.
- Document any prior history of transfusions, Rhogam, or abortions
- An antibody titer should be determined at the first prenatal visit, at 16-18 weeks of gestation, and approximately every 4 weeks thereafter.

If titer remains 8 or lower

Follow regularly, as often as monthly titers until delivery or if multiple titers remain stable

Significant sensitization by titers and/or prior history of affected pregnancy

- Initial ultrasound at 18 weeks for anomalies, dates, and ultrasound middle cerebral artery (MCA) Doppler peak systolic velocity (PSV)
- Ultrasounds every 1-2 weeks for repeat MCA PSV

PROTOCOL #16 - Maternal Fetal Medicine, University of New Mexico

Ultrasound measurements for isoimmunized pregnancies:

- Standard biometric measurements
- Amniotic fluid index
- Evidence of hydrops
- Serial peak systolic middle cerebral artery velocities (MCA PSV) using Doppler ultrasound. An increase in the MCA PSV is associated with moderate and severe anemia. The sensitivity in detecting the anemia is 100%. The pathophysiology is based on the notion that the anemic fetus preserves oxygen delivery to the brain by increasing cerebral flow of this low viscosity blood. The MCA PSV can help determine the timing of a second intrauterine transfusion in fetuses with severe anemia. By using a cut-off of greater than 1.50 MOM in the MCA PSV, most transfusions can be delayed due to reassuring noninvasive test results (see algorithm for the management of Rhesus Alloimmunization) the optimal interval for these measurements are not established but the recommendations are every week. The use of the MCA velocity should be limited to less than 35 weeks of gestation due to increase in the false positive rate increases after this. The MCA Doppler velocity assessment can be used as early as 18 of gestation in situations where a previous infant or fetus has been affected.

If abnormal ultrasound findings at any time: PUBs if prehydropic changes or critical MCA PSV (1.5 MoM)

PUBs protocol for fetal transfusion if Hct is 30% or less (Refer to Protocol #30)

- Transfusions should be with Type O, RH-negative, cytomegalovirus-negative, washed, and irradiated packed cells cross-matched with maternal blood
- A request for packed cells with a Hct of between 75 –85%. The blood to be transfused should be checked with a hemocue in the procedure room before the transfusion
- Repeat transfusions are planned for when the fetal hematocrit is predicted to be between 25% - 30%
- The intrauterine transfusions should be to a hematocrit of 40-45%
- Platelets should be available for transfusion if the fetus has had multiple transfusions.
- Administer steroids prior to fetal transfusion if possible
- The interval between transfusions with severe hemolytic anemia should be 7-14 days between the first and second transfusions. Subsequent transfusions are one to three weeks depending on the clinical status and the gestational age.
- Patients should then be delivered at fetal maturity or at 34-36 weeks.
- Direct Coombs and reticulocyte count should be performed and IVT should be given if the hematocrit is less than 30%.
- The amount of blood given is calculated by the formula:

$$\text{Volume}_{\text{transfused}} = \frac{\text{EFW(g)} * 0.14 * (\text{Hct}_{\text{final}} - \text{Hct}_{\text{initial}})}{\text{Hct}_{\text{transfused}}}$$

PROTOCOL #16 - Maternal Fetal Medicine, University of New Mexico

Alternatively: multiply EFW (g) by the coefficient that correlates with desired increase in fetal Hct

Target Hct Increase	Coefficient
10%	0.02
15%	0.03
20%	0.04
25%	0.05
30%	0.06

Management of the Newborn

- A. Pediatric consultation should be obtained prior to delivery of all sensitized mothers.
- B. Do not strip the cord toward the newborn infant. Keep baby at the levels of the placenta. Make every effort not to manually remove the placenta.
- C. Obtain Coombs, ABO, Rh and bilirubin on cord blood. In addition, a second tube of anticoagulated blood should be obtained for hematologic studies, i.e., hematocrit, hemoglobin, and/or reticulocytes.
- D. A pediatrician should be present for the delivery of those patients with an antibody titer of 16 or more of an antibody known to cause iso-immunization.

CONSULTATION: Twenty-four hour consultation is available by calling the Maternal Fetal Medicine service at the University of New Mexico Hospital. 1-888-866-7257.

Selected References:

Obstet Gynecol. 2006 Aug;108(2):457-64. ACOG Practice Bulletin No. 75: management of alloimmunization. American College of Obstetricians and Gynecologists.

BJOG. 2010 May;117(6):722-9. Epub 2010 Feb 22. Diagnostic accuracy of noninvasive polymerase chain reaction testing for the determination of fetal rhesus C, c and E status in early pregnancy. Gutensohn K, Müller SP, Thomann K, Stein W, Suren A, Körtge-Jung S, Schlüter G, Legler TJ. Department of Transfusion Medicine, University Hospital, Hamburg, Germany. email@kai-gutensohn.de