Evaluating the need for Rh immune globulin in some unusual situations

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In most situations the use of Rh Immune Globulin (RhIG) for the prevention of Rh\(_o\)(D) immunization in Rh-negative women of child-bearing age is routine. The following nine unusual situations are based on telephone calls received by Technical Services of Ortho Diagnostic Systems. Comments are not meant to be all-inclusive and the author suggests consultation when in doubt about a particular case.

**Case One**

*Situation:* An Rh-negative woman is bleeding at 35 weeks gestation. Until now her pregnancy has been uneventful. She was given Rh Immune Globulin (RhIG) at 28 weeks gestation. Should she receive an additional dose now because of the bleeding?

*Comments:* Yes, the fact that the mother is experiencing vaginal bleeding does not necessarily mean that there is also a fetal-maternal hemorrhage (FMH); however, one should assume that an FMH may be concomitant.

The half-life of gamma globulins is 21–23 days. Therefore, in this case, at least two “half-lives” have expired since the 28-week injection. This amount of time has reduced the RhIG to about 75 µg, which is sufficient to suppress the response of only three or four mL of red cells. Screening tests for FMH are not designed to detect small quantities of fetal cells. For example, the package insert of one of the commercially available screening kits states “Demonstration of volumes of fetal red cells less than 7.5 mL but greater than 2.5 mL will depend on the care taken in performing the test.” Because three or four mL of fetal cells might not be detected by a FMH screening test, a fail-safe approach should be taken with a negative test and it is recommended that one vial of RhIG should be given.

If a screening test for FMH is positive, the amount of the bleed should be determined by doing a Kleihauer-Betke (K-B) or enzyme-linked antiglobulin test (ELAT), and, depending on the results, the appropriate number of vials of RhIG should be given. It is best to ignore the residual RhIG from the 28-week injection in calculating the current needs.

**Case Two**

*Situation:* RhIG was given to an Rh-negative woman at 28 weeks gestation. The patient is now three weeks past the expected date of delivery. Should RhIG be given now?

*Comments:* Yes, another injection of RhIG should be given if 12 weeks have elapsed since the last injection. Based on the half-life of gamma globulins (21–23 days), the amount of RhIG present at the end of 12 weeks will be insufficient to suppress immunization from even a small amount of blood. Bowman has stated “. . . we don’t let a woman go more than seven days past the 12 weeks before calling her in and giving her the second injection.”

**Case Three**

*Situation:* An Rh-negative woman was delivered of a healthy Rh-positive baby. The test for FMH was negative, and a single dose of RhIG was given. The woman was in the hospital for 5 days because of postpartum complications. On the fourth day after delivery, the obstetrician ordered an antibody screening test. The reason for the order was to “evaluate the effectiveness of the RhIG.”

*Comments:* There is no scientific evidence to support
the contention that the absence of circulating antibody indicates an inadequate dose of RhIG, as the exact action of RhIG in suppressing the immune response is not known. There are no data to support speculation that antigen sites are blocked by antibody, leaving red cells immunologically inert and that all sites may not have been blocked unless excess antibody is detected. The site of action is probably at a more basic immunologic level. Many studies have shown that the recommended dose suppresses antibody production and it is meaningless to look for antibody in the serum.5

**Case Four**

*Situation:* A patient received eight units of Rh-positive blood in the emergency room. The patient was later found to be Rh-negative and the physician came to the blood bank to determine the best course of action.

*Comments:* Based on the following facts, it would require 128 vials of RhIG to suppress the immune response to eight units of blood:
- 480 mL whole blood per unit
- 1 vial RhIG suppresses 30 mL whole blood
- each unit of blood requires 16 vials of RhIG
- 8 units of blood = 128 vials of RhIG.

Before going to such measures, one question is important. Is the patient male or female and, if female, what is her reproductive potential? The package insert for RhoGAM* Rh sub(o)(D) Immune Globulin (Human) states “RhIG may be administered intramuscularly to prevent isoimmunization in eligible Rh-negative premenopausal females who receive Rh-positive red cells by transfusion, whether inadvertently or in association with leukocyte or platelet therapy.” In other words, one should carefully weigh the consequences of immunization against the cost and trauma of administering massive intramuscular doses of RhIG to prevent immunization of any patient except females who may still bear children.

**Case Five**

*Situation:* An Rh-negative woman has had two previous pregnancies and received antepartum and postpartum RhIG with both pregnancies. She is pregnant again, and her initial antibody screening test is positive; the antibody has been identified as anti-Rh sub(o)(D).

*Comments:* There are several possible scenarios that could account for this immunization. First, the woman could have had an unprotected (spontaneous or therapeutic) abortion since the last full-term pregnancy. Second, there might have been an undetected excessive FMH at the termination of the last pregnancy. Third, there might have been a FMH prior to the 28-week antepartum injection of RhIG. Statistics show that about 0.14 percent of women who have been properly treated during past pregnancies still become immunized prior to 29 weeks gestation.6 The most likely cause is transplacental passage of fetal cells during pregnancy prior to the 28-week injection of RhIG. In addition, a prior unrecognized or concealed pregnancy cannot be discounted.

**Case Six**

*Situation:* An Rh-negative woman had amniocentesis done at 15 weeks gestation to determine the possibility of an inherited defect. Should a full dose (300 µg) of RhIG be given?

*Comments:* Yes, a full dose of RhIG (300 µg) should be administered in any pregnancy that is expected to continue, regardless of the time of the amniocentesis. The micro dose of RhIG (50 µg) should be used only at the termination of pregnancy up to and including 12 weeks gestation.

If RhIG is given at 15–16 weeks gestation, a regular antepartum dose at 27–28 weeks must be given, because no more than 12 weeks should elapse between doses. The 12-week rule is based on both the half-life of RhIG and the concept of augmentation. There are limited studies that suggest there may be an enhancement of the immune response in the presence of a small amount of antibody, which is the opposite of the conditions required for suppression.7 Twelve weeks after a 300-µg dose of RhIG, the amount of immune globulin will have been reduced to less than 20 µg. Augmentation of the immune response is thought to be possible when fetal cells enter the circulation at the time when only a few micrograms of RhIG remain. These conditions could exist if more than 12 weeks elapse before another injection is given.

**Case Seven**

*Situation:* An Rh-negative woman is pregnant with twins, and amniocentesis was done at 16 weeks for genetic purposes. The twins are dizygotic and have
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separate amnionic sacks; therefore, amniocentesis was performed at two separate sites. Should two vials of RhIG be given?

Comments: One vial of RhIG (300 µg) is recommended following any amniocentesis. If there is any reason to believe that difficulty was encountered (e.g., a bloody tap), a FMH screening test can be performed to determine if there was sufficient bleeding to warrant doing a quantitative test.

Case Eight
Situation: Following a normal delivery, the rosette screening test for FMH was strongly positive while the K-B test was negative.

Comments: First, both tests should be repeated. Unless the K-B test is done frequently and by experienced technologists, it would be best to ask for consultation from a reference laboratory. The K-B test detects cells containing fetal hemoglobin, regardless of whether the cells are of fetal or maternal origin. On the other hand, a rosetting test determines the presence of D-positive cells (presumably fetal cells) in a majority of D-negative (maternal) cells. The above case description is typical if the mother is, in fact, D-positive or D<sup>+</sup> rather than D-negative.

Case Nine
Situation: An Rh-negative woman was delivered at home 5 days ago and has just now called the doctor to inquire about receiving RhIG. Should it be given at this late date?

Comments: Postpartum prophylaxis should be administered as soon as possible, preferably within 72 hours of delivery. The time of 72 hours was selected rather arbitrarily when the clinical trials were done to establish the efficacy of RhoGAM. It was assumed to be sufficient time for treatment to be given even in unusual circumstances. For this reason, there are no data to validate how much longer than 72 hours the injection will be effective, but it is unreasonable to believe that it would be effective at 72 hours and suddenly no longer effective at 75 or 80 hours. RhIG should be given after 72 hours; however, it should be recognized that the longer the time period, the less likely immunosuppression will be achieved.

References

*Trademark Ortho Diagnostic System

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