

Prenatal

Diagnosis and Risk Assessment

If patient has positive RBC antibody screen

- Follow with antibody ID and titer

If antibody is known to cause HDFN (D, K, c, E, others)

- Refer to MFM with specific skill in conducting intrauterine transfusions (suggested 30-50 lifetime IUT procedures and 10+ procedures annually; may be out of state; contact Allo Hope Foundation for a recommended provider)
- Order UNITY Fetal Antigen test as early as 10 weeks gestation for patients with D, K, C, c, E or Fya antibodies
- Order paternal antigen phenotyping, especially if fetal antigen testing is not available (important to determine zygosity, may require reference laboratory)
- Consider amniocentesis for patients with other antibodies not included in UNITY test, though this could increase antibody titer. Otherwise monitor as if fetus is antigen positive

If fetus is negative for the antigen(s) in question

- Fetus is not at risk for HDFN, regardless of maternal antibody titer; manage pregnancy normally. No further titer assessments needed

If titers are critical (≥ 4 for Kell, ≥ 16 for other antibodies)

- Do not allow fetal antigen status determination to delay referral to MFM

If titers are below critical

- Monitor titers every month until 24 weeks, then every two weeks thereafter, even if initial titer is too low to titer. Prompt referral to MFM still necessary

Fetal Monitoring

Prompt, early referral or pre-pregnancy consultation with MFM is critical for timely monitoring and intervention. Some patients may require treatments which must be initiated before 13 weeks gestation.

If patient has critical titers

- Middle cerebral artery (MCA) Doppler ultrasounds can begin as early as 15 weeks gestational age (wGA) and should be initiated no later than 16 wGA

Once MCA Doppler scans have been initiated

- Continue to scan weekly as hemolytic fetal anemia can develop in less than one week

When the patient reaches 32 wGA

- Begin weekly BPP or NSTs until delivery regardless of titer

Treatment

If patient is at risk for Early-Onset Severe HDFN (titers of ≥ 64 for Kell, ≥ 512 for D, or history of severe HDFN)

- Patient may benefit from IVIG with or without therapeutic plasma exchange. IVIG has been shown to delay time to first IUT by three weeks or more. Most effective when initiated before 13 wGA.

An MCA-PSV at or above 1.5 MoM for gestational age

- Indicates possible severe anemia requiring intrauterine blood transfusion (IUT)
- A severely anemic fetus may not show visible signs of anemia (hydrops) other than an elevated MCA Doppler value
- IUT outcomes decline significantly if fetus is hydropic. Do not wait for ascites or hydrops to develop
- Antenatal corticosteroids can falsely lower MoM values for up to 48 hours. Treatment decisions should not be based on MoMs during this time period. Only administer corticosteroids after decision to transfuse/deliver

Delivery

In advance of delivery

- Offer to facilitate NICU tour and pediatric hematology consult for family
- Prepare cross-matched blood for alloimmunized mother and infant at time of delivery

If fetus is known to be or may be antigen positive

- Deliver by 37-38 wGA regardless of antibody titer

Neonatal

After delivery families can expect:

Cord blood drawn and tested at birth

- For Direct Antiglobulin Test (DCT/DAT)
- For bilirubin, hematocrit/hemoglobin, reticulocytes

Frequent bilirubin assessment

- Consistent with AAP hyperbilirubinemia guidelines for infants with neurotoxicity risk factors

Potential NICU admission

- For prematurity, phototherapy, exchange or top-up transfusion, neonatal IVIG

After discharge families can expect:

Outpatient monitoring

- Daily outpatient bilirubin assessments until consistent downward trend without phototherapy
- Weekly Hgb/Hct and retic at least 6 weeks and up to three months after birth
- Anemia often doesn't require transfusion until 2 weeks or more after delivery