



## Special Considerations for Pregnancies at Risk of Early Onset Severe HDFN

*Early onset severe hemolytic disease of the fetus and newborn (HDFN) is generally described as an alloimmunized pregnancy where the fetus becomes anemic before 24 weeks gestation. These cases warrant extreme vigilance and highly specialized treatment by maternal fetal specialists with expertise managing severe HDFN and performing intrauterine transfusion before 24 weeks gestation. If you suspect your pregnancy may develop into early onset severe HDFN, refer to this resource as a special supplement to Allo Hope Foundation's (AHF's) existing resources.*

### Clinical Circumstances Associated with Increased Risk of Early Onset Severe HDFN:

- A history of previous fetal loss to HDFN
- A history of needing an intrauterine transfusion (IUT) before 24 weeks gestation in a previous pregnancy
- An antibody titer of 64 or higher for anti-Kell, or 512 or higher for D
- A middle cerebral artery (MCA) Doppler ultrasound MoM score of 1.5 or higher prior to 24 weeks gestation

If you have any of the above risk factors, it is important to **prepare before becoming pregnant or as soon as you find out you meet any of these circumstances during your pregnancy.** While not every baby will require early intervention, preparation is essential because treatment for fetal anemia is extremely time sensitive.

If you do not have any of the above risk factors, it is wise to have a plan in place with your provider for the possibility of IUTs should they become needed at any point in your pregnancy. This plan may include being referred from your local MFM to an MFM with specific expertise in IUT. Refer to our [excellent care checklist](#) to help you select a highly qualified provider for IUTs.

### Crucial Aspects that Directly Impact Your Baby's Outcome

Previous studies have shown a four times higher risk of death in babies needing IUT before 20 weeks gestation. Finding a specialist provider early who will provide timely, proactive care is extremely important (Lindenberg 2013).

For babies at risk of severe, early onset HDFN the two most important factors of your care that directly shape the outcome of your pregnancy are:

1. Timing of your care: fetal anemia does not wait for insurance approval, openings in the schedule, test result delays or for MCA scans to start. To protect your baby from early anemia, care planning and preparation, preventative treatments and fetal monitoring must start EARLIER than the anemia. Excellent, late care is inadequate care. Learn more about critical periods for time sensitive care in the table below.



2. Who provides your care: Your choice of medical provider greatly influences how HDFN affects your baby. Most MFMs have very little experience managing severe, early onset HDFN since it is so rare. The care necessary for a safe and healthy outcome is incredibly specialized, nuanced, and time sensitive.

How to prepare for a pregnancy at risk for early onset severe HDFN:

- Arrange a preconception visit with your maternal fetal specialist to discuss your treatment plan before becoming pregnant, if possible.
- Some obstetric clinics do not see pregnant patients until 8-12 weeks gestation. It is important to be seen by your provider immediately at confirmation of pregnancy to begin treatment planning.
- For pregnancies with history of previous loss, IUT before 24 weeks gestation in a previous pregnancy, and/or current Anti-D titers  $\geq 512$  or Anti-K titers  $\geq 64$ , discuss weekly intravenous immune globulin (IVIG) infusions and plasmapheresis with your provider. IVIG should ideally start before 13 weeks gestation and continue until an IUT is needed. This has been shown to delay fetal anemia.
- Find out baby's antigen status as early as possible so that the care team knows whether the baby is at risk for HDFN, *though this should not delay baby's monitoring or treatment while waiting for a result*. Knowing the baby's antigen status can help prevent unnecessary intervention. A baby who is negative for the antigen(s) in question is not at risk for HDFN (for example, if you have anti-D antibodies, you need to find out if the baby is positive or negative for the D antigen). You can do this by:
  - Having the baby's antigen status checked at or after 10 weeks gestation by a blood draw on mom, called cell free fetal DNA (cffDNA), or fetal antigen NIPT. In the U.S., this is offered by BillionToOne's Unity Screen for D, C, c, E, K, and Fya antigens, and by Natera for D. Other countries may also have country-specific availability to do fetal antigen NIPT.
  - Having the father tested for *antigen phenotyping (in the case of RHD, genotyping should be used instead)* for the *antigen* that corresponds to your *antibody* (\*not an antibody screen\*). For example, if you have Anti-E, the father needs antigen phenotyping for the E antigen.
    - If the father is negative for the E antigen, the baby does not have the antigen and is not at risk for HDFN.
    - If the father is antigen positive and homozygous, baby does have the antigen and will be at risk for HDFN.
    - If the father is heterozygous, baby has a 50% chance of having the antigen and being at risk for HDFN.
  - Having an amniocentesis to confirm the baby's antigen status, however, this is not typically preferred as it comes with a small risk of serious complications, can increase the maternal antibody titer, and generally cannot be done before 16 weeks gestation.
- Arrange for weekly MCA Doppler ultrasounds to monitor for fetal anemia beginning at 15-16 weeks gestation (ideally 15 in cases of possible severe disease). It is important that these are conducted every week.
- Find a maternal fetal specialist who has expertise managing severe, early HDFN, and exceeds the suggested standards for IUT competency (has performed at least 30-50 IUTs and continues to do about 10 or more annually) AND has special expertise performing early IUTs. This may be your



current provider, or it may be a maternal fetal specialist quite a distance away. If your current provider does not have this expertise, request a consultation with a specialist listed on AHF's recommended provider list or contact [info@allohopefoundation.org](mailto:info@allohopefoundation.org).

- Reach out to your support system and discuss your potential needs for your high-risk pregnancy, such as childcare, transportation, emotional support, etc. Discuss the possibility of frequent appointments, treatments, and necessary travel with your work

*It is time to take **immediate action without delay** when:*

- MCA Doppler ultrasound indicates an MoM value of 1.5 or higher
- Ultrasound shows any signs of cardiac dysfunction, fluid buildup in one or more organs (ascites or hydrops)

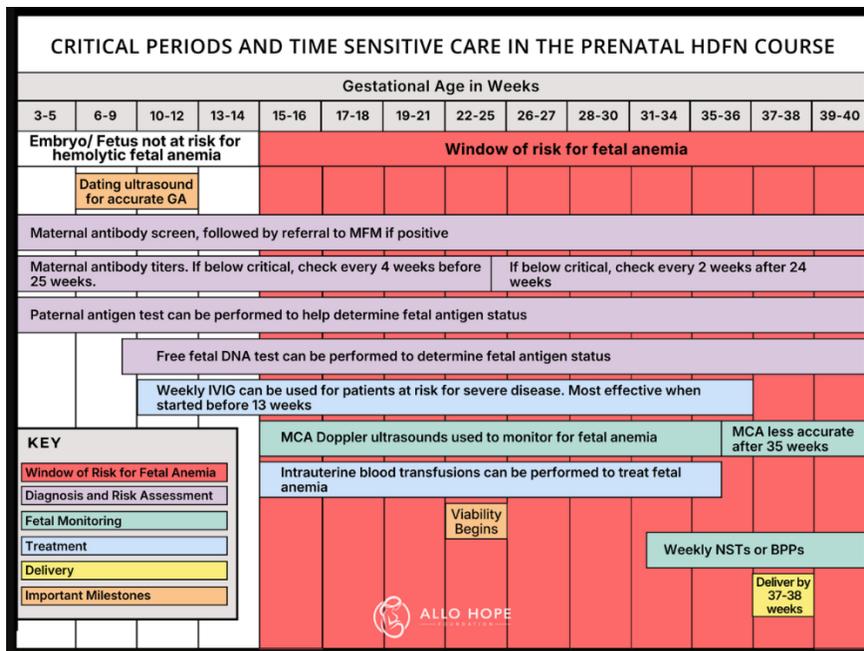
*Immediate action* means seeing a maternal fetal specialist recommended by AHF **within 24 hours**. If you need help and don't know what to do, no matter your circumstances, contact AHF immediately at [info@allohopefoundation.org](mailto:info@allohopefoundation.org) or message an admin in the "Antibodies in Pregnancy: An AHF Support Group" on Facebook.

This is a stressful but temporary challenge, and we are here to support you.



You may wish to show these considerations to your provider:

- Patients with history of hemolytic fetal anemia before 24 weeks gestation, fetal or neonatal loss from HDFN, or with titers 64 or above for most clinically significant red cell antibodies (4 or above for Kell) *may* develop fetal anemia prior to 24 weeks gestation and should be closely monitored by initiating weekly MCA Doppler ultrasounds at 15 weeks gestation at an experienced fetal center. Although rare, patients can have severe early onset HDFN even in their first sensitized pregnancy.
- Prepare a rapid referral plan at confirmation of pregnancy and refer if Dopplers become elevated before 24 weeks gestation (at or approaching 1.5 MoM regardless of visible ascites or hydrops). Ensure the referring specialist is aware of this plan.
- Do not administer steroids after an elevated 1.5 MoM as this can falsely lower MCA Doppler results; allow this to be administered only after intake at the IUT site and plans for IUT have been made.
- Please refer to recently published clinical practice guidelines for alloimmunized pregnancy management (Moise 2025) and the available resources below regarding best practices for early onset severe HDFN
- Early onset HDFN is extremely rare, and many providers do not have enough case volume in this condition to develop expertise in these cases. Please refer to a provider recommended on the Allo Hope Foundation website (see “Find a Doctor” page)
- Direct any inquiries to [info@allohopefoundation.org](mailto:info@allohopefoundation.org) and/or to a maternal fetal specialist on our medical advisory board (if practicing outside of the U.S., we will do our best to suggest a referral option):
  - Dr. Juan Gonzalez-Velez, UCSF
  - Dr. Kara Markham, University of Cincinnati
  - Dr. Ken Moise, University of Texas Austin
  - Dr. Saul Snowise, Midwest Fetal Care Center
  - Dr. Thomas Trevett, Georgia Perinatal Consultants
  - Dr. Leonardo Pereira, Oregon Health and Science University



## Resources

Lindenburg IT, Van Kamp IL, Van Zwet EW, Middeldorp JM, Klumper FJ, Oepkes D. Increased perinatal loss after intrauterine transfusion for alloimmune anaemia before 20 weeks of gestation. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2013 Jun;120(7):847-52. [Read here.](#)

Lindenburg IT, Wolterbeek R, Oepkes D, Klumper FJ, Vandenbussche FP, Van Kamp IL. Quality control for intravascular intrauterine transfusion using cumulative sum (CUSUM) analysis for the monitoring of individual performance. *Fetal diagnosis and therapy*. 2011 Feb 8;29(4):307-14. [Read here.](#)

**Moise Jr KJ, Markham KB, Spinella PC, Sherwood MR, Robinson KA, Wilson LM, Malone J, Espinoza J, Dizon-Townson D, Mercer L, Miller R. A Clinical Practice Guideline for the Management of Pregnancy Alloimmunized to Red Blood Cell Antigens. *JAMA Network Open*. 2025 Nov 24;8(11):e2544649.**

Moise E, Moise KJ, Nwokocha M, Lowry K, Hutson E, de Winter DP, Delphi IUT Study Group, Antolin E, Audibert F, Baschat AA, Bebbington M. Critical procedural steps in intrauterine transfusion: Delphi survey of international experts. *Ultrasound in Obstetrics & Gynecology*. 2025 Jan;65(1):78-84. [Read here.](#)

Zwiers C, Lindenburg IT, Klumper FJ, De Haas M, Oepkes D, Van Kamp IL. Complications of intrauterine intravascular blood transfusion: lessons learned after 1678 procedures. *Ultrasound in Obstetrics & Gynecology*. 2017 Aug;50(2):180-6. [Read here.](#)

*Updated 2026. The Allo Hope Foundation and its staff, board members and volunteers are never incentivized financially or by any other means to recommend a doctor. AHF is not liable for any outcomes that result from the recommendation of a specific doctor. This document should not be considered medical advice and should be discussed in consultation with the patient's care team.*

