Best Practice Guide: Screening and Follow-up for Transfusion-related anti-D Alloimmunization

In the event that a female of childbearing potential (FCP) receives Rh(D)-positive blood products, consider these strategies to mitigate risk of morbidity and mortality in subsequent HDFN.

Updated September 2025

Key context:

- Rh(D)-positive LTOWB and RBCs are becoming more commonly used for Rh(D) unknown or negative status females with life-threatening bleeding. Standardization of screening for alloimmunization and counseling is needed for those who develop antibodies.
- Rh(D) negative products are always the first choice when available. However, when Rh(D) is not available or will unreasonably delay resuscitation, use of Rh(D)-positive products may occur.
- Modeling studies project a 0.3% risk of subsequent fetal death due to HDFN in Rh(D)-negative FCP after receipt of Rh(D)-positive blood products.[1] A diagnosis of anti-D alloimmunization can only lead to significant HDFN in a future pregnancy if the female develops critical antibody titers (16 in most centers) and becomes pregnant with an Rh(D)-positive child.
- HDFN requiring in-utero treatment with intrauterine transfusion occurs in approximately 13-23% of pregnancies where the fetus is antigen positive and titers are at or above critical values.[2,3] Fetal/neonatal mortality is susceptible to significant management variability (1%-20%, depending on center).[1,4,5]
- Severe morbidity and mortality to HDFN is almost entirely preventable with close monitoring and timely, skilled intervention, best planned in advance with a maternal/fetal expert with a high volume of HDFN cases (10 or more intrauterine transfusions per year).[6] At times, this requires out-of-state travel for the patient and collaboration across specialties, making early diagnosis and treatment planning critical.

[1] Yazer MH, Panko G, Holcomb JB, Kaplan A, Leeper C, Seheult JN, Triulzi DJ, Spinella PC. Not as "D" eadly as once thought–the risk of D-alloimmunization and hemolytic disease of the fetus and newborn following RhD-positive transfusion in trauma. Hematology. 2023 Dec 31;28(1):2161215.

[2] de Winter DP, Kaminski A, Tjoa ML, Oepkes D. Hemolytic disease of the fetus and newborn: systematic literature review of the antenatal landscape. BMC Pregnancy and Childbirth. 2023 Jan 7;23(1):12.

[3] Sánchez-Durán MÁ, Higueras MT, Halajdian-Madrid C, Avilés García M, Bernabeu-García A, Maiz N, Nogués N, Carreras E. Management and outcome of pregnancies in women with red cell isoimmunization: a 15-year observational study from a tertiary care university hospital. BMC pregnancy and childbirth. 2019 Oct 15;19(1):356.

[4] de Winter DP, Verweij EJ, Debeer A, Devlieger R, Lewi L, Verbeeck S, Maurice P, Jouannic JM, Guillemin MG, Mailloux A, Dos Santos MC. Variations and opportunities in postnatal management of hemolytic disease of the fetus and newborn. JAMA network open. 2025 Jan 2;8(1):e2454330-.

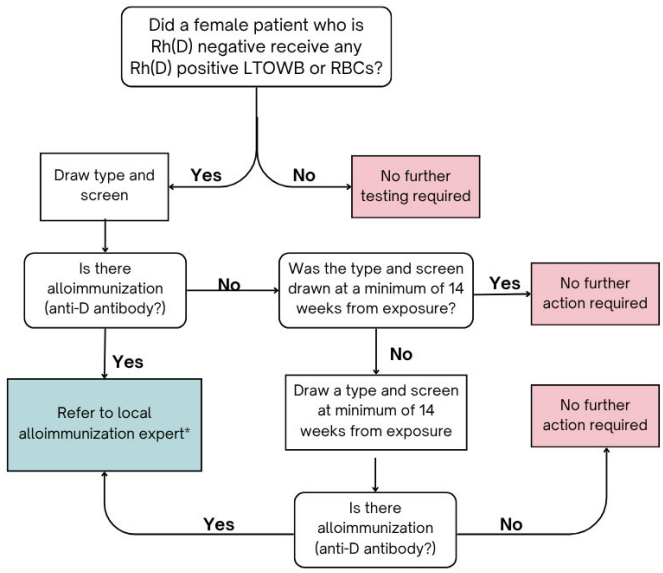
[5] de Winter DP, Lopriore E, Thorup E, Petersen OB, Dziegiel MH, Sundberg K, Devlieger R, de Catte L, Lewi L, Debeer A, Houfflin-Debarge V. Variations in antenatal management and outcomes in haemolytic disease of the fetus and newborn: an international, retrospective, observational cohort study. The Lancet Haematology. 2024 Dec 1;11(12):e927-37.

[6] Mustafa HJ, Sambatur EV, Shamshirsaz AA, Johnson S, Moise Jr KJ, Baschat AA, Verweij EJ, Javinani A, Kilby MD, Lopriore E, Rose R. Monitoring and management of hemolytic disease of the fetus and newborn based on an international expert Delphi consensus. American journal of obstetrics and gynecology. 2025 Mar 1;232(3):280-300.

Clinical considerations:

1. Rh Immunoglobulin (RhIg) in Rh(D)-negative FCP should not be used if the patient has received more than a small quantity of Rh(D)-positive RBC/LTOWB during their resuscitation (1-2 units).
2. RhIG should not be used in RhD-negative males or women who are no longer of childbearing potential regardless of the quantity of RhD-positive RBC/LTOWB transfused.
3. Antibody screening should be conducted at a minimum of 14 weeks to a maximum of 6 months after exposure to RhD-positive blood products for any FCP. If antibody screening is performed earlier than 14 weeks from exposure for any reason, repeat antibody screening should be performed at a minimum of 14 weeks from exposure since antibody testing could be falsely negative (see algorithm below).

RH(D) POSITIVE TRANSFUSION IN FEMALES CLINICAL DECISION TREE



*For females who are not considering pregnancy in near future, referral to pathology/hematology may be considered. For females who may become pregnant in the near future, consultation with a maternal fetal medicine (MFM) professional is suggested. Not all MFMs routinely treat HDFN. For specific referral recommendations, visit the Allo Hope Foundation website. All listed MFMs are available for virtual consultation.

Follow-up resources for patients:

Two templates are attached for patient follow-up after receipt of Rh(D)-positive blood products. **Template 1** is to be sent after receipt of Rh(D)-positive product when antibody screening has not yet been conducted. **Template 2** is to be sent if the antibody screen is subsequently positive for anti-D antibodies.