TITLE: Rh NEGATIVE STATUS & RhoGAM  
EFFECTIVE DATE: January 19th, 2013

POLICY STATEMENT:
While RhoGAM is generally considered safe, no drug is risk free. Informed consent should include several different considerations related to administration, including possible risks. Counseling regarding the increased risk of prenatal sensitization and documentation of this discussion in the prenatal record is recommended. RhoGAM administration is based on well-designed cohort or case-controlled trials, rather than on randomized controlled trials. This means that antepartum RhoGAM should be routinely provided to eligible candidates and that there is at least fair evidence that benefits outweigh the risks.

Despite its success, RhoGAM administration is somewhat controversial. Immune globulin is a blood product derived from human plasma. This may be of particular significance for women who hold religious beliefs that prohibit the use of blood products. The issue of clients who refuse blood products for religious reasons has not been addressed in the literature. During the preparation process, human plasma is screened for viruses as prescribed by the FDA. There is a small risk of contracting pathogen that is currently unknown and thus not included in the current screening protocol, but decades of experience with its administration have not demonstrated any deleterious effects.

Another concern is that until 2001, Thimerosal was used as the preservative in RhoGAM. A recent modification in RhoGAM preparation has eliminated this problem. Thimerosal is a mercury derivative used as a preservative to which certain individuals who are sensitive may possibly experience potentially serious allergic reactions and potential neurologic damage to the fetus. This had raised questions from clients concerned about immunization preservatives. A number of companies market RhoGAM. According to the Ortho Company that manufactures RhoGAM RIG, Thimerosal-containing syringes would have reached their expiration date by April 2003. Since Thimerosal is no longer used as the preservative, concerns about its inclusion in RIG are no longer warranted.

BLOOD BORNE PATHOGEN
EXPOSURE CATEGORY: I (Involves exposure to blood, body fluids, or tissues)

FUNCTION: Care of Patients

POINTS OF EMPHASIS:
If a feto-maternal hemorrhage (FMH) occurs when an Rh negative mother is carrying an Rh positive fetus, her immune system reacts to the antigen and forms an antibody to eliminate it. This process is called Rh isoimmunization, also commonly referred to as sensitization. The causative factor leading to Rh isoimmunization is called the sensitizing event. Once maternal anti-D antibodies have formed, they cross the placenta, attach to fetal red blood cells, and hemolyze the fetal RBCs. Once sensitized, the immune response worsens with each subsequent incompatible pregnancy.

Approximately 15% of all pregnant women are Rh negative. Approximately 17% of these Rh negative women would become isoimmunized perinatally without preventative measures. Of those isoimmunized, 90% of cases would occur at the time of birth and 10% in the antepartum period because of FMH. Most of these antepartum FMH occur following the 28th week of gestation. If the fetus is Rh positive and no preventative measures are taken, 0.7% to 1.8% of Rh negative women may experience prenatal isoimmunization.

Antepartum Rho (D) immune globulin is protective against the effects of FMH. A small amount of fetal blood can enter the maternal circulation most often during the birth process, particularly during operative deliveries. FMH may also occur during spontaneous or elective abortion, vaginal bleeding during late pregnancy, trauma, antepartum hemorrhage, fetal death, and stillbirth. Invasive procedures, such as amniocentesis, chorionic villus sampling,
cordocentesis, and fetal manipulation, such as external version and fetal surgery, may also lead to maternal exposure to fetal blood. However, FMH can occur in the absence of observable trauma, risk, or surgery.

“An estimated three in 1,000 births are associated with a fetomaternal hemorrhage greater than 30mL and require more than one 300-microgram vial of Rh immune globulin for adequate Rh immunoprophylaxis” (Sandler & Gottschall, 2012, p 1431).

**EQUIPMENT:**
1. Informed Consent
2. Lab draw equipment
   a. Red top tube (not the gtt) or a lavender tube for cord blood
   b. Lavender tube 0.5ml for infant heel stick
3. RhoGAM

**PROCEDURE:**
1. Blood typing, Rh and antibody screens are recommended to be screened on every pregnant client. The antibody can be reevaluated at the 28-week visit and subsequently, as determined necessary. The likelihood of sensitization after the initial antepartum Coombs test is less than 0.18%. ACOG recommends this repeat testing be individualized, as there is insufficient evidence to recommend for or against routine repeat testing at 28 weeks’ gestation.
2. Several maternal blood tests are used for identification and management of Rh negative women. If the antibody test is negative, the woman has not been sensitized. However, if the indirect Coombs is positive, serial quantitative levels are drawn to detect and follow patterns of change. Laboratory variation exists with regard to titers, and therefore values that represent fetal risk are laboratory specific. In general, titers of greater than 1:4 represent isoimmunization and titers exceeding 1:16 signal concern for the development of fetal hydrops, with risk increasing as titer values rise.
3. Several tests exist to detect and quantify feto-maternal hemorrhage (FMH). The most common of these is the Kleinhauer-Betke (KB). The KB is used to estimate the presence and the amount of fetal RBCs in the maternal circulation following FMH. This might be prudent following a motor vehicle accident and other abdominal traumas. Other tests include the erythrocyte rosette test, the enzyme-linked antiglobulin test, and flow cytometry. Each of these tests have different attributes and limitations.
4. RhoGAM should be given in dose related to time and reason of administration.
   a. It should be administered in a dose related to the amount of fetal blood that has entered the maternal circulation. During the second and third trimester, the full 300 microgram dose is given, which can cover up to 1.5 milliliters. If a hemorrhage greater than 15 milliliters is suspected, the RhoGAM dose should be adjusted to the rate of 20 micrograms/milliliters of fetal blood.
   b. In early pregnancy, the risk of feto-maternal hemorrhage is markedly less than during later pregnancy, and the total volume of fetal blood is very small. Therefore, small doses of MICRhoGAM are used in the amount of 50 micrograms.
   c. Adverse reactions to Rh(D)-immune globulin are rare (1:60,000) and include formation of anti-D antibodies despite treatment, and localized reaction at the site of injection.
5. RhoGAM should be refrigerated but not frozen prior to administration. The RIG syringe should be inspected for clarity. A cloudy appearance or the presence of particulate matter would be an indication of potential contamination.
6. The deltoid muscle may be preferable to the gluteal muscle for administration of RhoGAM. If the injection is given in the gluteal region it may only reach the subcutaneous tissue and absorption will be delayed. According to the package insert, women should be observed for 20 minutes following injection to detect any possible allergic reaction although they are rare.
7. Women should be informed about potential side effects that most commonly include local inflammation, malaise, chills, rashes, and in rare instances anaphylaxis. Special consideration should be given if a woman has had past allergic reactions to any human immune globulin such as immunoglobulin A or has an immune deficiency. If a woman reacts to one dose of RIG, consultation with an immunologist is advisable prior to any future administration.
8. Optimally, RIG should be administered at approximately 28 weeks gestation and within 72 hours of a sensitizing event. If the injection was not given within 72 hours because of an error, it still should be
administered as soon as possible to provide some benefit. The half-life of RIG is 24 days. One study showed administration provided protection even when given within 9 to 10 days and other authors have indicated benefit up to 28 days after birth.

9. If birth occurs within 3 weeks of an antepartum injection of a standard 300 ug dose, the postpartum dose of RIG may be held unless massive FMH is suspected. Further, women who had not delivered 12 weeks after the administration of antepartum RIG should receive a second dose. The administration of one 300 ug antepartum dose of RIG will not result in a positive direct Coombs of the baby.

10. RhD-negative women should also have the blood of her baby typed after birth. If she has a RhD-positive baby, she can then be offered a postnatal injection of RhoGAM 300 micrograms.

11. Birth assistants are responsible for labeling the cord blood with the mother’s last name, and either “Infant Boy” or “Infant Girl.” Date and time are also necessary.

12. Birth assistants are to write STAT on the label, place the specimen in the refrigerator within a specimen bag and provide a laboratory order to the family. (See forms for preprinted laboratory orders.)

13. The specimen will need to be taken into the St. Vincent Laboratory (or a previously arranged laboratory in the client’s community) within twenty-four hours of birth. STAT results should be faxed to Believe Midwifery Services within two hours.

14. If newborn blood is determined to be Rh positive, RhoGAM is indicated; however, the mother will require a RhoGAM work-up to verify that no maternal-fetal blood exposure has occurred, which would require additional dosage of RhoGAM. Therefore, if positive results are found, the mother will be instructed to visit the St. Vincent/Women’s laboratory for a RhoGAM work-up and await results and subsequent administration of RhoGAM.

a. The first step in determining the dose of Rh immune globulin for postpartum Rh immunoprophylaxis is a qualitative laboratory screen for the presence of fetal red blood cells in a sample of maternal blood. In principle, this screen can be performed using any one of several laboratory assays capable of detecting fetal red blood cells, including a rosette fetal red blood cell assay, an acid-elution assay, or a column gel assay.
   i. The acid-elution assay is tedious, labor-intensive and reserved almost exclusively for the comparatively few blood samples requiring quantification.
   ii. The column essay can be used, also, as a first-step screen, but this assay is not sufficiently standardized for routine use.
   iii. In the US, nearly all (more than 99%) laboratory screens for the presence of fetal red blood cells in maternal blood are performed using one of the two commercially marketed kits for the rosette fetal red blood cell screen.

15. If the mother has previously arranged newborn blood typing and obtaining RhoGAM via another avenue (such as through her insurance mail delivery program, through her local hospital or lab, or through a local pharmacy) then she can opt to obtain the RhoGAM herself and have it administered by a nurse with Believe Midwifery Services at her 48 hours home visit.

16. If the RhoGAM was not administered within the recommended 72 hours for whatever reason, it should still be administered as soon as possible for up to 28 days although it is less likely to be effective.

**Recommendations for Administration of Rh Immune Globulin**

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<th>Mother</th>
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317-415-7657 Laboratory
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## Rh NEGATIVE & RhoGAM

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### REFERENCES


**Originated:** September, 2007

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**Penny Lane MSN, CNM, IBCLC**

**DATE:** 1/18/2013

**Holly Hopkins MSN, CNM**

**DATE:** 8/23/2011

**Michelle Burton**

**DATE:** 6/4/2013