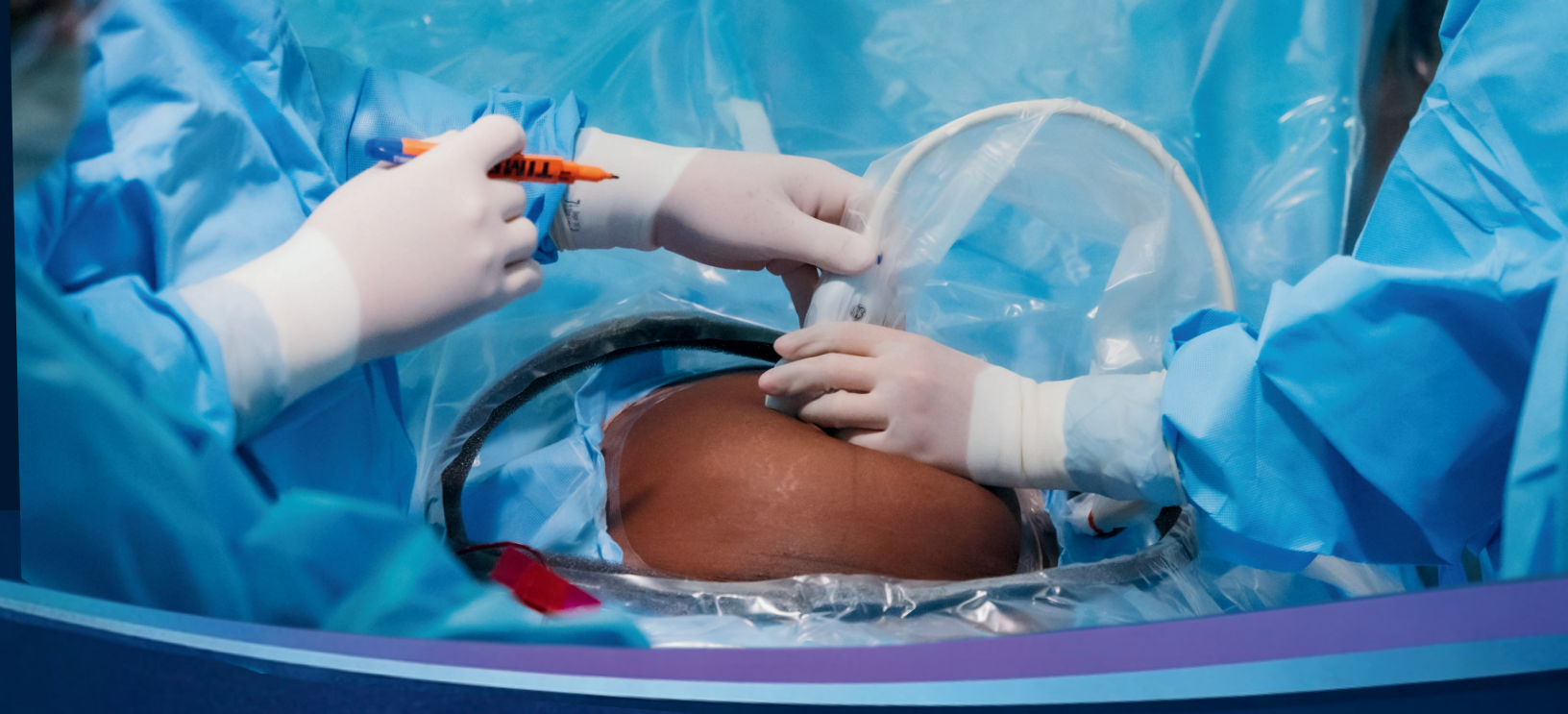

HDFN CARE IS EVOLVING

POINT-OF-CARE IMPLEMENTATION CHECKLIST

Clinical Practice Guidelines

for Red Cell Alloimmunized Pregnancies

ALLO HOPE FOUNDATION

Management of Pregnancy Alloimmunized to Red Blood Cell Antigens: Point of Care Implementation Checklist

This checklist translates evidence-based clinical practice guidelines into actionable steps for clinicians managing pregnancies complicated by red cell alloimmunization. It is intended to support timely referral, appropriate surveillance, and prevention of severe hemolytic disease of the fetus and newborn (HDFN). This tool does not replace clinical judgment or the full guideline.

Reference:
Moise KJ, Markham KB, Spinella PC, Sherwood MR, Robinson KA, et al. A Clinical Practice Guideline for the Management of Pregnancy Alloimmunized to Red Blood Cell Antigens. JAMA Network Open. 2025;8(11):e2544649.

ABBREVIATIONS:

IUT = intrauterine transfusion
IVIG = intravenous immune globulin
LTOWB = low titer group O whole blood
MCA = middle cerebral artery
MFM = maternal fetal medicine
NIPT = noninvasive prenatal testing
PSV = peak systolic velocity
RBC = red blood cell
wGA = weeks gestational age

> Parenthetical references following each checklist item identify the supporting guideline recommendation and practice point, allowing direct cross-referencing with the 2025 Evidence-Based Clinical Practice Guidelines.

1. IMMEDIATE ACTIONS AT DIAGNOSIS

Applies to Pregnant Patients

□ Refer to Maternal–Fetal Medicine promptly after diagnosis of red cell alloimmunization, regardless of antibody type or titer (1.1)
□ Document key risk history (antibody ID, date identified, titer, prior affected fetus or neonate?)

Applies to Non-Pregnant Patients

□ Refer to Maternal–Fetal Medicine specialist for preconception counseling (1.1)
- Applies to patients considering another pregnancy
- Applies to Rh(D)-negative patients who have previously received Rh(D)-positive RBCs or LTOWB

2. INITIAL FETAL RISK ASSESSMENT

Maternal Antibody Titers

□ Perform antibody titers, preferably at the same laboratory, run in tandem with prior samples (3.2)

Fetal Antigen Status

If alloimmunization involves D, C, c, E, K, or Fya:
□ Order cell-free fetal DNA (cffDNA/NIPT) after 10 wGA to determine fetal red cell antigen status (refer to country-specific capabilities if outside of United States) (1.2)

If alloimmunization involves other clinically significant antigens:
□ Order cell-free fetal DNA (cffDNA/NIPT) after 10 wGA to determine fetal red cell antigen status (refer to country-specific capabilities if outside of United States) (1.2)
□ Manage fetus as antigen-positive unless proven otherwise (1.4)
- Consider amniocentesis ≥15 weeks only if clinically necessary
- Do not allow amniocentesis to delay IUT

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Early Onset Severe Disease

□ Assess for early-onset severe HDFN risk (2a, 2b)
- Anti-D titer ≥512? □ Yes □ No
- Anti-K titer ≥64? □ Yes □ No
- Prior pregnancy with fetal loss? □ Yes □ No
- Prior pregnancy with fetal anemia <24 wGA ? □ Yes □ No

□ If you answered yes to any of the questions above, consider IVIG (2a, 2b)
□ If you answered no to all of the questions above, skip to step 3
□ Consider using plasmapheresis prior to IVIG in select severe cases (generally three double-volume exchanges in a week followed by the first IVIG infusion) (2.8)
□ Initiate IVIG before 13 wGA when possible. If fetal antigen status pending → continue IVIG until antigen-negative confirmed (2.1, 2.5)

IVIG Specifications

- Dose: 1 g/kg weekly (based on baseline weight; no escalation) (2.4)
- Inform patient of potential IVIG side effects and risks: (2.2)
- Administer first dose in monitored setting (2.3)
- Monitor maternal hemoglobin in type A, B, or AB patients (2.6)

4. MONITORING FOR FETAL ANEMIA

□ Initiate weekly MCA-PSV Doppler surveillance by 16 wGA if:
- Cricital titer reached OR
- History of previously affected fetus/neonate (2.4)

□ Consider initiating weekly MCA-PSV Doppler surveillance at 15 wGA if:
- Prior severely affected pregnancy
- Highly immunogenic antibodies: anti-D, C, c, E, K, Jka (4.3, 4.6)

MCA-PSV Doppler Technique (4.4)

- Should be performed with proper technique by an experienced sonographer+MFM (4.4)
- Fetus quiescent
- Angle of insonation as close to 0° as possible
- Obtain ≥3 measurements
- Use manual calipers
- Record highest acceptable value

5. ESCALATE WHEN MCA-PSV ≥1.5 MOM

□ MCA-PSV ≥1.5 MoM → Prepare for cordocentesis and IUT within 24–48 hours (4.5)
□ In some cases with borderline elevation → consider repeating MCA-PSV within 24 hours before intervention (4.5)
□ Withhold antenatal corticosteroids until final IUT decision has been made, as steroids can falsely lower MCA-PSV for up to 48 hours (4.7)

Timing is Critical (4.5)

- Do not wait for signs of fetal hydrops to intervene
- Survival following IUT is significantly lower in a hydropic fetus
- Once a ≥ 1.5 MoM has been reached, delaying definitive diagnosis and treatment may lead to worsening anemia, development of fetal hydrops, adverse neurologic sequelae, and fetal death

6. INTRAUTERINE TRANSFUSION (IUT)

□ Ensure cordocentesis and IUT are performed by experienced operator. (3.1)
□ Perform IUTs through 35 wGA unless technically limited (5.0)

Criteria for Experienced IUT Operator (5.3)

- Has performed ~30–50 total IUTs and
- Performs ≥10 IUTs annually to maintain proficiency
- Has proper access to blood banking and neonatal services
- Has capability for urgent delivery if indicated

7. DELIVERY PLANNING

□ Begin weekly antenatal testing by 32 wGA (6.1)
□ Before delivery, arrange neonatal consultation (6.6)
□ Prior to delivery perform maternal crossmatch for red cell units (6.4)
□ If IUT performed → plan delivery 2–3 weeks after final IUT (5.2)
□ If no IUT but antigen-positive or unknown antigen fetus → deliver 37 0/7–38 6/7 wGA regardless of titer (6.3)
□ Upon delivery, evaluate cord blood for: (6.7)
- blood type
- direct antiglobulin test (DAT)
- hemoglobin/hematocrit
- reticulocyte count
- total bilirubin

Delivery Considerations

- Red cell alloimmunization is not an indication for cesarean delivery (6.5)
- Delayed umbilical cord clamping at delivery can still be practiced in pregnancies affected by HDFN (5.4)

NEW

CLINICAL PRACTICE GUIDELINES

for red cell alloimmunized pregnancies

Access Full Publication in JAMA Network Open

Access additional guideline tools, updates, and resources as they become available.

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