Rh Alloimmunization Prevention: Pregnancy & Postpartum

POLICY
BIRTH CENTER
Patient Care
Issued: August 2014
Last Approval: December 2020

I. PURPOSE

To outline recommendations and information about preventing RhD alloimmunization during pregnancy and the postpartum period.

II. REFERENCES

American College of Obstetricians and Gynecologists. (2017) ACOG practice bulletin 181: Prevention of Rh D Alloimmunization. 130 e57-70. Washington, DC.

III. DEFINITIONS

None.

IV. PROCEDURES

A. GENERAL

a) Administration of Rh Immunoglobulin (RhIG) is indicated in RhD negative women who have not been previously alloimmunized to RhD.

b) A Type and Screen (T&S) sample should always be drawn *before* administration of RhIG to evaluate for presence of alloimmunization to RhD.

i) If a T&S has been performed at UCSF Blood Bank within the last 30 days, there is no need to order a new T&S.

ii) If Blood Bank receives only a RhIG order with no T&S test within the last 30 days, they will call and request a T&S order and sample before issuing the RhIG.

c) The UCSF Blood Bank does not provide MICRhoGAM® (50 µg) and issues the full dose of RhoGAM® (300 µg) regardless of gestational age.

d) In patients with low platelet counts (<50,000/mm^3) or other bleeding disorders/coagulopathy, the intravenous preparation of RhIG (WinRho® SDF) should be ordered. A full dose of WinRho is 300 µg and is available in the UCSF Pharmacy.

e) For outpatient clinics, RhIG should be ordered through pharmacy. For inpatient/hospital triage, RhIG is ordered through appropriate APeX order sets and will be provided by the Blood Bank.

f) RhIG should be administered as soon as possible, within 72 hr. after a sensitizing event. However, if inadvertently RhIG is not given in the 72-hr. window, it should not be withheld. Administration of RhIG up to 13 days of sensitizing event has been shown to provide some benefit in preventing alloimmunization to RhD.

g) Fetomaternal hemorrhage (FMH) estimation may be done by fetal bleed screen (rosette test) performed by the Blood Bank, or Kleihauer-Betke (K-B) acid elution test performed by the Hematology Lab. Fetal bleed screen detects RhD-positive cells and is a qualitative screening test, whereas K-B test is quantitative and based on identification of fetal hemoglobin (HbF) in red cells.

i) If the fetal/neonatal RhD type is unknown (e.g. antepartum or stillbirth), fetal bleed screen is not useful and a K-B should be ordered instead.

ii) In mothers with medical conditions associated with increased baseline HbF levels (e.g. hereditary persistence of fetal hemoglobin, delta/beta thalassemias, and sickle cell disease), positive K-B tests should be interpreted with caution. In such cases,

flow cytometry-based send out tests detecting both HbF and RhD may need to be considered.

h) All patients with variant RhD types, including those who are confirmed to have weak D types 1, 2, 3, 4.0 or 4.1 by genotype testing should be managed as RhD-negative.[1]

i) In cases where a large FMH requires multiple RhIG doses to be administered, additional RhoGAM® doses can be administered intramuscularly at separate sites every 12 hours until the desired dosage has been reached. Alternatively, for enhanced patient comfort, the intravenous preparation of RhIG (WinRho® SDF) may be considered.

B. ANTEPARTUM

For Outpatient Clinic: Order RhIG through pharmacy

For Inpatient/hospital triage: Order RhIG using the appropriate APeX order set:

- *'RhoGAM/WinRho only-Antepartum Rh-negative Mom'* for routine RhIG prophylaxis at 28 weeks gestation

- *'Rhogam/WinRho and Kleihauer Betke-Antepartum Rh-negative Mom*' for cases when RhIG prophylaxis is given for a specific sensitizing event, with high risk of FMH

a) Events with NO risk of alloimmunization-*RhIG IS NOT REQUIRED*

i) Empty sac (no embryo ever documented in sac)

b) Events with potential alloimmunization risk-*RHIG IS REQUIRED*

- For all following listed indications, *regardless of the gestational age*, one full dose of RhIG (300 µg) should be administered (UCSF Blood Bank does not provide the 50-µg dose). Order 1 dose RhIG (300 µg) using the appropriate APeX order set *'Rhogam/WinRho and Kleihauer Betke-Antepartum Rh-negative Mom*', which also includes a T&S and K-B order.

- Prior to administration of RhIG, a T&S should be performed (within last 30 days) to determine RhD alloimmunization status. Patients who are proven to have already been alloimmunized to RhD are not candidates for RhIG prophylaxis.

- Each sensitizing event should be treated individually, regardless of when the prior RhIG dose was administered.[2]

[1] Patients with RhD variants weak D type 1, 2, 3, 4.0 and 4.1 are not considered to be at risk for RhD alloimmunization, therefore an inter-organizational Work Group on *RHD* Genotyping has recommended such patients be managed as RhD-positive. However, per ACOG 2017 Practice Bulletin, due to lack of comprehensive cost-benefit analysis, clinicians are advised to manage these patients as RhD-negative and administer RhIG when clinically indicated.

[2] Per ACOG 2017 Practice Bulletin, when a potentially sensitizing event (e.g. delivery) occurs within 3 weeks of the last RhIG administration, a K-B test may be performed and in the absence of any circulating fetal cells, RhIG may be withheld.

- Presence of residual passive anti-D from prior RhIG administration as evidenced by a positive T&S should NOT be used to determine whether RhIG is needed.[3]
- K-B test is not required in the 1st trimester, since the full dose of RhIG (300 µg) is more than adequate to prevent alloimmunization secondary to ANY volume of FMH.
- K-B test should be performed when a potentially sensitizing event occurs in the 2nd and 3rd trimester to estimate FMH volume and determine need for additional doses of RhIG.[4]

i) Complete therapeutic (medical or surgical) abortion

ii) Complete spontaneous abortion

iii) Threatened abortion: bleeding but continued pregnancy[5]

iv) Evacuation of molar pregnancy

v) Procedures with high risk of FMH

(1) Amniocentesis

(2) Chorionic villus sampling

(3) Cordocentesis or other percutaneous fetal procedures

(4) External Cephalic Version

(5) Intrauterine therapeutic interventions (transfusion, surgery, insertion of shunts, laser)

vi) Ectopic pregnancy

vii) Abdominal trauma

viii) Intrauterine fetal death and stillbirth - 2nd or 3rd trimester

ix) Antenatal hemorrhage (AH) - 2nd or 3rd trimester

(1) Similar to all other indications listed above, one full 300 µg dose of RhIG should be given, and K-B performed to determine if additional doses may be required.

[3] The half-life of RhIG is ~24 days. Anti-D can be detected in the maternal circulation for as long as 6 months after RhIG is given. A positive antibody screen due to passive anti-D does not indicate that enough anti-D remains in circulation to prevent sensitization.

[4] Per British guidelines, estimation of FMH volume is not required <20 weeks' gestation, since the routinely administered RhIG dose will always be adequate to prevent RhD alloimmunization regardless of the volume of the FMH.

[5] ACOG 2017 Practice Bulletin does not make any recommendations for RhIG prophylaxis for threatened pregnancy loss before 12 weeks due to insufficient evidence. Although FMH has been documented in 3-11% of women with a threatened pregnancy loss from 7-13 weeks gestation, RhD alloimmunization is very rare. Therefore, several national guidelines recommend against giving RhIG for threatened pregnancy loss, particularly if bleeding stops before 12 weeks of gestation. However, other guidelines recommend RhIG for all patients with threatened miscarriage, or when vaginal bleeding is heavy, repeated, or associated with abdominal pain, particularly if these events occur as gestational age approaches 12 weeks.

(2) For continuous AH, need for additional RhIG doses can be assessed by repeating K-B test every 2 weeks.[6]

(a) In such clinical scenarios, maternal cell-free DNA testing to ascertain fetal RhD status may be considered, in order to avoid unnecessary repeat testing and RhIG administration with an RhD-negative fetus.

c) Routine prenatal prophylaxis (28 weeks)

i) Outpatient clinic

(1) Order and draw T&S before administering RhIG

(2) There is no need to wait for the T&S results before dispensing RhIG

(i) RhIG should be given at that visit before the patient leaves

ii) Inpatient

(1) Order 1 dose RhIG (300 µg) using the appropriate APeX order set *'RhoGAM/WinRho only-Antepartum Rh-negative Mom'*, which also includes a T&S order.

(a) Blood Bank must have a T&S within the past 30 days before issuing RhIG in order to ensure patient has not already been alloimmunized to RhD.

(2) If RhIG is given at 28 weeks and patient has not given birth 12 weeks later (at 40 weeks gestation), another prenatal dose of RhIG may be considered.[7]

(3) Routine prophylactic 28-week dose should be administered regardless of prior RhIG administered for potential sensitizing events earlier in pregnancy.

(4) Antibody screen results showing residual anti-D from prior RhIG administration should NOT be used to decide if RhIG is needed.

(5) If patient declines RhIG because father of the baby (FOB) is RhD negative:

(a) Counsel patient about the risk of alloimmunization if father's RhD information is incorrect, or paternity questionable (mean non-paternity rate is approximately 3%)

(i) Can offer blood RhD typing to FOB, if paternity is certain

(ii) Encourage RhIG if any question of paternity

(iii) Consider non-invasive fetal RhD genotyping (maternal cell-free DNA testing)

[6] Per ACOG 2017 Practice Bulletin, this is a more conservative approach than the intuitive, but unproven strategy of using persistence or absence of passive anti-D in repeat antibody screens performed every 3 weeks, to determine when K-B testing and additional doses of RhIG may be indicated.

[7] RhIG appears to persist for approximately 12 weeks in most patients, so in the past some authorities advised giving a second dose of RhIG to women who had not given birth 12 weeks after their 28-week antenatal dose (at 40 weeks). However, Per ACOG 2017 Practice Bulletin, there is insufficient evidence at this time to make a recommendation for or against this practice.

C. POSTPARTUM

a) The following tests should be ordered for all RhD negative mothers, regardless of past RhIG doses administered:

i) *'Rhogam / WinRho + Fetal Bleed Screen - Postpartum Rh-negative Mom'*. This order set includes:

(1) Fetal bleed screen test (rosette test)

(a) Draw a large (6-7 mL) purple top (EDTA) from mother/OB patient

(b) Sample should be obtained as close to **1 hour** after delivery as possible (after at least 30-45 minutes has passed).

(i) Samples drawn *earlier* than 1 hour may potentially underestimate the FMH since fetal cells may not have adequately mixed with maternal blood, leading to possible under-dosing of RhIG

(2) 1 dose of RhIG (300 µg), issued from Blood Bank

b) Newborn Cord/Peripheral Blood Testing (Rh negative mother) or Newborn Cord/Peripheral Blood Testing (O positive mother) available within the *'Delivery Room Neonatal (Nsg / Allied Health)'* APeX order set

(1) For determination of newborn's RhD and direct antiglobulin test (DAT)

(2) Draw a small (5 mL) purple top (EDTA) from the cord blood

(3) If a cord blood sample is not available, a peripheral blood sample may be used for the 'Cord Blood Test' panel, although Blood Bank should be alerted of the specimen substitution.

c) If the neonatal cord (or peripheral blood) sample tests as RhD-positive, RhD-negative/serologic weak D-positive (or RhD-unknown), one 300 µg dose of RhIG will be issued by the Blood Bank.

i) If the fetal bleed screen is positive (or invalid), Blood Bank will initiate a reflex K-B test and send maternal sample to hematology for testing.

(1) Need for additional doses of RhIG (in addition to the one 300 µg already issued) will be calculated based on the K-B results and communicated to clinical team.

ii) If the fetal bleed screen is negative, no additional doses of RhIG are needed.

d) Post-partum RhIG should be administered regardless of whether the patient has recently received prenatal RhIG or not. Presence or absence of residual passive anti-D in the antibody screen should not be used to determine need for RhIG.[8]

[8] Per ACOG 2017 Practice Bulletin, if the patient has received RhIG in the 3 weeks prior to delivery, a K-B test may be performed and if positive, RhIG administered accordingly. If the K-B is negative, RhIG may be withheld.

D. CALCULATION OF RhIG DOSE

The following table provides the total number of 300 µg RhIG doses needed based on the result of the K-B test. NOTE: These numbers are based on a maternal blood volume of 5000 mL (~ 70 kg body weight).

% Fetal cells (per K-B result)	Number of 300 µg vials to inject
<0.3	1
0.3-0.8	2
0.9-1.4	3
1.5-2.0	4
2.1-2.6	5

For mothers who have a larger blood volume (>5300 mL), this table may underestimate the number of vials needed, especially with larger FMH volumes. For such patients, it is more appropriate to use the RhIG calculator provided by the College of American Pathologists, which calculates maternal blood volume (and RhIG dose) based on maternal height and weight: https://ucsf.box.com/s/evsy7qf5rvcyfkhy0rp5lo2c050mnqn2

V. RESPONSIBILITY

For questions regarding this procedure contact the Birth Center Clinical Nurse Specialist or Perinatal Educator.

VI. HISTORY OF THE PROCEDURE

Author: Mari-Paule Thiet MD, Morvarid Moayeri, MD, PhD
Issue Date: August 2014
Revised by: M. Killion RN CNS, July 2014
Last Revision/Review: M. Duck, RN CNS, M. Moayeri MD, E. Lomeli, J. Gonzalez, December 2020

VII. APPENDIX

None.