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WITH HER: HEAL, EMPOWER, RESPECT- EVERY STEP OF THE WAY

Theme:

The New Era of Red Cell Alloimmunization
Precision Diagnosis. Fetal Surveillance. Novel Therapies



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From the President's Desk



Dear Members,

It gives me immense pleasure to connect with you through this edition of the AOGD Bulletin. The recent AOGD Conference held last month was a great success and a wonderful reflection of the enthusiasm, academic excellence, and professional camaraderie of our members. I extend my sincere appreciation to everyone who contributed to its success.

The theme of this edition focuses on an important and enduring challenge in obstetric practice—**Rh alloimmunization in pregnancy**. Over the years, my own experience in obstetric practice has reminded me that Rh alloimmunization is not simply a laboratory finding; behind every positive antibody screen is a pregnancy that may require careful surveillance, counselling, and coordinated decision-making. I have seen how a sensitized pregnancy can create considerable anxiety for the expectant mother and her family. At the same time, I have also witnessed how early recognition, appropriate monitoring, timely referral, and advances in fetal medicine can transform the outcome of pregnancies that were once associated with considerable fetal and neonatal morbidity.

These experiences have reinforced for me one important principle: **Prevention is always better than intervention**. A simple blood-group assessment and appropriate antibody screening can identify women at risk, while timely administration of anti-D immunoglobulin can prevent sensitization in eligible RhD-negative women. Missed opportunities for prophylaxis still occur, and continued awareness among healthcare professionals remains essential. Every opportunity to prevent Rh alloimmunization therefore deserves our attention.

From my experience, one of the most important lessons is the value of **teamwork and continuity of care.** The successful management of an alloimmunized pregnancy often requires close collaboration between the fetal medicine specialist, transfusion medicine team, and neonatologist. Equally important is clear communication with the mother and her family, so that they understand the condition, the purpose of surveillance, and the possible interventions.

Rh alloimmunization also reminds us that obstetrics is a specialty where prevention, vigilance, and timely intervention can profoundly influence outcomes. Our responsibility is not only to manage sensitized pregnancies with expertise but also to ensure that every eligible woman receives appropriate preventive care.

I hope this edition of the AOGD Bulletin will encourage greater awareness and discussion about the prevention, diagnosis, surveillance, and management of Rh alloimmunization and other red-cell antibodies in pregnancy. Let us continue to translate advances in science into safer pregnancies and healthier mothers and babies.

With warm regards,

Dr Neena Malhotra

Head of Department, Obstetrics and Gynaecology, AIIMS, New Delhi

President, AOGD

From the Secretarial Desk



Dr K Aparna Sharma
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Dear AOGD Members,

The continued enthusiasm, valuable feedback, and active engagement of our members with the AOGD Bulletin have been truly encouraging and reinforce our commitment to fostering evidence-based practice, academic excellence, and continuous learning in women's healthcare.

We are pleased to present this issue of the AOGD Bulletin, dedicated to the theme "The New Era of Red Cell Alloimmunization: Precision Diagnosis, Fetal Surveillance & Novel Therapies."

Red cell alloimmunization remains an important and complex challenge in obstetric and fetal medicine, with significant implications for fetal and neonatal outcomes. Over the years, however, remarkable advances in immunohematology, antibody characterization, non-invasive fetal antigen genotyping, and fetal surveillance have transformed our approach to these pregnancies. The integration of MCA-PSV Doppler, individualized risk assessment, and advances in intrauterine transfusion has enabled earlier recognition and more precise management of fetal anemia.

This issue brings together contemporary evidence and expert perspectives covering the spectrum of red cell alloimmunization—from screening and antibody identification to fetal antigen determination, prediction and surveillance of fetal anemia, intrauterine transfusion, neonatal considerations, and emerging therapeutic strategies. Particular emphasis has been placed on translating these advances into practical, evidence-based clinical care.

The evolving landscape is taking us beyond conventional protocols towards precision diagnosis, personalized surveillance, and timely intervention. By bringing together established practices and emerging innovations, this issue aims to enhance clinical decision-making and encourage further research and collaboration in this rapidly advancing field. This episode of the AOGD bulletin hopes to be a practical guidebook for daily management of Rh Negative Pregnancy for students and practitioners alike.

We extend our sincere appreciation to our editorial team, esteemed contributors, reviewers, and the entire AOGD community for their dedication and academic contributions. Their collective efforts continue to enrich our educational initiatives and strengthen our commitment to improving maternal and fetal healthcare.

We look forward to your continued support, valuable feedback, and active participation in our future academic endeavours as we continue to advance knowledge, innovation, and excellence in women's and fetal healthcare.

AOGD Secretariat
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From the Editor's Desk



Dr Reeta Mahey



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Dr Swati Tomar

Dear Colleagues

It is with great pleasure that we present this issue of the AOGD Bulletin, dedicated to the theme **"The New Era of Red Cell Alloimmunization: Precision Diagnosis, Fetal Surveillance & Novel Therapies".** This issue is focusing on a subject that beautifully reflects how rapidly fetal medicine is evolving.

Red cell alloimmunization in pregnancy is entering a new era—one where precision diagnosis, individualized fetal surveillance, and timely intervention are transforming outcomes.

Advances in antibody identification and quantification, non-invasive fetal genotyping, and MCA-PSV Doppler surveillance have enabled earlier and more accurate detection of fetal anemia. At the same time, innovations in intrauterine transfusion and emerging fetal therapies are expanding the possibilities for managing even complex cases.

This issue of the AOGD Bulletin brings together contemporary evidence and practical insights to help clinicians navigate this evolving landscape. Our aim is to move beyond traditional protocols towards precision, prediction, and personalized care—ultimately improving outcomes for mothers and their babies.

On behalf of the Editorial Team, we sincerely thank all the contributors, and members of the AOGD family whose dedication has made this issue possible. We hope this edition serves as a valuable resource for clinicians, academicians, and trainees.

We would like to express our special appreciation and gratitude to Prof. K. Aparna Sharma, who graciously accepted our invitation to serve as the Guest Editor for this special issue. Her expertise, academic leadership, and valuable guidance have been instrumental in shaping and enriching this edition.

Happy reading!

The Editorial Team

Red Cell Alloimmunisation: The Opening Perspective

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EPIDEMIOLOGY AND EVOLVING BURDEN OF ALLOIMMUNISATION

During pregnancy, the process of formation of maternal antibodies against foreign antigens present on the fetal red blood cells (RBCs), triggered by Rh alloimmunised pregnancy is called red cell alloimmunisation. This could happen in non-pregnant state following blood transfusion or tissue transplantation.

Before the introduction of anti-D immune globulin, the prevalence of RhD sensitisation was around 10-15%, and contributed significantly to haemolytic disease of the fetus and newborn (HDFN) worldwide. In the latter half of 20th century, after discovery of anti-D Ig and its approval for clinical use led to a sharp decline in RhD alloimmunisation to 0.2%.

In India due to limited healthcare access there is a wide gap between the desired and routine antenatal anti-D prophylaxis (RAADP) and it remains around 13-38% despite a low prevalence of Rh alloantibody of 1-2%. *ACOG recommends routine antenatal screening for ABO, RhD, and ICT at the time of booking for all the mothers, and an additional testing for antibodies at 28 weeks in RhD negative mothers.* The dose of Rh immune globulin (RhIg) was calculated via quantitative tests and a standard dose of 1500 IU/ 300 ug was decided that neutralises 15 mL of RhD-positive red blood cells or 30 mL of whole blood.

Although there is a higher genetic predisposition of Rh isoimmunization in the caucasians (10-15%), compared to the Southeast Asian countries (5%) but its clinical prevalence is low, reflecting a robust healthcare in place.

Apart from ABO and Rhesus systems, several other RBC antigen systems such as Kell, Duffy, Kidd, and MNS systems are clinically important. The International Society of Blood Transfusion (ISBT) currently recognises 48 blood group systems comprising 400 distinct antigenic molecules.

RHD genotyping is preferred over serology as it is more precise and helps to stratify alloimmunisation. Alloimmunization is a complex interplay of multiple clinical and obstetric factors including number of blood transfusions, age at first transfusion, previous major surgery, multiparity, birth of a male child.

During pregnancy, potentially sensitising events can be abortion or threatened abortion, amniocentesis, chorionic villus sampling (CVS), version procedures, abdominal trauma, ectopic pregnancy or molar pregnancy, fetal death, caesarean section, intraoperative cell salvage, assisted vaginal delivery, and post-maturity. Anti-D is given to prevent alloimmunisation from such events.Probability of sensitisation is more likely when RhIg prophylaxis is inadequate in events like caesarean, manual removal of placenta, stillbirth, abruptio placenta, abdominal trauma etc. Intrauterine transfusion (IUT), in addition to FMH itself, can serve as a trigger for RBC alloimmunization.

Antigen immunogenicity is determined by characteristics of both donor antigen and recipient immune response. Factors such as chemical composition, molecular structure, accessibility of antigen epitopes, immune status all contribute. Protein antigen RhD and kell provoke stronger T-cell-dependent responses and memory B-cell formation than carbohydrate antigens such as ABO and Lewis.

The immunogenic potential of a particular RBC unit may be altered by how the blood is collected, processed, modified and stored. This is particularly relevant in patients who are chronically transfused blood such as patients with sickle cell disease (SCD) and thalassemia and thus they require more extensive antigen matching.

PATHOPHYSIOLOGY OF MATERNAL SENSITIZATION AND FETAL DISEASE

The fetal-maternal interface is not an absolute barrier, and there is considerable trafficking of fetal RBCs into maternal circulation in the pregnancy. Around the time of delivery both the frequency and volume of feto-maternal haemorrhage tend to rise. First exposure leads to activation of maternal B lymphocytes and production of IgM antibodies, which are large in size(~900kDa) and hence cannot cross the placenta. Therefore, in the first pregnancy with Rh positive fetus, the fetus does not have hemolysis. In a subsequent pregnancy with Rh-D-positive fetus, re-exposure rapidly stimulates maternal memory B cells to produce IgG antibodies. These IgG antibodies (~150kDa) cross the placenta and bind to Rh-D antigens on fetal red blood cells. The antibody-coated cells are removed by macrophages, primarily in the fetal spleen, causing extravascular hemolysis and progressive fetal anemia.

Physiological responses in foetuses are reticulocytosis, increase in cardiac output and 2,3-diphosphoglycerate levels, appearance of erythroblasts in the fetal liver at a haemoglobin deficit of 7g/dl or greater. Reduced serum albumin levels presumably resulting from depressed synthesis by the fetal liver, which shifts to an erythropoietic function.

Screening for maternal alloimmunisation is based on Indirect Coombs Test (ICT). ICT is used because it measures the maternal IgG response. If antibody is detected, its titre is followed until it reaches critical value, thereafter fetal surveillance is done with MCA-PSV (Figure 1).

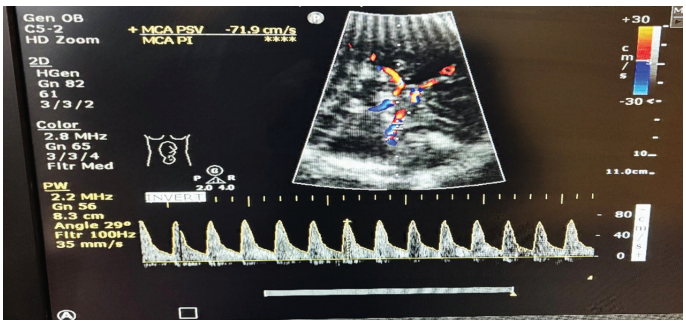


Figure 1: MCA-PSV monitoring

If initial titre levels are below critical titres (1:16), they should be checked every 4 weeks until 28 weeks, then every 2 weeks thereafter until delivery.However, if the titres are 1:16 or more, it should directly be followed up by MCA-PSV weekly and USG to look for features of hydrops. MCA-PSV of more than 1.5MoM is an indication for cordocentesis and IUT. Antenatal testing should be started at 32 weeks and induction should be considered by 38 weeks. Following birth, a Direct Coombs Test (DCT) is used to ascertain if maternal alloantibodies are bound to the newborn's RBCs.

Maternal IgG alloantibodies cross the placenta especially in the second and third trimester and may destroy fetal RBCs, causing Hemolytic Disease of the Fetus and Newborn (HDFN). At the severe end of the spectrum, miscarriage, hydrops fetalis, or intra-uterine fetal demise (IUFD) may occur. Maternal antibodies can remain in the neonatal circulation for several weeks, affected newborns may subsequently develop hyperbilirubinemia, delayed anaemia, neutropenia, or thrombocytopenia.

CLINICALLY SIGNIFICANT ANTIBODIES BEYOND ANTI D:

Immediately after the discovery of ICT, anti-kell antibody was isolated and named after Mrs Kelleher, whose newborn died of HDFN, making it the third most immunogenic antigen after ABO and Rh.

ANTI-KELL ALLOIMMUNISATION: PATHOPHYSIOLOGY, GENOTYPING, SURVEILLANCE AND MANAGEMENT

The Kell blood group system (KEL; ISBT 006) is highly polymorphic, comprising 38 antigens, and is clinically important because of its high immunogenicity and association with severe hemolytic disease of the fetus and newborn (HDFN). The K antigen (KEL1) is expressed early in fetal erythropoiesis and can be detected on fetal erythrocytes from approximately 10 weeks of gestation. Anti-K antibodies are predominantly IgG alloantibodies that cross the placenta and can cause severe fetal anemia. *Anti-K alloantibodies are present in 0.5-1 in 1000 pregnancies, and 13-19% of severe HDFN is attributed to it.*

The pathophysiology of anti-K-mediated fetal anemia is distinctive. In addition to immune-mediated destruction of circulating Kell-positive erythrocytes, anti-K antibodies exert a **direct suppressive effect on fetal erythropoiesis**. Kell antigens are expressed on erythroid progenitor cells, and experimental studies have demonstrated inhibition of Kell-positive erythroid burst-forming units and colony-forming units following exposure to anti-K antibodies. Consequently, fetal anemia results from both impaired erythroid production and peripheral hemolysis. This mechanism may result in profound anemia with an inappropriately low reticulocyte and erythroblast response compared with the degree of anaemia.

The same mechanism explains the **poor correlation between maternal anti-K antibody titre and severity of fetal anemia**. Antibody titre represents the concentration of circulating maternal antibody but does not adequately reflect its biological effect on fetal erythroid progenitors. Severe fetal anemia may therefore develop despite a low or apparently stable titre. The critical titres of kell antibody on ICT testing in maternal blood is 1:4 (in contrast to RhD antibodies which is 1:16). Although serial titres may be performed as part of laboratory assessment, they should not be used in isolation to assess disease severity or determine the timing of intervention.

Following identification of clinically significant anti-K, **early referral to a fetal medicine unit is recommended**. Fetal Kell antigen status should be established where possible. Traditionally, this has involved paternal Kell phenotyping and molecular genotyping. Increasingly, **non-invasive fetal genotyping using cell-free fetal DNA (cffDNA) from maternal plasma** permits direct assessment of fetal KEL status without an invasive procedure. Targeted allele-specific PCR can identify KEL*01 (K1), while newer approaches include **digital PCR and droplet digital PCR (ddPCR)**, which offer highly sensitive detection of low-abundance fetal alleles. **Next-generation sequencing (NGS)** can further permit targeted sequencing of KEL polymorphisms and simultaneous analysis of multiple clinically relevant red-cell antigens. These approaches facilitate antenatal risk stratification by identifying fetuses that are antigen-negative and therefore not at risk of anti-K-mediated HDFN.

For a Kell-positive fetus, or when fetal antigen status cannot be reliably established, surveillance should primarily rely on **serial middle cerebral artery peak systolic velocity (MCA-PSV) Doppler**, rather than antibody titre. An MCA-PSV ≥1.5 multiples of the median (MoM) is suggestive of moderate-to-severe fetal anemia and warrants specialist

assessment, with fetal blood sampling indicated. **Intrauterine transfusion (IUT)** remains the principal antenatal treatment for significant fetal anemia. Following IUT, serial MCA-PSV surveillance is required to identify recurrent anemia, while timing of subsequent transfusion and delivery should be individualized according to gestational age, fetal condition and neonatal facilities.

For patients who have had previous pregnancies severely affected by HDFN, weekly administration of intravenous immunoglobulin and plasmapheresis might be considered. FcRn-blocking agents such as the monoclonal antibody Nipocalimab are currently under trials. Limiting unnecessary blood transfusions in reproductive-age-group women is therefore an important preventive measure; some international guidelines also prefer Kell-negative RBC units for them.

IMPACT ON THE FETUS AND NEWBORN: SPECTRUM OF HEMOLYTIC DISEASE

The fetal manifestations of HDFN may include decreased movements, elevated middle cerebral artery peak systolic velocity (MCA-PSV), hydrops and echogenic bowel. This may result in anemia, jaundice, and hepatosplenomegaly in the newborn. Severe cases can lead to hydrops fetalis, kernicterus, and heart failure. Early recognition and treatment with phototherapy or exchange transfusion can prevent complications.

In pregnancies complicated by highly aggressive antibodies, IVIG and plasmapheresis may be used in an attempt to delay the onset of fetal anemia. Once significant anemia develops, management may require intrauterine transfusion (IUT) or delivery, followed as needed by an exchange transfusion, phototherapy, and IVIG. Delayed neonatal anemia can be treated with folic acid and weekly erythropoietin with serial hemoglobin and bilirubin measurements for follow-up. In the largest cohort of fetuses treated with IUT, the neurodevelopmental impairment was reported in 4.8%, while the overall long-term outcomes were favourable.

For a woman planning a subsequent pregnancy, early referral to a high risk maternal-fetal medicine team is recommended for close prenatal surveillance.

KEY POINTS

- In India due to limited healthcare access there is a wide gap between the desired and routine antenatal anti-D prophylaxis (RAADP) and it remains around 13-38% despite a low prevalence of Rh alloantibody of 1-2%.
- ACOG recommends routine antenatal screening for ABO, RhD, and ICT at the time of booking for all the mothers, and an additional testing for antibodies at 28 weeks in RhD negative mothers.
- Maternal IgG alloantibodies cross the placenta especially in the second and third trimester and may destroy fetal RBCs, causing Hemolytic Disease of the Fetus and Newborn (HDFN).
- • The Kell blood group system is high immunogenicity and association with severe hemolytic disease of the fetus and newborn (HDFN). Besides immune-mediated destruction of circulating Kell-positive fetal erythrocytes, anti-K antibodies have a direct suppressive effect on fetal erythropoiesis. Maternal anti-K antibody titres correlate poorly with the severity of fetal anemia; therefore, mere positivity warrants monitoring with middle cerebral artery peak systolic velocity (MCA-PSV) and referral to a fetal medicine centre.

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Precision Screening: From Antibody Detection to Fetal Risk Prediction: An Algorithmic Approach

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INTRODUCTION

Red-cell alloimmunization remains an important cause of haemolytic disease of the fetus and newborn (HDFN). A positive maternal antibody screen, however, does not necessarily indicate that the fetus is at risk and will require intrauterine transfusion (IUT). Current management of isoimmunized pregnancies has moved beyond a mere titre-based approach towards identifying at-risk fetuses by combining antibody identification testing, previous obstetric history, fetal blood group testing by cfDNA with ultrasound surveillance for development of fetal anaemia by 2 weekly MCA PSV monitoring from 16 weeks onwards.

The 2025 British Society for Haematology (BSH) guideline recommends blood grouping and red-cell antibody screening at booking and again at 28 weeks.[1] The principal objective after detection of an antibody is to identify whether the fetus is actually at risk and planning antenatal surveillance accordingly. This is particularly relevant for anti-D, anti-c and anti-K, which are associated with significant fetal and neonatal morbidity.[1]

UNIVERSAL ANTENATAL ANTIBODY SCREENING

All pregnant women should undergo ABO and RhD grouping and an antibody screen at booking. Repeat screening at 28 weeks detects antibodies that may develop later in pregnancy and should be performed before routine anti-D prophylaxis, where indicated.[1] All Rh (D) negative women should be offered indirect Coomb's test (ICT) at the booking visit and again at 28–32 weeks before administration of anti-D prophylaxis.

A positive screen should warrant a structured evaluation before serial fetal surveillance. The essential questions that need to be addressed are the following:

1. What is the type of antibody that is giving a report of ICT positive?
2. Is it clinically significant for HDFN?
3. Has there been a previous affected pregnancy?
4. Does the fetus carry the corresponding antigen?
5. Is the fetus likely to develop anaemia or need intrauterine transfusion?

This progression from antibody detection to fetal risk prediction forms the basis of precision screening.

ANTIBODY IDENTIFICATION AND CLINICAL SIGNIFICANCE

Antibody identification is the first determinant of risk. There are more than 50 alloantibodies that can cause alloimmunization, but the most important ones are Rh 'D', 'c', 'E', 'Kell', Lewis, Duffy, Kidd and MNS. Rh D still accounts for about half of such cases. Anti-D, anti-c and anti-K are the antibodies most frequently associated with severe HDFN requiring antenatal intervention. [1] Identifying these less common antibodies is essential as rare 'K' and 'k' antigens of the Kell group cause severe, early-onset fetal anaemia because they not only cause haemolysis but also suppress erythropoiesis. Their identification may warrant more frequent monitoring even at titres as low as 1:2. Knowing these atypical antibodies is also essential for crossmatching blood when intrauterine transfusion is needed. Therefore, merely stating that a pregnant women is "antibody positive" is an inadequate diagnosis. The laboratory should identify the antibody, and titres should be done to ascertain the critical titre.

CRITICAL TITRE AND ITS LIMITATIONS

The critical titre is defined as the maternal antibody level above which there is a significant risk of severe haemolytic disease of the fetus and newborn (HDFN), specifically fetal hydrops or severe anaemia. The critical titre is taken as 1:16 or 1:32 depending on the lab cutoffs. However, there are limitations to this 'critical' titre - higher titres do not directly correlate with severity of fetal anaemia and do not predict fetal disease with equal accuracy for all allo-antibodies. The major exception to this is presence of anti-K antibodies. Anti K causes fetal anaemia from both haemolysis and suppression of erythropoiesis; therefore, maternal titre correlates poorly with disease severity.

Crossing of the critical titres warrants referral of the patient to a fetal medicine specialist and shifting antenatal care to a tertiary care centre. Women with anti-K should be referred for specialist fetal medicine assessment when the antibody is first identified. [1]A history of previous affected pregnancy

may override a seemingly reassuring antibody titre level.

Low titres of ICT could be falsely positive or due to passive immunization. Passive anti-D may persist and cannot be reliably distinguished from immune anti-D by reaction strength alone. Thus, a history of inadvertent anti-D injection in the last 4-6 weeks should be elicited, and serial quantitative assessments are essential to rule out or confirm passive immunization. [1]

PREVIOUS AFFECTED PREGNANCY: THE HIDDEN RISK FACTOR

The previous obstetric history is the most powerful predictor of risk of developing anemia in the current pregnancy. History of previous fetal anaemia or hydrops, intrauterine transfusion (IUT), unexplained fetal loss or stillbirth, severe neonatal jaundice, exchange transfusion, neonatal anaemia, or prolonged neonatal admission for HDFN should be taken.

Women with a previous pregnancy affected by HDFN should be referred to fetal medicine early, preferably before 16 weeks, irrespective of the current antibody titre.[1] Previous severe HDFN should therefore outweigh a reassuring current titre. The gestational age at which disease developed in the previous pregnancy and the timing and number of previous IUTs guides surveillance in the current pregnancy.

PATERNAL TESTING

Once a clinically significant maternal antibody is identified, the next step is to identify whether the fetus is carrying the corresponding antigen. Paternal antigen testing is useful. If the biological father is antigen-negative, the fetus cannot inherit the antigen and is not at risk of HDFN from that specific antibody. If the father is antigen-positive, paternal phenotyping/zygosity, i.e. whether the father is homozygous or heterozygous, may help estimate fetal risk. If the father is heterozygous for Rh-D antigen, there is a 50% chance that the fetus may be Rh-negative, and intensive surveillance will not be needed. However, paternal testing for zygosity has limitations, including uncertain paternity, in cases of assisted conception with donor egg/ donor sperm and due to difficulties in obtaining paternal samples. Therefore, recent guidance supports direct fetal antigen genotyping using cell-free fetal DNA (cffDNA) where available. [1,2]

CELL-FREE FETAL DNA

Non-invasive fetal antigen genotyping using cell-free fetal DNA (cffDNA) from maternal plasma represents a major advance in management of Rh isoimmunized pregnancies. It has reported sensitivities and specificities of nearly 100% with a false negative rate of 0.1%–0.3%. It allows identification of fetal RBC antigens D, c, C, e, E and Kell. Current BSH guidance supports non-invasive fetal genotyping for RHD, RHCE and KEL*01 (K), where appropriate. [1] It is important that samples are not sent too early in pregnancy as the levels of cfDNA rise with gestation. The false negative rate for RHCE (for c) and RHD (for D) genotyping performed at or after 16 weeks' gestation is less than 1%.

WHICH ANTIBODIES REQUIRE FETAL SURVEILLANCE?

Fetal surveillance is indicated when there is a clinically significant maternal antibody and an antigen-positive or potentially antigen-positive fetus, particularly in the presence of anti-D, anti-c or anti-K; antibody titres meeting relevant referral thresholds; rising antibody concentrations and a previous pregnancy affected by HDFN.

For anti-D and anti-c, serial antibody titre assessment remains useful until critical titres are reached. For anti-K, early fetal medicine specialist referral is essential because titre is a less reliable predictor of fetal disease.

MCA PSV DOPPLER SURVEILLANCE

Once the fetus is considered at risk, surveillance is done by 2-weekly MCA PSV measurements which is the primary non-invasive technique for detecting fetal anaemia.[3] Assessment should be done using the standardized Doppler technique.[3,4] MCA-PSV ≥1.5 multiples of the median (MoM) is associated with a significant risk of moderate-to-severe fetal anaemia and requires treatment by IUT. [3] These pregnancies should be managed in a centre with expertise in invasive fetal therapy. When significant fetal anaemia is suspected prior to 34 weeks, fetal blood sampling with preparation for IUT is considered.[3] Once fetal surveillance with MCA PSV has commenced, repeated measurement of a high maternal antibody level does not provide additional clinical information.[1]

CONCLUSION

The management of red-cell antibodies in pregnancy has evolved from antibody detection to fetal risk prediction. A positive antibody screen should initiate a structured pathway: identify the antibody, quantify titres, review the previous obstetric history and determine fetal antigen status. cfDNA-based fetal antigen genotyping enables better identification of the fetus at risk. Identify the antibody. Identify the susceptible fetus. Identify fetal anaemia before hydrops develops.

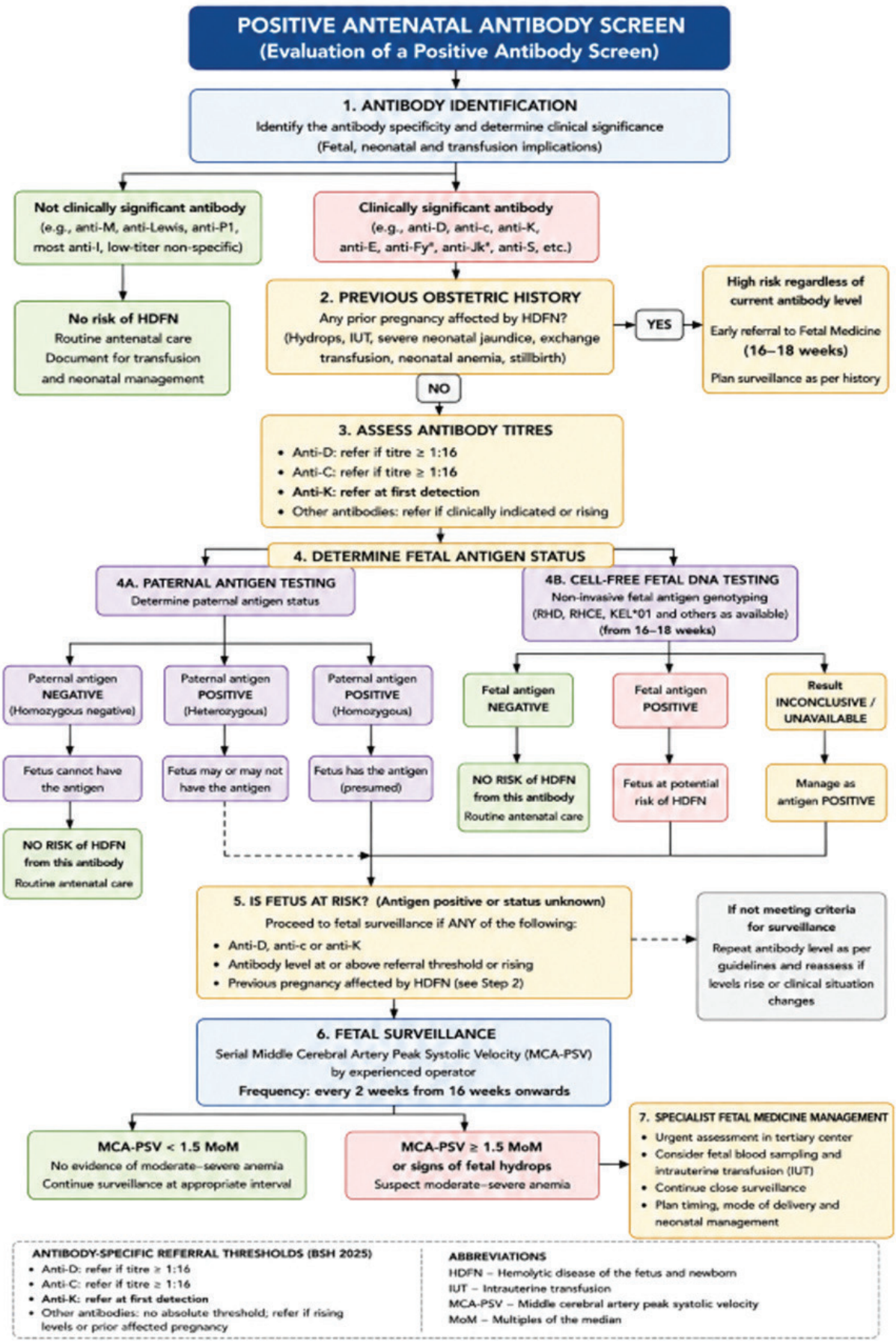


Figure 1. Algorithm for evaluation of a positive antenatal antibody screen and assessment of fetal risk.

KEY TAKE-HOME MESSAGES

- A positive antibody screen is not equivalent to fetal disease.
- Universal antibody screening should be performed at booking and again at 28 weeks.
- Anti-D, anti-c and anti-K carry the greatest risk of severe HDFN.
- Critical titres do not directly predict fetal haemoglobin.
- A previous pregnancy affected by HDFN is a major independent risk factor.
- Fetal antigen status should be determined whenever feasible using paternal testing and/or cffDNA fetal antigen genotyping.
- MCA-PSV is the principal non-invasive test for detecting fetal anaemia.
- MCA-PSV ≥1.5 MoM should prompt urgent specialist fetal medicine assessment.

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Watching the Fetus: Fetal Surveillance for Fetal Anemia

MIDDLE CEREBRAL ARTERY DOPPLER: PRINCIPLES, INTERPRETATION, AND A CLINICAL DECISION MAP

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1. INTRODUCTION

Fetal anemia is a hematological state in which fetal red-cell mass or hemoglobin concentration falls more than 2 standard deviations below the gestational-age-specific mean. It is conventionally graded as mild (hemoglobin deficit 2–4 g/dL below the mean for gestational age), moderate (deficit 4–7 g/dL), or severe (deficit >7 g/dL, or fetal hematocrit <30%, typically corresponding to a hemoglobin <7 g/dL in the third trimester). Left unrecognized, moderate-to-severe fetal anemia can progress through a well-described sequence: reduced blood viscosity and oxygen-carrying capacity → compensatory increase in cardiac output → myocardial strain and high-output cardiac failure → extramedullary hematopoiesis and hepatosplenomegaly → hypoproteinemia → ascites, pleural/pericardial effusion, and skin edema, culminating in generalized fetal hydrops. Hydrops fetalis secondary to severe anemia was historically associated with perinatal mortality approaching 20–30% even with treatment, and near 100% if untreated.

Before 2000, surveillance relied on serial amniocentesis with spectrophotometric measurement of amniotic fluid bilirubin (ΔOD450) plotted on the Liley or Queenan curves — an invasive test carrying a procedure-related pregnancy-loss risk of approximately 1%, and one further complicated by the risk of worsening alloimmunization through fetomaternal hemorrhage. Mari et al. (New England Journal of Medicine, 2000) demonstrated in a multicentre study of 111 fetuses at risk of anemia that Doppler measurement of the peak systolic velocity (PSV) in the fetal middle cerebral artery (MCA) predicted moderate-to-severe anemia with a sensitivity of 100% and a false-positive rate of 12%, at a threshold of 1.50 multiples of the median (MoM). This finding, subsequently validated in the multicentre trial by Oepkes et al. (NEJM, 2006, n=165), established MCA-PSV Doppler as the primary, non-invasive surveillance tool, essentially replacing amniocentesis-based bilirubin assays in modern practice.

This chapter reviews, in detail: the causes and grading of fetal anemia; the hemodynamic and physiological basis of the MCA-PSV rise; the precise scanning technique required for reproducible measurement; the mathematics and clinical interpretation of MoM-based thresholds; a practical, gestational-age-specific decision map for surveillance and invasive management; recent technological and evidence-based advances (2018–2025); commonly encountered technical pitfalls; and a quick-reference summary.

1.1 Causes of Fetal Anemia Requiring Surveillance

A structured aetiological approach helps determine the appropriate surveillance protocol and starting gestation:

Table 1. Principal causes of fetal anemia and their mechanisms.

Category	Examples	Mechanism
Red cell alloimmunization	Anti-D (most common, ~85% of severe cases historically); anti-Kell (causes anemia via marrow suppression, not just hemolysis — anemia can be disproportionate to titre); anti-c, anti-E, anti-Fya	Maternal IgG crosses placenta from ~16 weeks onward → extravascular hemolysis (or, for Kell, additional erythroid progenitor suppression)
Infective	Parvovirus B19 (risk of fetal anemia ~10% after maternal infection <20 weeks; highest risk 4–12 weeks post-exposure)	Virus targets erythroid progenitor P-antigen → profound but usually self-limited marrow suppression
Twin pregnancy complications	Twin anemia-polycythemia sequence (TAPS, spontaneous ~3–5% of monochorionic twins, or post-laser in ~2–13%); TTTS recipient/donor imbalance	Unbalanced flow through small (<1mm) arteriovenous placental anastomoses causing slow, chronic donor-twin anemia
Inherited hemoglobinopathy	Homozygous α0-thalassemia (Hb Bart's hydrops fetalis; all 4 α-globin genes deleted)	Absent α-globin chain synthesis → unstable Hb Bart's (γ4) with high oxygen affinity → tissue hypoxia and hydrops, typically by 22–28 weeks
Fetomaternal hemorrhage	Acute (e.g., abruption, trauma) or chronic FMH	Direct fetal blood loss into maternal circulation; Kleihauer-Betke test aids maternal-side confirmation
Other	Congenital infection (CMV, syphilis, toxoplasmosis); fetal tumours (sacrococcygeal teratoma, chorioangioma); G6PD deficiency; hereditary spherocytosis	Marrow suppression, high-output consumption/sequestration, or intrinsic red-cell fragility

2. PATHOPHYSIOLOGY: WHY ANEMIA RAISES CEREBRAL BLOOD FLOW VELOCITY

Fetal anemia reduces blood viscosity and oxygen-carrying capacity. In response, a cascade of compensatory hemodynamic changes occurs:

1. Reduced blood viscosity secondary to lower hematocrit facilitates increased laminar flow velocity through the vascular tree.
2. Tissue hypoxia stimulates a redistribution ("brain-sparing") response, preferentially increasing blood flow to the brain, heart, and adrenal glands at the expense of peripheral and splanchnic circulations.
3. The combination of reduced viscosity and preferential cerebral perfusion produces a measurable rise in peak systolic velocity within the fetal middle cerebral artery, proportional to the severity of anemia.

This relationship, first systematically described by Mari and colleagues in 2000, underpins the entire basis of MCA-PSV as a surveillance tool: PSV rises before ultrasound signs of hydrops become apparent, permitting anticipatory rather than reactive management.

2.1 The Mari Regression Equation

Mari's original reference standard expressed the expected (median) MCA-PSV for a structurally normal, non-anaemic fetus as a log-linear function of gestational age:

$$\text{Median MCA-PSV (cm/s)} = 1.525 \times e^{(0.0027 \times \text{GA in weeks})}$$

A measured PSV is then expressed as a multiple of this predicted median (MoM = measured PSV ÷ predicted median PSV for GA), which normalizes for the physiological rise in velocity across gestation and allows a single numerical threshold (1.5 MoM) to be applied from approximately 18 to 35–37 weeks. Because peak velocities and vessel calibre continue to change near term, some centres apply a modified or gestation-capped correction beyond 35 weeks; local departmental protocols and ultrasound machine software (which typically has the Mari curve pre-programmed) should be followed for exact cut-offs.

3. MCA DOPPLER: PRINCIPLES AND TECHNIQUE

Reliable MCA-PSV measurement is technique-dependent. Reproducibility requires strict adherence to a standardized acquisition protocol, summarized in the flowchart below.

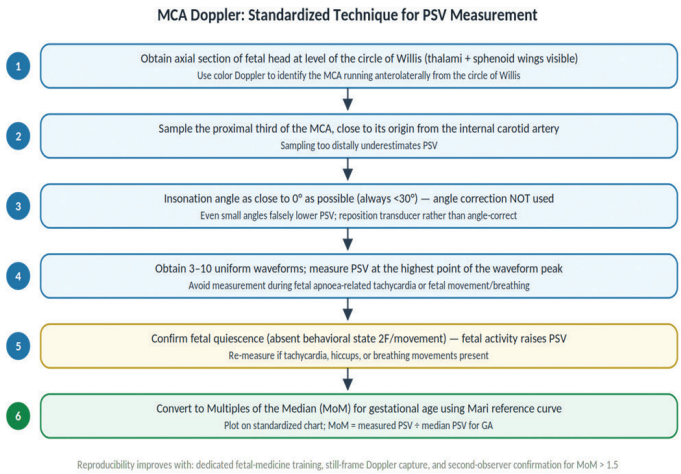


Figure 1. Standardized stepwise technique for MCA-PSV Doppler acquisition.

- The MCA is identified in an axial plane at the level of the circle of Willis using color Doppler; it courses anterolaterally and is visualized as a bright color signal close to the skull base.
- The sample gate is placed in the proximal third of the vessel, immediately after its origin from the internal carotid artery — velocities decline distally, so sampling error here is a common source of false-negative results.
- The angle of insonation between the ultrasound beam and vessel should approach 0°, and must never exceed 30°. Unlike umbilical or uterine artery Doppler, angle correction is not applied, because at near-zero angles the cosine correction factor becomes unreliable and can introduce error.
- Measurements should be taken during fetal quiescence — fetal breathing, movement, and hiccups elevate heart rate and cerebral flow velocity, causing overestimation of the PSV.
- Multiple (3–10) technically satisfactory waveforms should be obtained, and the PSV taken from the highest, most well-defined systolic peak.

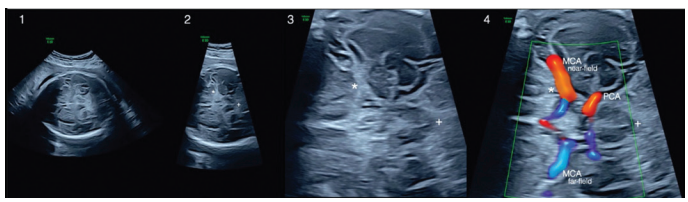


Figure 3. Sequence for obtaining the MCA Doppler waveform. (1) Transverse view of the fetal head at the level for insonation. (2) Sweep towards the skull base; the lesser wings of the sphenoid are identified (*), with the field of view reduced. (3) Further optimization by decreasing depth and applying zoom; the cerebral peduncles are visualized (+). (4) Colour Doppler is activated with a small box; both MCAs and the posterior cerebral arteries (PCA) are visible, allowing the MCA to be distinguished from the PCA by anatomical landmarks.

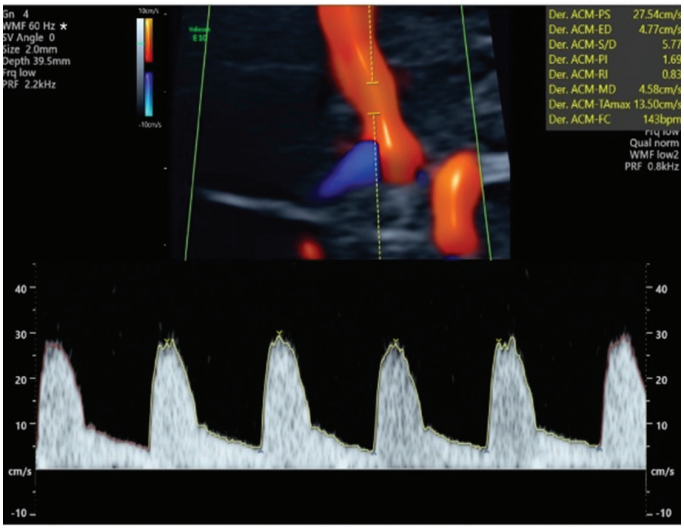


Figure 4. Correctly optimized pulsed-Doppler interrogation of the MCA. The vessel occupies more than 50% of the screen, four similar waveforms have been obtained, the high-pass (wall) filter is set to 60 Hz, and the sample volume is placed at the centre of the vessel with a width of 2 mm.

4. INTERPRETATION: MOM THRESHOLDS AND CLINICAL MEANING

Because absolute PSV values rise physiologically with gestational age, measured velocities must be expressed as multiples of the median (MoM) for gestational age, most commonly using the reference equations derived by Mari et al. This normalization allows a single threshold to be applied across gestation.

Table 2. Interpretation of MCA-PSV MoM values and corresponding clinical action.

MCA-PSV (MoM)	Interpretation	Approx. Sensitivity for Mod–Severe Anemia	Recommended Action
< 1.0 MoM	Below median — anemia very unlikely	—	Continue routine interval surveillance
1.0–1.29 MoM	Normal range	—	Continue routine surveillance per protocol
1.3–1.49 MoM	Borderline — increased vigilance	Grey zone	Shorten surveillance interval (weekly)
≥ 1.5 MoM	High probability of moderate–severe anemia	~88–100%	Refer for cordocentesis ± intrauterine transfusion
≥ 1.5 MoM post-IUT	Reduced reliability (donor cell rheology)	Reduced specificity	Interpret with hydrops signs; base timing on Hb decline curve

A threshold of 1.5 MoM has been validated across multiple cohorts (Mari 2000[1]: sensitivity 100%, false-positive rate 12%; Oepkes 2006[2]: sensitivity 88%, specificity 78% when compared head-to-head against amniocentesis) as achieving high sensitivity for detecting moderate-to-severe fetal anemia. Below this threshold, the negative predictive value exceeds 95% in most series, allowing safe continuation of non-invasive surveillance and avoidance of unnecessary invasive testing.

4.1 Post-Transfusion Follow-Up

Following intrauterine transfusion (IUT), MCA-PSV loses much of its predictive value for 2–3 weeks because adult donor red cells alter fetal blood rheology (higher hematocrit, different cell deformability), which independently raises flow velocity regardless of true fetal hemoglobin. Follow-up should therefore combine a modelled hemoglobin-decline estimate with clinical and ultrasound surveillance rather than relying on the MoM threshold alone.

- Do not re-apply the 1.5 MoM threshold in the first 2–3 weeks after IUT; a normal or low MCA-PSV in this window does not reliably exclude recurrent anemia.
- Estimate the expected fetal hematocrit decline using the standard post-transfusion model (~1% hematocrit, or approximately 0.3 g/dL hemoglobin, per day) to predict when the next transfusion is likely to be needed.
- Schedule repeat IUT empirically, typically every 2–4 weeks, based on this decline curve rather than on a single Doppler measurement.
- Continue ultrasound surveillance for resolution or recurrence of hydrops (ascites, skin edema, pleural/pericardial effusion) and monitor cardiac function and ductus venosus Doppler as adjunct markers of decompensation.
- MCA-PSV can still be trended qualitatively across serial post-IUT scans — a rising trend is informative even if the absolute MoM is not — and becomes fully reliable again once donor cell turnover is complete, generally by 4 weeks post-transfusion.
- Interpret any borderline or unexpected post-IUT Doppler finding in the context of the hemoglobin decline curve and hydrops signs rather than in isolation, and involve the tertiary fetal medicine team managing the transfusion series.

5. CLINICAL DECISION MAP FOR FETAL ANEMIA SURVEILLANCE

The following decision map integrates risk stratification, Doppler surveillance, and escalation to invasive

management into a single working algorithm suitable for departmental protocols. Surveillance timing is individualized: for red-cell alloimmunization, MCA-PSV is started at 16–18 weeks or, in a woman with a previous affected pregnancy, 8–10 weeks before the gestation at which the earliest prior intrauterine transfusion (IUT) or fetal loss occurred. For parvovirus B19 exposure, weekly surveillance for 8–12 weeks post-exposure/seroconversion is typical, as the anemia risk window is concentrated in this period. Cordocentesis for confirmation of fetal hematocrit and, where indicated, IUT is generally deferred until 18 weeks (below this gestation the procedure carries a substantially higher loss rate) and is performed at a tertiary fetal medicine centre with immediate access to neonatal intensive care.

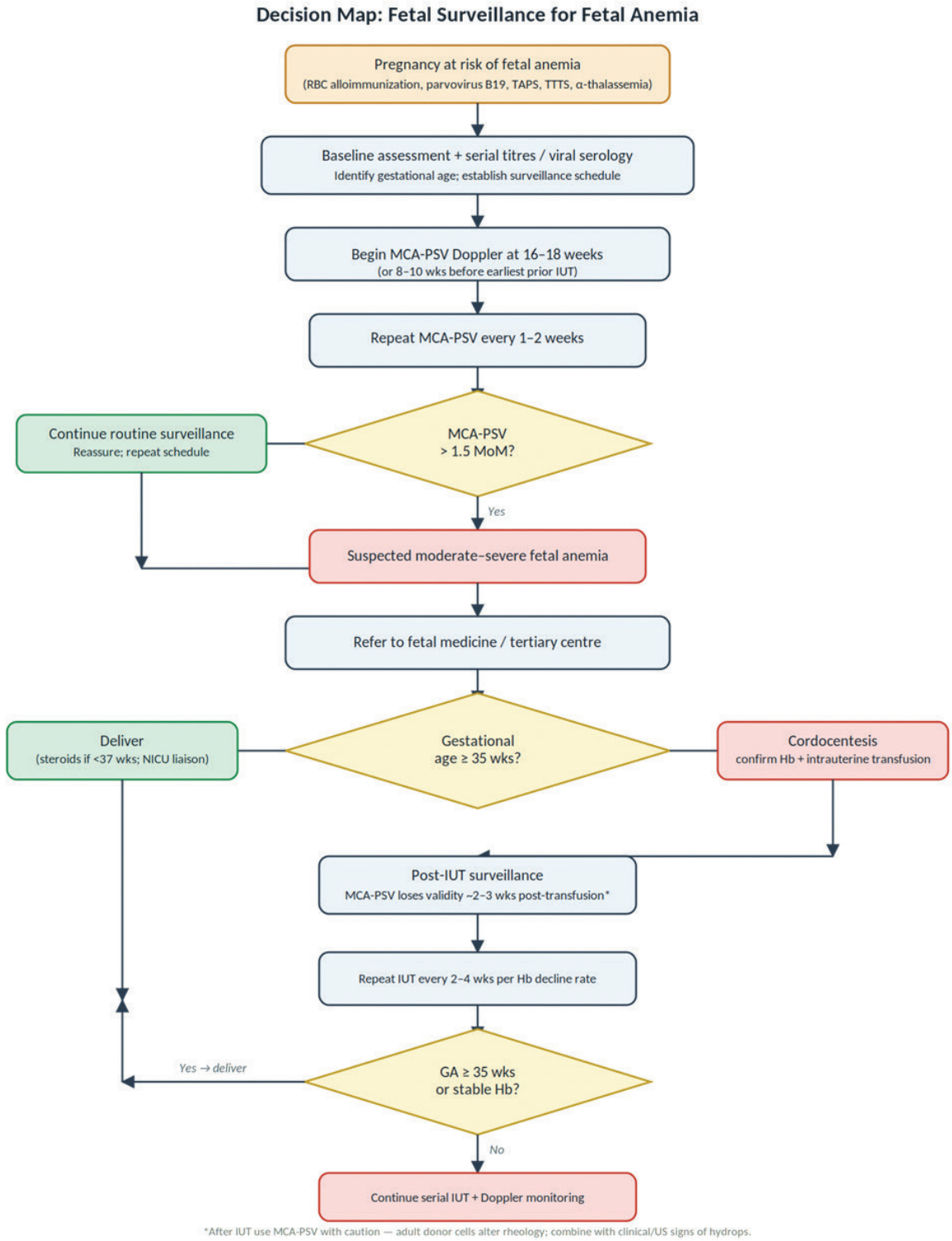


Figure 2. Decision map for surveillance and management of pregnancies at risk of fetal anemia.

Following a confirmed severe anemia diagnosis (fetal hematocrit typically <30% or Hb deficit >7 g/dL), IUT is performed via the umbilical vein (intrahepatic portion or cord insertion), transfusing group O, CMV-negative, irradiated, leukodepleted red cells cross-matched against maternal serum to a target post-transfusion hematocrit of approximately 40–45%. Repeat transfusions are typically required every 2–4 weeks, as adult donor cells have a shorter intrauterine lifespan and fetal hematocrit falls by approximately 1% per day post-transfusion. Delivery is generally planned for 35–37 weeks in a well-controlled, transfusion-responsive fetus, with earlier delivery considered if hydrops fails to resolve or if repeated IUT becomes technically difficult.

6. RECENT ADVANCES

MCA Doppler surveillance continues to evolve, with recent work focused on reducing operator dependence, refining reference standards, and exploring non-invasive alternatives or adjuncts.

Table 3. Recent advances relevant to fetal anemia surveillance.

Advance	Description	Clinical Relevance
AI-assisted Doppler acquisition	Machine-learning algorithms (reported in pilot/validation studies, 2021–2024) auto-identify the MCA, optimise insonation angle in real time, and flag suboptimal waveforms before the operator freezes the image	Reduces operator-dependent variability; supports non-expert sonographers in low-resource and peripheral settings
Automated angle-independent PSV estimation	Vector-flow / power-Doppler-derived techniques under prospective evaluation to reduce reliance on manual angle minimization	May reduce both false-positive and false-negative results driven by angle misestimation, historically the single largest source of technical error
Updated, larger multi-ethnic reference curves	Re-derivations of Mari's original 1999–2000 cohort (n=222) using larger, more diverse contemporary populations to test generalisability of the 1.5 MoM cut-off across ethnicities and modern ultrasound equipment	Improved precision of thresholds, particularly near term and at early gestations (<20 weeks) where the original dataset was sparse
Combined biomarker / multi-parameter risk models	MCA-PSV combined with ductus venosus Doppler, cardiothoracic ratio, and (for parvovirus) viral load trends	Improves risk stratification and timing of intervention in the 1.3–1.5 MoM 'grey zone'
Point-of-care & tele-Doppler networks	Remote real-time image transmission and store-and-forward Doppler review by tertiary fetal medicine centres, expanded significantly since 2020	Extends specialist-level surveillance and second-opinion review to peripheral, rural, and resource-limited units
Non-invasive fetal Hb estimation research	Investigational fetal MRI T2* relaxometry and quantitative susceptibility mapping, and near-infrared spectroscopy approaches, reported in small feasibility cohorts	Potential future adjunct to Doppler in equivocal cases; not validated for routine clinical decision-making at this time
AI-based quantitative echogenicity/texture analysis	Machine-learning image-texture analysis of fetal liver, spleen, and placental greyscale echogenicity, trained to detect subtle parenchymal changes associated with extramedullary hematopoiesis and early hydrops, reported in exploratory cohorts (2022–2025)	Investigational adjunct to MCA-PSV; may flag anemia risk from routine greyscale images even before Doppler thresholds are crossed, but not yet validated for independent clinical decision-making
Refined post-transfusion surveillance models	Protocols combining serial Doppler trend (rather than a single absolute MoM) with mathematical modelling of the expected ~1%/day post-transfusion hematocrit decline	Improves timing precision for repeat IUT, partially mitigating the known reduced validity of MCA-PSV in the 2–3 weeks following transfusion

While these developments are promising, MCA-PSV Doppler using the standard technique described above remains the evidence-based first-line surveillance tool; emerging technologies are, at present, best regarded as adjuncts pending further prospective validation.

7. PITFALLS AND TECHNICAL ERRORS

Awareness of common sources of error is essential to safe interpretation of MCA-PSV, since both false-positive and false-negative results carry clinical consequences — the former leading to unnecessary invasive procedures, the latter to missed severe anemia.

Table 4. Common technical pitfalls in MCA-PSV Doppler and their mitigation.

Pitfall	Effect on PSV	Mitigation
Insonation angle > 0°	Falsely lowers PSV (underestimates anemia)	Reposition probe for angle as close to 0° as possible; never angle-correct
Sampling distal MCA	Falsely lowers PSV	Sample proximal third, near circle of Willis origin
Fetal movement/ tachycardia/ hiccups	Falsely raises PSV (overestimates anemia)	Wait for fetal quiescence; repeat measurement
Excess transducer pressure on head	Variable, unpredictable effect on flow	Use minimal, consistent probe pressure
Measurement post-IUT	Reduced validity of MoM thresholds	Interpret cautiously; corroborate with hydrops/ultrasound signs
Inter-observer variability	Inconsistent MoM classification near threshold	Standardized training; second-observer confirmation near cut-off

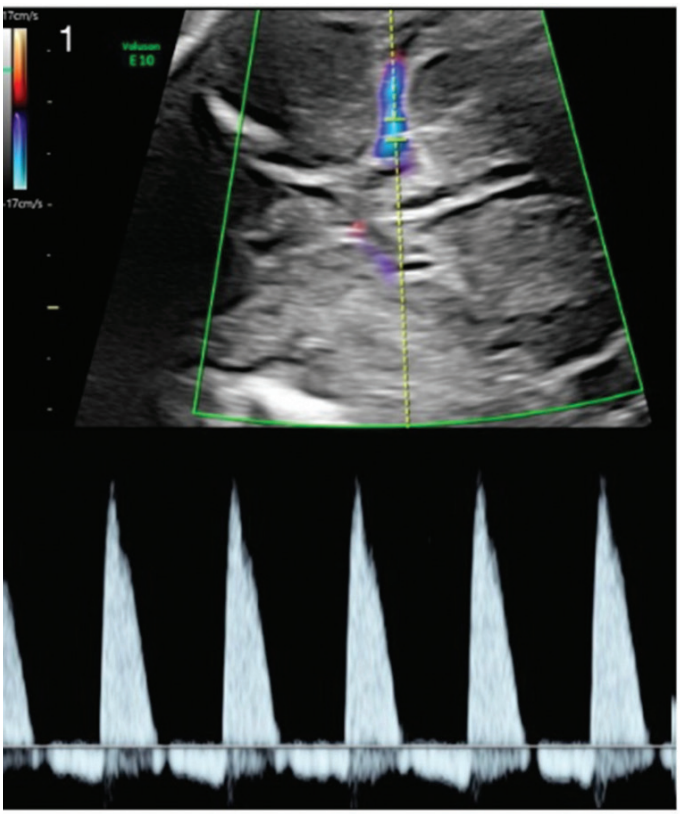


Figure 5. Poor technique: excessive transducer pressure on the fetal scalp produces reversed end-diastolic velocities in the MCA on both colour and pulsed Doppler — an artefactual finding that can also be seen in fetuses with obstructive hydrocephalus.

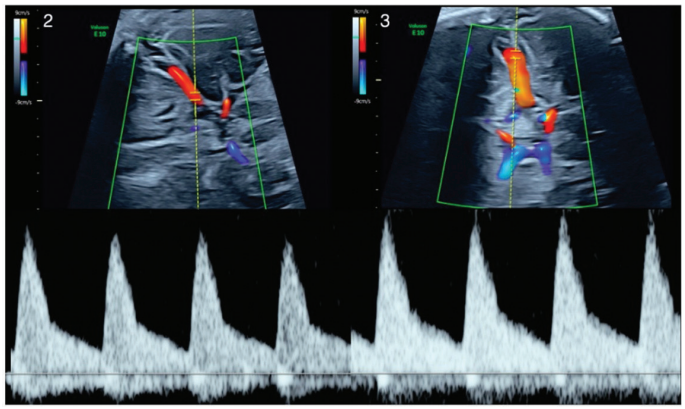


Figure 6. Two further technical pitfalls. Left: an inadequate insonation angle, which can cause false-negative results in the diagnosis of fetal anemia. Right: the MCA sampled in its distal portion, close to its bifurcation and away from its origin at the internal carotid artery — a common source of falsely low PSV readings.

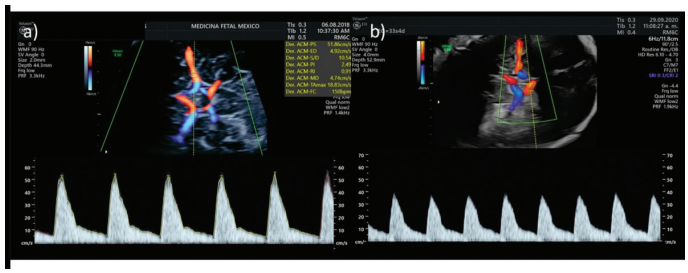


Figure 7. Vessel misidentification pitfall. Insonation of the middle cerebral artery (a) should not be confused with the anterior cerebral artery (b): the two vessels produce a similar waveform and similar peak systolic velocities, but only the MCA is validated for anemia surveillance.

8. SUMMARY TABLE: QUICK REFERENCE

Table 5. Quick-reference summary of key thresholds and management points.

Parameter	Quick Reference
Onset of MCA-PSV surveillance	16–18 weeks (or 8–10 weeks before earliest previous IUT)
Surveillance interval	Every 1–2 weeks in at-risk pregnancies
Threshold for referral / cordocentesis	MCA-PSV ≥ 1.5 MoM for gestational age
Sampling site	Proximal third of MCA near origin from internal carotid artery
Insonation angle	As close to 0° as possible; always < 30°; no angle correction
Post-IUT reliability window	Reduced accuracy for approximately 2–3 weeks after transfusion
Delivery threshold (uncomplicated)	Around 35–37 weeks or when anemia risk/benefit favours delivery over IUT

9. INTERACTIVE TOOL: MCA-PSV CALCULATOR

To support bedside use of the thresholds discussed above, an interactive MCA-PSV calculator has been developed. Given the gestational age and the observed MCA peak systolic velocity, it computes the expected median PSV and the multiples of the median (MoM), plots the result against the reference and 1.5 MoM threshold curves, and returns a plain-language interpretation.

Formula used for the expected median PSV: $PSV = e^{(2.31 + 0.04643 \times GA)}$, where GA is gestational age in decimal weeks. As with any calculator, results should support, not replace, clinical judgment.

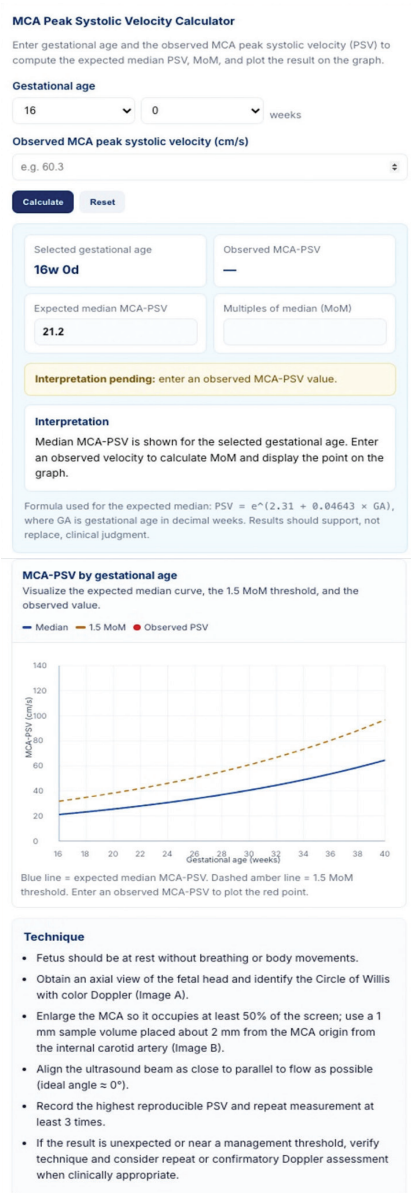


Figure 8. MCA-PSV calculator interface, showing input/results panel (left) and the reference chart (right). Interface concept inspired by perinatology.com-style clinical calculators; this implementation was built for this chapter and is not sourced from or affiliated with perinatology.com.

Technique reinforced by the tool

- Fetus should be at rest, without breathing or body movements.
- Obtain an axial view of the fetal head and identify the Circle of Willis with colour Doppler.
- Enlarge the MCA so it occupies at least 50% of the screen; use a 1 mm sample volume placed about 2 mm from the MCA origin from the internal carotid artery.
- Align the ultrasound beam as close to parallel to flow as possible (ideal angle ≈ 0°).
- Record the highest reproducible PSV and repeat the measurement at least three times.
- If the result is unexpected or near a management threshold, verify technique and consider a repeat or confirmatory Doppler assessment when clinically appropriate.

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Saving the Fetus: Intrauterine Fetal Therapy

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1. INTRODUCTION

Intrauterine intravascular transfusion (IUT) is a medical procedure that involves delivering specially prepared donor red blood cells directly into the umbilical vein of the fetus, guided by ultrasound imaging. The decision to carry out IUT is made by a team of specialists, including obstetricians and experts in maternal-fetal medicine, who carefully weigh the benefits and risks.

2. INDICATIONS

The majority of transfusion are done for immune hydrops. However, there are other indications for which an IUT may be needed.

Table 1: Indications for IUT

Immune fetal anaemia (RhD and Non RhD alloimmunisation)
Homozygous alpha thalassemia,
Parvovirus B19 infection,
Chronic fetomaternal haemorrhage
Twin-twin transfusion syndrome
Twin-anemia polycythaemia sequence

Instead of waiting until severe anemia (a haemoglobin deficit of at least 7 grams per decilitre) or fetal hydrops (a haemoglobin level typically <5 g/dL) develops, intervention at a moderately reduced fetal haemoglobin level, which is two standard deviations below the mean value for gestational age, results in a better fetal outcome.

3. DIAGNOSIS OF FETAL ANAEMIA

Advances in imaging techniques have greatly enhanced the management of patients with Rh-isoimmunization. Doppler ultrasound, a non-invasive tool, is particularly valuable for assessing fetal anemia. A fetus is considered to have severe anemia if the peak systolic velocity (PSV) in the middle cerebral artery (MCA) is 1.5 times the median (MoM) or higher, measured between 18 and 35 weeks of gestation. At least three values of middle cerebral artery Doppler should be taken prior to confirming fetal anaemia. Other ultrasound signs of severe anemia can include hydrops, which is characterized by ascites, pericardial effusion, pleural effusion, subcutaneous edema, as well as polyhydramnios and placentomegaly. A fetus exhibiting hydrops is likely to have severe anemia with a hemoglobin level deficit of 7 grams per deciliter or more.

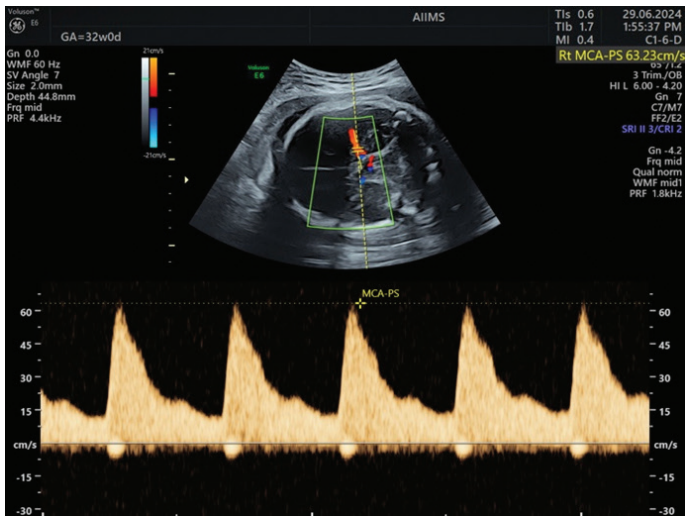


Figure 1. Middle cerebral artery Doppler in normal fetus at 32 weeks showing PSV 63.23cm/sec is <1.5 MOM as shown in Mari's chart below

Figure 2. Expected peak velocity of systolic blood flow in the MCA as a function of gestational age as given by Mari et al

Weeks of gestation	Multiple of median (cm/sec)		
	1.29	1.50	1.55
18	29.9	34.8	36.0
20	32.8	38.2	39.5
22	36.0	41.9	43.3
24	39.5	46.0	47.5
26	43.3	50.4	52.1
28	47.6	55.4	57.2
30	52.2	60.7	62.8
32	57.3	66.6	68.9
34	62.9	73.1	75.6
36	69.0	80.2	82.9
38	75.7	88.0	91.0
40	83.0	96.6	99.8

4. TIMING

Intrauterine transfusions for severe fetal anemia are usually conducted between 18 and 34 weeks of pregnancy. Before 18 weeks, these transfusions are seldom effective because of poor visualization and the small size of key anatomical structures. After 34 weeks, the procedure is generally seen as riskier compared to delivering the baby early for neonatal treatment of severe anemia.

5. ROUTE

Intraperitoneal transfusions have been utilized as bridge therapy before 18 weeks of gestation until access to the umbilical vein is theoretically possible later in gestation. Intravascular transfusion via the umbilical vein is the preferred route due to its safety and ease of access. The umbilical vein at the placental insertion is the most commonly used site. As long as the fetal position is favourable, transfusion into the intrahepatic section of the umbilical vein is a valid substitute for transfusion at the placental insertion point. Table 1 shows sites of intrauterine transfusion and their advantages and disadvantages.

Table 2. Sites of intrauterine transfusion with advantages and disadvantages

Site	Advantages	Disadvantages
Placenta loop	Easy penetration	Fetal Bradycardia
Free loop		Fetal bradycardia Difficult Penetration
Intrahepatic	Fewer chances of fetal bradycardia	More organ trauma More stress to the fetus

6. SELECTION OF RED BLOOD CELL UNIT FOR INTRAUTERINE TRANSFUSION

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- The packed red blood cells (PRBCs) to be used for Intrauterine transfusions (IUT) require certain modifications in PRBCs routinely available with the blood centers which are tested for blood group, clinically significant antibodies and infectious markers (HIV, HBV. HCV, Syphilis and Malaria with hematocrit of around 50-70% and leukocytes in the range of 108 to 109. Selection of appropriate blood components for IUT is necessary to ensure survival of transfused red cells.
- PRBCs for IUT should be Leukoreduced to prevent fetal CMV transmission. A method which ensures 3-log reduction (<5x106 leukocytes/PRBC) has been shown to provide safety comparable to CMV seronegative blood.
- Another modification on PRBCs intended for IUT is irradiation. PRBC is given a small dose (25 Gy) of irradiation (gamma ray / X-ray) which causes donor leukocytes to become non-viable and prevents donor leukocytes from mounting an immune response to the fetus, thus mitigating transfusion associated graft vs host disease (TAGvHD). Irradiation is to be done as close to the time of transfusion as possible.
- PRBC hematocrit should be adjusted to 75-80% by centrifugation and removing supernatant plasma or preservative. This modification allows to deliver a slightly higher RBC mass in small volumes. Excess potassium or other metabolites accumulated during storage are also removed along with plasma/ preservative.
- Blood group of PRBC is selected such that it is compatible with maternal ABO/RhD type, maternal alloantibodies and fetal blood group. The common practice is to select O RhD negative PRBCs for IUT. If maternal alloantibodies are identified, an antigen negative PRBC (to maternal antibody) is selected.
- The practice of selecting O RhD negative PRBCs for all subsequent IUTs in a fetus may result in depletion of the inventory of O RhD negative PRBCs resulting in unavailability of O RhD negative PRBCs for other patients. When fetal blood group is known, selecting non-O RhD negative PRBCs for IUT which are compatible with both mother and fetus can conserve O RhD negative inventory and improve the search for compatible antigen-negative units. (Table 2) Fetal blood type is usually possible after first IUT and subsequent IUTs may utilize non-O RhD negative units. This strategy may not be useful if fetal blood group cannot be identified with certainty due to any reason such as in case of twin pregnancy.

Table 3: Selection of blood group of PRBC for IUT

Maternal blood group	Fetal blood Group	Choice of Blood Group for IUT
Selection of ABO group		
O	O	O
	A	O
	B	O
	AB	O
A	O	O
	A	A
	B	O
	AB	A>O
B	O	O
	A	O
	B	B
	AB	B>O
AB	O	O
	A	A
	B	B
	AB	AB>B/A/O
Selection of RhD group		
RhD positive	RhD positive	RhD positive
	RhD negative	RhD negative
RhD negative	RhD positive	RhD negative
	RhD negative	RhD negative
Please note: O RhD negative PRBCs are selected if fetal blood group is not known (e.g. 1st IUT) or fetal blood group cannot be identified with certainty (e.g. Twin pregnancy)		

- Lastly, the selected PRBC must be as fresh as possible to limit the storage changes. PRBCs collected within seven days are usually preferred for IUT. In practice, RBCs till 10-14 days of collection may be utilized if pre-storage leukoreduction is being practiced especially when no compatible units could be found in fresh units as such units have shown to have minimal storage lesions2. Testing these PRBCs for HbS has also been recommended specially in a sickle cell disease endemic zone.
- To summarize, PRBCs intended for IUT should be Leukoreduced, Irradiated, preferably within 7-10 days of storage, negative for HbS with the hematocrit adjusted to 75-80% and should be compatible with both mother and fetus (if blood group is known).

7. CALCULATION OF TRANSFUSION VOLUME

The volume of blood to be transfused is determined by three parameters:

- The pretransfusion fetal haematocrit
- The estimated fetoplacental blood volume
- The haematocrit of the donor blood

To determine the volume of red blood cells required for an intravascular transfusion, the fetoplacental volume is approximated. It has been discovered that during pregnancy, the fetoplacental volume in relation to the estimated fetal weight by ultrasound is rather consistent. To get this volume (in millilitres), multiply the expected fetal weight (g) by 0.14.27. Next, using the following formula, the volume to be transfused during a fetal intravascular transfusion is determined:

$$\text{V transfused (ml)} = \frac{\text{Hct (final)} - \text{Hct (initial)} \times \text{V fetoplacental (ml)}}{\text{Hct (transfused)}}$$

where V is volume and Hct is haematocrit.

The formula for the volume of intraperitoneal transfusion (IPT) was determined decades ago to allow maximum infusion of RBCs without compromising umbilical venous blood flow from excessive intraabdominal pressure.

IPT volume = (Gestational age in weeks – 20) × 10

Thus, a fetus at 30 weeks would receive: (30 – 20) × 10 = 100 mL

8. PREPARATION FOR IUT

- Written informed consent should be obtained before the procedure, including discussion of:
  - Indication and expected benefits
  - Alternative management
  - Need for repeat IUT
  - Procedure-related complications
  - Possibility of emergency delivery and neonatal intervention
- Intravenous access (maternal) is obtained.
- Some medical professionals provide a first-generation cephalosporin (1 to 2 grams) as a preventive antibiotic within an hour of the procedure beginning; however, there is currently no information on the efficacy of antibiotic prophylaxis in this context.
- In case of IUTs after 26 weeks (beyond period of viability):
  - It is advisable to, administer a course of antenatal corticosteroids
  - There should be a facility for emergency caesarean section and a NICU back up.
  - Clear liquids may be consumed by the patient up to two hours prior to the planned treatment. Six to eight hours prior to the treatment, it is recommended to refrain from consuming any other oral intake
- Pre-procedure Checklist: Correct patient and indication, gestational age, fetal viability, fetal position, placental location, hydrops status, planned access site, availability and compatibility of blood, required transfusion volume, maternal IV access and consent

Figure 3: IUT Consent form template

Patient information sheet and consent form Intrauterine Transfusion

1. What is intrauterine transfusion?

Intrauterine Transfusion (IUT) is a procedure in which blood from donor is transfused through fine vessels in cord to treat fetal anemia. It is one of the most successful in utero therapeutic procedures.

2. What are goals of treatmen

Goals of intrauterine transfusion are to prevent or treat fetal heart failure (hydrops), which can be caused by anemia, and to allow the pregnancy to continue so the baby can be more developed when it is born.

3. How to select patients for IUT?

Pregnancies with moderate to severe fetal anemia diagnosed by doing Doppler of fetal vessel (MCA) are optimal candidates for IUT at 18 to 35 weeks of gestation. In these cases, the actual hematocrit/hemoglobin is then determined by obtaining fetal blood via percutaneous umbilical blood sampling

4. What are Pre op maternal preparations?

Before the initial IUT, a course of antenatal corticosteroids is administered when the fetus is at a gestation age where the patient and her physician agree that emergency cesarean birth would be performed if indicated because of fetal compromise. Patients are instructed to avoid oral intake for six to eight hours before the procedure. Intravenous access is obtained and prophylactic antibiotic are given immediately before procedure.

5. How is the IUT procedure performed?

Intrauterine transfusion is performed in the hospital; usually an admission for 1-2 days is needed. The fetus may be given additional medicine to stop movement. No anesthesia for mother is required and it's done under continuous ultrasound guidance to determine the position of the fetus and placenta. The surgeon inserts a needle into your abdomen and then into the umbilical cord vein. O negative blood is cross matched with mother is passed through the needle into the fetus. The doctor will prescribe antibiotics and medication to prevent labor. Fetal transfusions may need to be repeated every few weeks until the fetus is ready to be born which is around 34-35 weeks.

Follow-up – A follow-up ultrasound examination is scheduled for the following day as most cases of fetal loss occur within the first 24 hours post procedure. Patient can be discharged next day after ultrasound examination.

6. What are risks associated with the procedure?

Fetal bradycardia and bleeding from the puncture site are the most common complications of IUT, but usually resolve without consequences.

Procedure related fetal loss is around 1.6 % and procedure related complications like preterm rupture of membranes, infections, emergency cesarean delivery is around 3%

7. What are outcomes in alloimmunized pregnancies?

Survival after IUT is over 90 percent in our center. Survival is less when severe anemia develops before 20 weeks of gestation

During your evaluation, we will provide a detailed review of your baby's condition and treatment options in order to help you and your family decide what the best treatment plan may be.

Consent for IUT

I, ..., & my husband/ family member understood the condition (fetal anemia) that my unborn babies are suffering from, in detail. The expected progression of the problem, its likely consequences & complications thereof as well as the various management options that are available to us at this gestational age were explained. The possible fetal interventions with the pros and cons of each and the costs involved were also discussed in detail. All possible complications to the mother and fetus were also explained in detail and include preterm delivery, premature membrane rupture, bleeding, infection, miscarriage and even fetal demise. No anesthesia is required for the procedure, as a fine needle is inserted in maternal abdomen for blood transfusion to fetus. Maternal risks and risk to the mother's life are therefore minimal but not nil. We accept the risks involved after fully understanding them and agree to go ahead with intrauterine transfusion (IUT) on our free will.

Patient's signature Husband/Relative's signature

Date/ time Date/ time

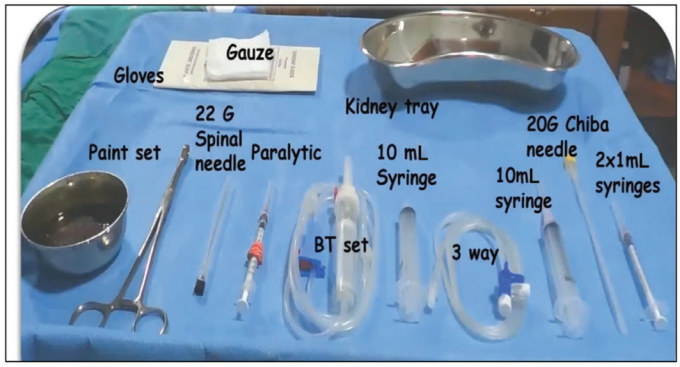


Figure 4: Set up of Trolley for IUT

9. PROCEDURE OF IUT

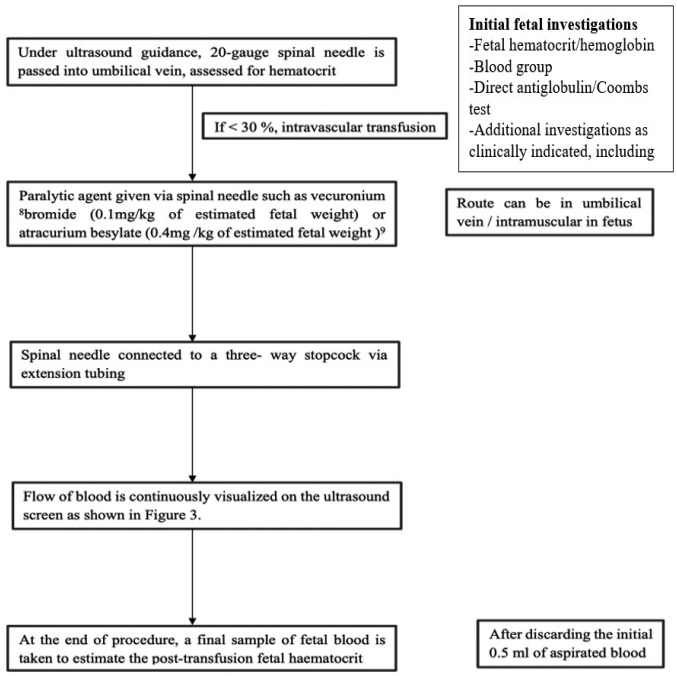


Figure 5. Flow chart of procedure of IUT



Figure 6. Needle positioned within the umbilical vein at cord insertion

Name	Age
UHID	Date of Procedure
Diagnosis: Procedure: Surgeons:	

Paralytic agent:	Site of insertion:

Needle used	
Placenta Site (Cord insertion/free loop/intrahepatic)	
Number of attempts	
Pre IUT Hb/ HCT	
Volume transfused (ml)	
Post IUT Hb/HCT	
Diagram (placenta and site of IUT)	
Post procedure FCA	
Post procedure NST	
Any additional procedure (amniocentesis/ cordocentesis)	

Additional points:

JR: SR:

Sign: Sign:

Figure 7: Documentation of Procedure

10. FOLLOW-UP

The target haematocrit level for fetal blood transfusion is set at 45–50%. In fetuses beyond the period of viability, post procedure fetal surveillance is conducted by monitoring the fetal heart rate with cardiotocography for about an hour. The mother is advised to track daily fetal movements and attend antenatal clinic appointments every week for ultrasound evaluations, including measurement of middle cerebral artery peak systolic velocity (MCA-PSV), umbilical artery flow velocimetry, and to check for any signs of fetal compromise.

- MCA PSV is less effective for timing subsequent intrauterine transfusions because the fetal middle cerebral artery blood flow changes when it is replaced by adult red blood cells, which are smaller, less rigid, and have different oxygen-carrying capacities.
- For MCA PSV measurements, a cut-off of 1.69 multiples of the median (MoM) is preferable.

The interval between the first and second intrauterine transfusions is generally around 1–2 weeks. The goal of the transfusions is to maintain the fetal hematocrit at a physiological level using adult RhD-negative red blood cells, thereby suppressing the production of fetal RhD-positive red blood cells. However, the hematocrit typically decreases between transfusions due to fetal growth, plasma expansion, and the dilution of RhD-negative cells, as well as the ongoing hemolysis of remaining RhD-positive cells. After the first transfusion, the hematocrit usually falls at a rate of 1% or more per day. Following the second transfusion, fetal erythropoiesis is usually suppressed, and the rate of hematocrit decline is about 0.8–1.2% per day. Subsequent transfusions can be scheduled at 3–4 week intervals, depending on the post-transfusion hematocrit levels achieved.

PRACTICAL PEARL FOR SCHEDULING SUBSEQUENT TRANSFUSION:

The goal is to maintain the fetal hematocrit **above 30 percent**. For the Second, Third, and Fourth Transfusions**, t**he empirically transfusion time:

- 10 days after the first transfusion
- 2 weeks after the second transfusion
- 3 weeks after the third transfusion

Another reasonable approach is to base the interval between transfusions on the expected decline in fetal hemoglobin:

- After first transfusion: 0.4 g/dL/day
- After second transfusion: 0.3 g/dL/day
- After third transfusion: 0.2 g/dL/day.

The strategy is different for hydropic or highly anemic fetuses that arrive early in the second trimester. Initially, transfusion is performed on these fetuses in order to attain a hematocrit of about 35%. The goal of a second transfusion, which takes place 48 hours later, is a final hematocrit of 45 to 50%.

BEFORE IUT:

- ☐ Indication confirmed
- ☐ Consent obtained
- ☐ Maternal sample sent
- ☐ Compatible blood available
- ☐ Donor Hct documented
- ☐ Blood appropriately irradiated/leukodepleted
- ☐ Ultrasound machine checked
- ☐ Procedure tray complete
- ☐ IV access secured
- ☐ Fetal status documented
- ☐ Placental location/access site confirmed
- ☐ Hydrops status documented
- ☐ Emergency delivery/neonatal support available

DURING IUT

- ☐ Fetal paralysis/analgesia administered as indicated
- ☐ Intravascular position confirmed
- ☐ Pre-transfusion fetal Hct obtained
- ☐ Transfusion volume independently verified
- ☐ No air in circuit
- ☐ Volume transfused documented
- ☐ Continuous fetal heart-rate surveillance
- ☐ Complications recognized and managed promptly

AFTER IUT

- ☐ Post-transfusion Hct obtained
- ☐ FHR documented
- ☐ MCA-PSV documented
- ☐ Hydrops reassessed
- ☐ Next surveillance/IUT planned
- ☐ Delivery plan reviewed
- ☐ Complete procedural documentation

Figure 8: Summary of IUT checklist: Ready Reckoner

WHEN TO STOP FETAL TRANSFUSIONS

IUTs are generally not performed after **35+0 weeks of gestation**.

TIMING OF DELIVERY

Labor is induced approximately **three weeks after the**

last IUT, typically at **37+0 or 38+0 weeks of gestation**, or caesarean birth is scheduled if indicated for standard obstetric indications. Delaying delivery until term gestation has the advantage of allowing hepatic maturity, which can result in enhanced bilirubin conjugation and a decreased need for exchange transfusion.

11. OUTCOMES

Short-term outcome

Intravascular transfusion significantly enhances survival for fetuses severely affected by Rh isoimmunization, with overall survival rates exceeding 80%. Non-hydropic fetuses demonstrate even better outcomes, with survival rates over 90%, whereas hydropic fetuses have around 70% survival following intrauterine treatment. Notably, when hydrops is reversed through intrauterine transfusion, survival rates can soar to 98%, compared to just 39% when hydrops persists. Fetuses who undergo intrauterine transfusions typically need fewer days of phototherapy but may require additional red blood cell transfusions compared to those who do not receive this procedure. Recent studies have indicated survival rates of up to 90% in hydropic fetuses, with a reported average survival rate of 93% across various studies. The mean gestational age at delivery for these cases was approximately 34.5 weeks (±1.94 weeks), underscoring the effectiveness of intrauterine treatment in improving perinatal outcomes.

Erythropoiesis suppression is not unusual following multiple intravascular transfusions. These newborns have essentially no reticulocytes in their blood, with donor red blood cells making up the majority of their blood volume. Passively acquired maternal antibodies are retained in the neonatal circulation for a few weeks since exchange transfusion is rarely necessary for these babies. As a result, the baby may require multiple top-up red cell transfusions over the course of one to three months.

Long-term outcome

Advancements in fetal treatment techniques have significantly improved the survival rates of critically ill and severely anemic fetuses. The frequency of neurodevelopmental damage in children who received intrauterine transfusions for fetal alloimmune anemia is rather low, at 4.8%, according to a study called the LOTUS trial, which involved 291 infants followed for up to 8 years. In particular, it was found that 6 children (2.1%) had cerebral palsy, 9 children (3.1%) had severe developmental delays, and 3 children (1.0%) had bilateral deafness.

12. COMPLICATIONS

Each technique used for intrauterine blood transfusion carries potential complications that might necessitate emergency delivery and lead to preterm birth, along with its associated risks and potential perinatal death. Preterm prelabor rupture of membranes (PPROM), infection (chorioamnionitis), preterm labor, and fetal distress (non-reassuring fetal heart rate patterns) are recognized consequences following intrauterine blood transfusion. Furthermore, the necessity of repeated transfusions may raise the possibility of further antibody production, which could worsen the fetal hemolytic state by increasing antibody sensitization. Additionally, if the infant receives a transfusion while still in the womb, it may decrease the baby's own red blood cell production, necessitating further transfusions throughout and after the baby is born.

Over the years, intrauterine transfusion has a become a safer procedure. In a retrospective review of more than 1600 transfusions over 27 years, the procedure-related perinatal loss declined from 4.7% to 1.8% per fetus (P = 0.053)

13. CONCLUSION

Intrauterine intravascular transfusion (IUT) represents a critical intervention for managing severe fetal anemia, particularly in cases of Rh-isoimmunization and other hemolytic disorders. Advances in imaging techniques, such as Doppler ultrasound, have significantly improved the identification and management of affected fetuses, enabling timely and effective treatment. Despite the reduced need for IUT due to prophylactic anti-D immune globulin, its use remains essential in certain settings, especially in low and middle-income countries. The procedure, while generally safe, requires careful planning and monitoring to minimize risks such as preterm labor and fetal distress. Ongoing improvements in technique and management strategies have enhanced both short-term survival and long-term outcomes for treated fetuses. However, the complexity of IUT necessitates a multidisciplinary approach to ensure optimal results and mitigate potential complications. As with any medical procedure, continued research and refinement are vital to further improve safety and efficacy.

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Management of a neonate with Rh isoimmunization: A Practical Approach

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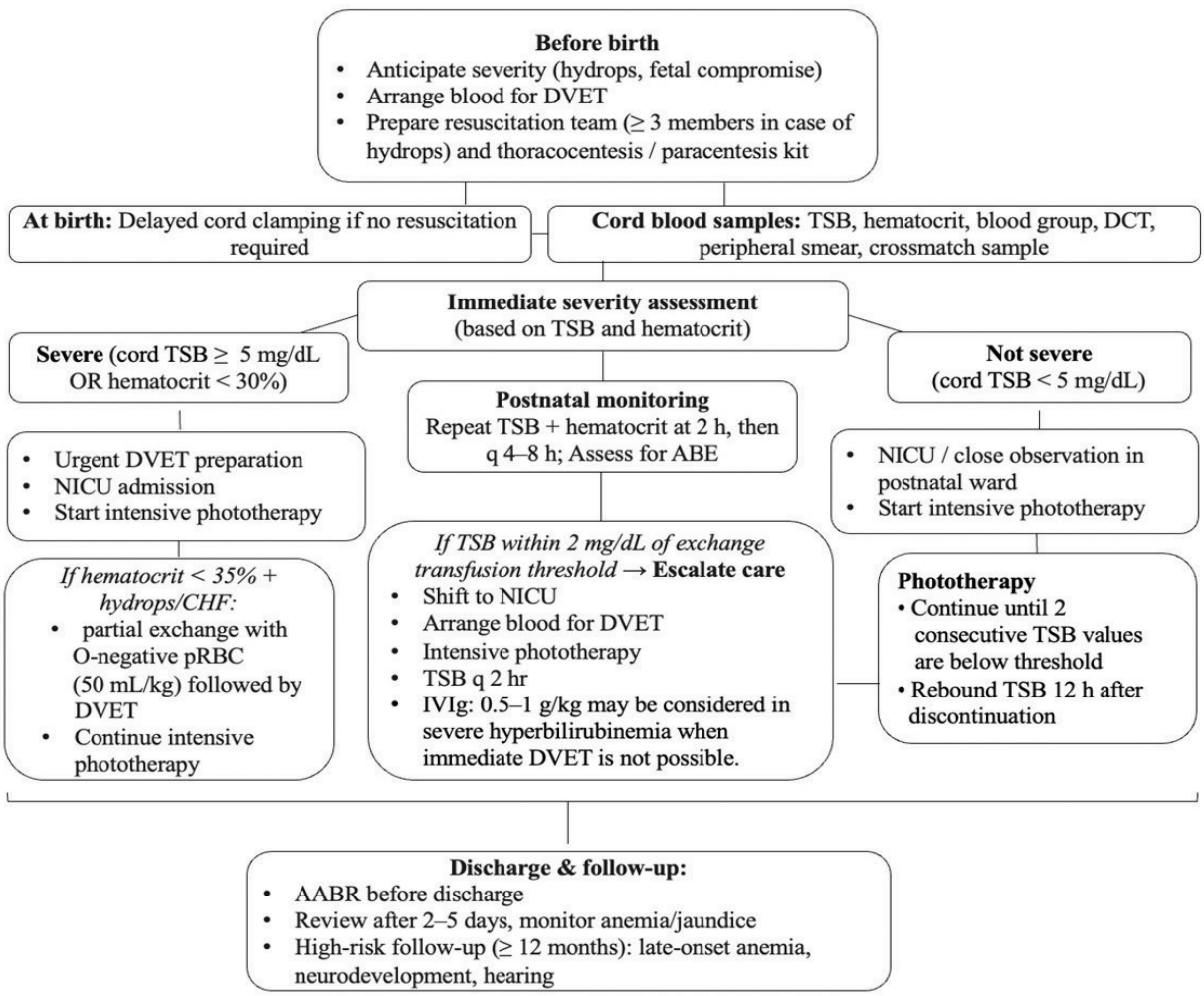
1. INTRODUCTION

Rhesus (Rh) hemolytic disease is the most common form of hemolytic disease of the fetus and newborn (HDFN), classically presenting with fetal or neonatal anemia and severe hyperbilirubinemia. In the absence of treatment, Rh HDFN has been associated with substantial risks of stillbirth (11%), neonatal mortality (24%), and kernicterus (13%).[1] With timely and appropriate antenatal and postnatal management, however, survival exceeds 90%.

Neonatal preparedness for Rh isoimmunization should begin before birth. These infants should preferably be delivered at a center with experience in managing severe hemolytic disease, with neonatology, obstetrics/fetal medicine, and transfusion medicine teams communicating in advance. The current review summarizes a practical approach to the management of Rh-hemolytic disease of newborn, in an Indian context. It may be noted that much of the available guidance is based on expert consensus rather than high-quality direct evidence. Flowchart 1 briefly outlines the neonatal management of Rh hemolytic disease.

Flowchart 1: Neonatal management of Rh hemolytic disease

(Abbreviations: AABR automated auditory brainstem response, ABE acute bilirubin encephalopathy, CHF congestive heart failure, DCT direct Coombs test, DVET double volume exchange transfusion, IVIg intravenous immunoglobulin, pRBC packed red blood cell, NICU neonatal intensive care unit, TSB total serum bilirubin)



2. MANAGEMENT IN THE DELIVERY ROOM

2.1 Delivery preparedness

- The neonatal team should be informed of the antenatal severity and planned timing of delivery. Particular attention is required when severe fetal anemia or hydrops have been documented. Blood should be arranged for anticipated exchange transfusion before the delivery. The required blood volume and preparation are described in the subsequent section.
- Infants with hydrops may have significant pleural effusions or ascites causing respiratory compromise and impaired ventilation. A suitably trained resuscitation team of at least three team members should therefore be present, with equipment immediately available for emergency thoracocentesis and/or paracentesis when clinically indicated.
- Respiratory compromise should be anticipated, particularly in infants with hydrops, severe anemia or prematurity. The resuscitation team should be prepared for respiratory support, including surfactant administration when indicated.

2.2 Immediate postnatal management

- If the infant does not require resuscitation, cord clamping should be deferred for at least 60 seconds, as it may improve hematocrit and reduce subsequent transfusion requirements.[2]
- Cord blood should be sent immediately for:
  - Total serum bilirubin (TSB)
  - Hematocrit
  - Blood group typing
  - Direct Coombs test (DCT)
  - Peripheral smear for evidence of hemolysis (schistocytes, nucleated red blood cells, reticulocytosis and polychromatophils)
  - Crossmatching
- Following one or more intrauterine transfusions (IUTs), interpretation of blood grouping and DCT requires caution: the infant may appear Rh-negative because of circulating donor red cells, and the DCT may be negative. In such cases, infant's blood group should be repeated at 6 months of age.

2.2.1 Exchange transfusion

- A cord TSB ≥ 5 mg/dL or hematocrit < 30% should prompt preparation for urgent DVET and transfer to the NICU. For DVET, the total blood volume can be calculated as:

  DVET blood volume = 2 × birth weight × blood volume + 20 mL for tubing loss

- Blood volume is approximately 80-90 mL/kg in term infants and 90-100 mL/kg in preterm infants, and can be estimated using Rawling's chart. The preferred preparation consists of two-thirds ABO-compatible Rh-negative pRBCs suspended in one-third AB plasma. In case the infant's blood group is unknown and urgent DVET is required, O-negative pRBCs suspended in AB plasma may be used. Use of leucodepleted and irradiated blood products is strongly recommended in neonates to minimize the risk of cytomegalovirus infection and graft-versus-host disease. Additionally, it is preferable, although not mandatory, to use fresh blood (< 5 days) for exchange transfusion.
- The 2022 American Academy of Pediatrics (AAP) guidance recommends reconstituted blood with a hematocrit of approximately 40% for exchange transfusion, providing a higher plasma/albumin concentration; however, superiority over other preparations has not been established.[3]
- DVET should be performed under continuous cardiorespiratory monitoring. Commonly reported adverse events include thrombocytopenia, hypocalcemia, necrotizing enterocolitis. Exchange transfusion is a resource-intensive procedure and should therefore be anticipated rather than arranged after deterioration has occurred. The required blood should be available before delivery in all cases.
- In case of severe anemia (hematocrit < 35%) with hydrops or features of cardiac failure, partial exchange transfusion (PET) with O-negative or other compatible pRBCs should be performed before double-volume exchange transfusion (DVET). In this scenario, PET helps rapidly improve anemia and oxygen carrying capacity without subjecting the hemodynamically unstable and severely anemic neonate to the longer DVET procedure. At the author's unit, PET is done with 50 mL/kg pRBC. Once stabilized, DVET can be done.

2.2.3 Phototherapy

- Intensive phototherapy should be initiated as early as possible in confirmed cases. In experienced centers, neonates with milder involvement may safely be managed in the postnatal ward, provided that effective phototherapy and frequent jaundice assessment can be carried out. However, if the jaundice is rising rapidly or intensive uninterrupted phototherapy can not be provided at the mother's side, it is prudent to shift

the neonate to the NICU for further management.

3. POSTNATAL PERIOD

3.1 Assessment of jaundice and anemia

- TSB and hematocrit should be reassessed at 2 hours of life and subsequently every 4-8 hours, depending on clinical severity. Phototherapy and exchange transfusion thresholds should be determined using the AAP 2022 charts for infants ≥ 35 weeks' gestation (charts for neonates with 'neurotoxicity risk factors') and the National Institute for Health and Care Excellence (NICE) 2010 charts for infants < 35 weeks.[3,4]
- Intensive phototherapy should be continued until two consecutive TSB values are below the treatment threshold; a rebound TSB should be obtained 12 hours after stopping phototherapy.5 The infant should also be monitored for worsening anemia and clinical features suggestive of congestive heart failure.

3.2 Escalation of care

- A TSB value within 2 mg/dL of the exchange transfusion threshold warrants escalation of care, including NICU admission, intensive phototherapy, and preparation for DVET. Feeding intake should be optimized, and intravenous hydration considered if oral intake is insufficient.3
- DVET should be undertaken when the TSB reaches the relevant exchange transfusion threshold despite intensive phototherapy, or earlier if there are clinical features of acute bilirubin-induced neurological dysfunction. A rapidly rising bilirubin despite phototherapy is an additional warning sign; some units consider DVET if the rate of rise of TSB is > 0.5 mg/dL/hr.
- Intravenous immunoglobulin (IVIg), at 0.5-1 g/kg over 2 hours, has been suggested for infants with isoimmune hemolytic disease and severe hyperbilirubinemia, particularly when immediate DVET is not possible. The dose may be repeated after 12 hours.3 However, the evidence for benefit remains uncertain, and a few studies have suggested an increased risk of necrotizing enterocolitis with IVIg. The NNF Clinical Practice Guidelines do not recommend IVIg for prophylactic or therapeutic use in neonatal hyperbilirubinemia secondary to alloimmune hemolysis.[5]

3.3 Management of anemia

- Anemia without severe jaundice can be managed with pRBC transfusion. At the author's center, a hematocrit threshold of 25% is used to guide pRBC transfusion prior to discharge. When transfusion is required, at least 15 mL/kg should be administered, at a rate not exceeding 5 mL/kg/hour. The transfused volume can be calculated using the following formula:

A desired hematocrit of 35% and pRBC hematocrit of 75% may be assumed.

- Folate supplementation should be considered because of increased erythropoietic demand. The author's center prescribes folate 2.5 mg once weekly (half of a 5-mg tablet) until 3 months of age in affected neonates.
- Late-onset, hypo-regenerative anemia is a well-described complication of Rh isoimmunization, particularly following IUT, DVET or pRBC transfusion. Ongoing hemolysis and suppression of erythropoiesis may result in anemia during the first few weeks to months of life. One small randomized trial reported that weekly darbepoetin until 8 weeks of life may reduce the number of transfusions required in infants treated with IUT, but its role remains uncertain.6single-centre, phase 2 randomised controlled trial to evaluate the effect of darbepoetin alfa on the number of erythrocyte transfusions in infants with haemolytic disease of the fetus and newborn. All infants who were treated with intrauterine transfusion and born at 35 weeks of gestation or later at the Leiden University Medical Center, Leiden, Netherlands, were eligible for inclusion. Included infants were randomised by computer at birth to treatment with 10 µg/kg darbepoetin alfa subcutaneously once a week for 8 weeks or standard care (1:1 allocation, in varying blocks of four and six, with no stratification
- Rarely, Rh-isoimmunized infants may also develop thrombocytopenia or neutropenia; these abnormalities generally follow a benign course and can be managed conservatively.[7]

3.4 Neurological and hearing assessment

- The infant should also be assessed repeatedly for bilirubin-induced neurological dysfunction (BIND). M-BIND scoring, incorporating mental status, muscle tone, cry characteristics and eye movements, provides a structured approach to neurological surveillance.
- Hearing loss is a characteristic abnormality associated with BIND, although its incidence has decreased with improved management, reported in approximately 1% of infants from a large western cohort.8 Automated auditory brainstem response (AABR) hearing screening should preferably be completed before discharge for all

affected neonates to ensure timely intervention.

4. DISCHARGE AND FOLLOW-UP

- The managing neonatal unit should develop systems to facilitate the postnatal follow-up for discharged infants for the assessment of jaundice and anemia and for readmission, if needed, for phototherapy and/or pRBC transfusion. The first follow-up should preferably be done within 2-5 days of discharge.
- pRBC transfusion should be considered when hematocrit falls below 21%, or below 25% if the infant is symptomatic (poor feeding, inadequate weight gain, respiratory distress). The risk of anemia requiring transfusion decreases after first 3-4 months of life.
- All Rh-isoimmunized infants should be followed in a high-risk clinic, with particular attention to hematological status, hearing and neurodevelopment, until an age of at least 12 months.
- Hyperferritinemia is common in Rh hemolytic disease, particularly among infants who have received IUT.9iron supplementation may be unnecessary or potentially even harmful. However, there is a paucity of literature to make evidence-based recommendations.\nMETHODS: All neonates with Rh isoimmunization and evidence of fetal anemia were eligible for inclusion in this cohort study. Primary outcomes were serum ferritin and hemoglobin at birth, 3, 6, 9, and 12 months. Additional outcomes were the requirement of top-up transfusion and iron therapy during infancy. Iron supplementation was given only if ferritin was <30 mcg/L. Subgroup analysis was performed based on receipt of intrauterine transfusion (IUT Early iron supplementation may therefore be avoided. In the author's unit, iron at 2–3 mg/kg/day is started at 12 months in infants who received IUT and at 6 months in those who did not.

5. KEY POINTS

- Prepare before delivery: Anticipate severity, involve neonatology and transfusion teams, and ensure blood is readily available.
- Assess immediately: Obtain cord TSB, hematocrit, blood group, DCT, smear and crossmatch sample.
- Treat before bilirubin injury occurs: Start intensive phototherapy early and escalate care as the TSB approaches the exchange threshold.
- Exchange when indicated: Recognize severe anemia, hydrops and BIND early; perform PET before DVET when severe anemia is accompanied by cardiovascular compromise.
- Continue surveillance after discharge: Monitor for late anemia, jaundice, hearing impairment and neurodevelopment.

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Early Severe Alloimmunization: Novel Noninvasive Therapy Beyond Today: New Evidence, Controversies and Future Directions

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INTRODUCTION

Early-onset severe red cell alloimmunisation with previous poor obstetric outcomes is a major clinical dilemma for the clinician, especially when severe fetal anaemia develops in very early gestation. At pre-viable gestations, intrauterine transfusion (IUT) carries increased procedural risks of fetal loss (8.5%), technical failure, and cord hematoma due to the small calibre of vessel.[1] Emerging research towards bridging the gap until safe IUT or viable delivery becomes feasible focuses on noninvasive therapies targeting maternal pathogenic immunoglobulins and their transplacental transfer such as Intravenous Immunoglobulins (IVIG). A major breakthrough occurred in 1981 when high-dose IVIG successfully treated idiopathic thrombocytopenic purpura, establishing its utility as an immunomodulatory therapy across hematology, neurology, and severe autoimmune conditions.

HISTORY OF IVIG THERAPY

The antenatal use of IVIG for red-cell alloimmunization evolved from isolated reports in the 1980s to more systematic case series from 1990 onwards, as a non-invasive strategy to mitigate severe hemolytic disease of the fetus and newborn (HDFN).[2] Margulies and Voto pioneered high-dose maternal IVIG administration, demonstrating that competitive blockade of placental Fc receptors and fetal reticuloendothelial Fcγ receptors could blunt hemolysis and antibody transport. An early 1991 experience included 24 women with severe anti-D sensitisation; IVIG 0.4 g/kg was administered on 4-5 consecutive days and repeated after 2-3 weeks, with reductions in anti-D titres and fetal anaemia. By 1997, a series on 69 women suggested a more favourable fetal course when IVIG was given before 20 weeks and IUT deferred until after 21 weeks, including a reported 36% reduction in fetal mortality.[2] An individual patient data meta-analysis (97 cases vs. 97 controls) demonstrated that maternal IVIG significantly delayed the timing of the first IUT (mean difference: 3.19 weeks compared to prior affected pregnancies).[3]

MECHANISM OF ACTION

The proposed actions of IVIG are complementary rather than singular: it may dilute the effective maternal alloantibody load, compete for placental Fc-mediated transport and reduce phagocytic clearance of antibody-coated fetal erythrocytes.[4] PETIT also discussed accelerated antibody turnover, a reduction in circulating maternal alloantibody and dampening of fetal macrophage activity. These effects may slow the haemolytic process; they do not restore haemoglobin once significant fetal anaemia is already present.[5] More recent mechanistic synthesis extends this model to suppression of B-cell activity and saturation of FcRn, alongside Fc-receptor blockade.[6]

CLINICAL EVIDENCE AND OUTCOMES

PETIT was a multi-centre retrospective comparison of 24 IVIG-treated pregnancies and 28 pregnancies managed without IVIG, all following a prior pregnancy with severe HDFN.[5] Relative to the preceding pregnancy, fetal anaemia appeared 15 days later with IVIG and 25 days later when treatment began before 13 weeks; however, the adjusted difference between treated and untreated groups was only 4 days and did not reach statistical significance (P=.564).[5]

Despite that statistical limitation, hydrops was observed in 4% versus 24%, and neonatal exchange transfusion in 9% versus 37%, in IVIG and non-IVIG pregnancies, respectively.[5] The 2023 case-control experience included 22 treated pregnancies. Two avoided IUT altogether; among women whose previous pregnancies ended in early loss, IVIG was associated with higher fetal haemoglobin and better perinatal survival.[7] For women with a previous loss before 20 weeks, the first transfusion in the subsequent treated pregnancy was postponed to at least 19.9 weeks, with a mean of 23.2 weeks.[7]

A single-centre study in India reported a cohort of 34 women with early severe alloimmunization and previous poor pregnancy outcomes, amongst whom 17 received IVIG and another 17 did not. They reported that the IVIG group had a reduced incidence of fetal hydrops and preterm delivery.[8]

WHERE IVIG FITS: PATIENT SELECTION AND TIMING

A clinical practice guideline recommends IVIG administration in an antigen-positive fetus when a previous pregnancy was complicated by fetal anaemia or HDFN-related loss before 24 weeks.[9] It also allows consideration in an antigen-positive pregnancy with an initial anti-D titre

of at least 512 or Kell titre of at least 64, even in the absence of a previously affected pregnancy. Fetal antigen status should therefore be defined early; the same guideline supports maternal cell-free fetal DNA testing after 10 weeks for RhD, RhC, Rhc, RhE, Kell and Fya. Importantly, both IVIG recommendations received unanimous panel agreement, yet the certainty of the supporting evidence was graded very low.[9]

PRACTICAL USE AND SURVEILLANCE

The therapeutic window is deliberately early. In the international Delphi exercise, 10-14 weeks garnered the strongest support for commencement. The preferred schedule was 1 g/kg weekly without a loading dose.[10]

While IVIG therapy is administered, middle cerebral artery peak systolic velocity (MCA-PSV) and signs of hydrops should be assessed weekly; once Doppler surveillance suggests fetal anaemia, IVIG is discontinued, and IUT becomes the treatment pathway.[10] There is still no randomised evidence defining the ideal gestation for initiation, and regimen decisions therefore remain individualised within an experienced fetal-therapy service.[5]

IVIG AS A BRIDGE TO IUT

For clinical practice, IVIG is best regarded as a gestational bridge: the intention is to buy time until IUT can be undertaken beyond the most vulnerable early window, not to replace transfusion. This is consistent with current guideline interpretation: many treated fetuses will ultimately require IUT, but the first procedure may be later and undertaken before anaemia becomes as profound.[4]

BENEFITS, DISADVANTAGES AND CONTROVERSIES

Accordingly, the pragmatic endpoint is not freedom from transfusion but a safer gestational age at which the first IUT is done beyond 18-20 weeks. This potential gain comes at substantial resource cost: the RCOG Scientific Impact Paper cites an approximate weekly IVIG cost of ?4,800 [4]. Indian makers price a 5 gms vial for approximately Rs 8,000 and a weekly expenditure would amount to nearly INR80-90,000. Infusion-related symptoms are frequent and generally minor; serious immediate reactions and delayed complications are much less frequent but need to be part of counselling, consent and monitoring.[4]

The major evidentiary weakness remains unchanged: the Cochrane review identified no randomized trial evidence, with benefit inferred largely from case series.[2] Later reviews have added more observational data, but heterogeneity in populations, treatment schedules and outcome definitions, together with the lack of large randomized trials, still limits certainty.[6] IVIG therefore belongs in selected, exceptionally high-risk pregnancies rather than as routine therapy for red-cell alloimmunization.

RECENT ADVANCES: NIPOCALIMAB

Nipocalimab offers a more targeted biological strategy. By blocking FcRn, it lowers circulating IgG and interferes with the receptor pathway responsible for maternal IgG transport across the placenta.I ts action is more focussed as compared to IVIG (Table 1). In the UNITY trial 13 women at high risk of early severe HDFN received weekly Nipocalimab. Amongst these seven (54%) women delivered at or beyond 32 weeks without IUT; six required IUT, with the first procedure at a median of 28+3 weeks.[11] These findings have provided the rationale for the ongoing phase 3 AZALEA trial, which is evaluating Nipocalimab in a larger cohort of pregnancies at risk of severe HDFN. Unlike the single-arm UNITY study, AZALEA is a randomised, double-blind, placebo-controlled multicentre trial designed to determine whether FcRn blockade can meaningfully reduce fetal anaemia and the need for invasive fetal therapy.[12] Until these confirmatory data are available, Nipocalimab should be regarded as a promising disease-modifying therapy rather than a replacement for established surveillance and IUT in routine clinical practice.

Table 1: Molecular action of IVIG and Nipocalimab

Feature	Intravenous Immunoglobulin (IVIG)	Nipocalimab
Molecule Type	Pooled, polyclonal human donor IgG	Recombinant, targeted monoclonal antibody (anti-FcRn)
Target Specificity	Non-specific; broad saturation of FcRn and Fcγ receptors	Highly specific; targeted FcRn receptor blocker
Maternal IgG Lowering	Modest acceleration of general IgG catabolism	Profound, rapid targeted degradation of maternal IgG/ anti-D
Placental Transfer Inhibition	Competitive saturation (mass-action displacement)	Complete physical/ competitive blockade of FcRn transcytosis
Fetal Action	Direct blockade of fetal splenic/hepatic macrophage Fcγ receptors	Upstream prevention; stops maternal antibody entry into fetal circulation

IVIG: HOPE, HYPE OR HERE TO STAY?

IVIG is here to stay and occupies a narrow but clinically relevant space: it is neither definitive therapy nor a treatment for established fetal anaemia, but it may buy valuable gestational time in pregnancies expected to develop HDFN very early. Whether that role expands will depend on prospective multicentre evidence and better definition of dose and timings.FcRn blockade may eventually provide a

more specific approach; until randomised data mature, it should remain investigational rather than routine.

Algorithm: Early Severe Alloimmunization - Where IVIG Fits in Modern Management

1. Confirm fetal antigen status

Establish fetal antigen status with maternal cell-free fetal DNA after 10 weeks for RhD, RhC, Rhc, RhE, Kell or Fya alloimmunization.

↓

2. Identify a high-risk pregnancy

Consider IVIG when an antigen-positive fetus follows a pregnancy complicated by fetal anaemia or HDFN-related loss before 24 weeks; very high anti-D or Kell titres are an additional consideration.

↓

3. Start early

If IVIG is chosen, the Delphi panel most strongly favoured starting between 10 and 14 weeks.

↓

4. Dose

Use IVIG 1 g/kg weekly without a loading dose, the regimen favoured by Delphi consensus.

↓

5. Monitor

Continue weekly MCA-PSV surveillance during treatment.

↓

6. If fetal anaemia is suspected

When Doppler findings indicate fetal anaemia, discontinue IVIG and plan IUT.

↓

7. Continue definitive fetal therapy as required

If serial IUT is required, the 2025 guideline supports continuing transfusions through the end of 35 weeks unless technical constraints preclude this.

IVIG = intravenous immunoglobulin; MCA-PSV = middle cerebral artery peak systolic velocity; IUT = intrauterine transfusion; HDFN = haemolytic disease of the fetus and newborn.

KEY POINTS

1. Think of IVIG as disease-modifying rather than haemoglobin-restoring: it may slow haemolysis but cannot correct established fetal anaemia.
2. The clearest candidates are antigen-positive pregnancies with a history of very early severe HDFN; exceptionally high anti-D or Kell titres may also warrant discussion.
3. When used, an early weekly regimen with weekly MCA-PSV assessment is the prevailing expert-consensus approach, with transition to IUT once anaemia is suspected.
4. Nipocalimab is biologically attractive as an FcRn-targeted option, but routine use should await randomised evidence.

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Calendar for AOGD Monthly Clinical Meeting 2026-2027

30th October 2026	DDU Hospital
27th November 2026	MAMC & LNJP Hospital
18th December 2026	Sir Ganga Ram Hospital
29th January 2027	Dr RML Hospital
26th February 2027	UCMS & GTB Hospital
19th March 2027	LHMC & SSK Hospital
30th April 2027	ESI, Basaidarapur Hospital

Journal Scan

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A CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF PREGNANCY ALLOIMMUNIZED TO RED BLOOD CELL ANTIGENS MOISE KJ JR, MARKHAM KB, SPINELLA PC ET AL. JAMA NETW OPEN. 2025 NOV;8(11)

Red Cell Alloimmunization in Pregnancy: Summary of the 2025 Guideline

Background: Red cell alloimmunization, consequent to transplacental transfer of incompatible fetal red blood cells (RBC) into maternal circulation, affects subsequent pregnancies with hemolytic disease of fetus and neonates (HDFN). Rhesus D (RhD) is the most antigenic and accounts for majority of HDFN, although alloimmunization to the Rhc, RhE, and Kell antigens are associated with severe HDFN.

Development of guidelines: The 2025 JAMA Network Open guideline by Moise et al., developed via multidisciplinary involvement of four working groups (trauma and transfusion medicine, hematology, maternal-fetal medicine/obstetrics, and neonatology). The evidence on key clinical knowledge gaps was provided as systematic reviews and metaanalyses by library scientists at Johns Hopkins University, addressing six PICO questions. These were then refined by Delphi consensus as recommendations and practice points, updates the management

Six recommendations were developed by the maternal-fetal medicine/obstetrics working group.

- **Recommendation 1: Determination of Fetal Red Blood Cell Antigen Status by cell-free fetal DNA (cffDNA)**
- Use of maternal cffDNA is recommended to accurately determine the fetal RBC antigen status and identify the at-risk fetus early in pregnancy. This is recommended after 10 weeks' gestaional age in pregnancies complicated by RhD, RhC, Rhc, RhE, Kell or Fya alloimmunization.
- The major change: cell-free fetal DNA testing after 10 weeks is now recommended for RhD, RhC, Rhc, RhE, Kell, and Fya alloimmunization (92.5% Delphi agreement, moderate certainty; ~100% sensitivity, ~98% specificity across 49 studies).
- This shifts care from surveillance of all alloimmunized pregnancies to targeting only antigen-positive fetuses, sparing antigen-negative pregnancies unnecessary monitoring.
- cffDNA was also favored over monitoring with MCA Doppler, as monitoring is not needed in an antigen-negative fetus saving unnecessary burden. Also, false positive MCA-PSV Doppler would unnecessarily lead to avoidable amniocentesis for fetal genotyping
- **Recommendation 2: Immunomodulation with intravenous immune globulin (IVIG) in select cases:**
- **Use of IVIG is recommended in patients with a documented antigen positive fetus with**
- **(2a) History of either fetal anemia or a fetal loss due to HDFN before 24 weeks' GA in a previous pregnancy.**
- **(2b) V**ery high titers (anti-D ≥512, anti-Kell ≥64), **regardless of prior pregnancy history.**
- **Gestational age at first IUT improves with IVIG treatment by 3.19 weeks. Also, fetus will have less severe anemia at the first procedure. IUTs performed before 20 weeks' gestation have a 3-fold increased perinatal loss compared to those performed later..**
- IVIG is not routine treatment and is reserved for high-risk cases. L**ower threshold is considered for** anti-K as it causes anemia partly via erythropoiesis suppression, not just hemolysis.

Recommendation 3 and 4: Earlier surveillance with MCA-PSV Doppler measurements to detect fetal anemia earlier
Weekly MCA-PSV should start by 16 weeks once antigen-positive status and critical titer (≥16 generally, ≥4 for Kell) or if there is history of HDFN in an antecedent pregnancy. The >1.5 MoM threshold for suspected significant anemia is unchanged.
The risk of significant disease in a low-titer pregnancy shoulds be weighed against the 12% false-positive rate of MCA-PSV screening for anemia, which would result in unnecessary invasive procedures with procedure related risks.
Weekly monitoring allows for early diagnosis of fetal anemia. Intraperitoneal transfusions as early as 15 weeks' gestation have been reported as a successful method of bridging the need for IUTs until a later gestational age when fetal intravascular access is more easily. Also, weekly monitoring with MCA doppler minimizes the risk of missing affected cases due to false-negative results.
Recommendation 5: Duration of intrauterine transfusion therapy (IUT)
Continuation of IUT is recommended until the end of the 35th week of pregnancy if technically feasible. (97.6% Delphi agreement).
Continuation of IUT till 35 weeks will allow a more advanced gestational age at delivery, thereby decreasing the risks of neonatal respiratory, infectious and neurologic morbidities which are highest in the late preterm infant. Also, a more advanced gestational age at delivery allows hepatic maturity with subsequent lesser need for neonatal exchange transfusion.
Recommendation 6: Delivery time for allo-immunised pregnancy not requiring intrauterine transfusion (IUT)
In these women who not not received an IUT, delivery is recommended at 37^{+0} to 38^{+6} weeks regardless of titer (92.7% Delphi agreement)

Comparison with Society for Maternal-Fetal Medicine (SMFM) 2015 guidelines

Following aspects differ with the SFMF guidelines:

1. **The routine use of cffDNA was not addressed in SMFM. Also its uses as early as 10 weeks' gestation is much earlier than the suggested 16-20 weeks gestation suggested in RCOG-2014.**

2. **IVIG use in cases with a history of early onset of HDFN or severe red blood cell alloimmunization was not previously addressed in SFMF or RCOG**

3. **Use of a Kell titer >4 for threshold for beginning MCA-PSV surveillance for fetal anemia was not addressed in SMFM, though RCOG guideline suggested that severe anemia can occur even at low Kell titers.**

4. **SMFM guidelines suggested initiating MCA-PSV Doppler at 18 to 20 weeks gestation; RCOG does not specify specific gestational age.**

5. **The continuation of IUTs until 35 weeks' gestational age and postponing delivery until a later gestational age is the new recommendation unlike proposed traditionally**

- **Hence the bigger shift** is toward risk-stratified care: antibody screening → identify significant antibody → cffDNA fetal antigen testing → surveil only true at-risk fetuses → MCA-PSV once thresholds are met → fetal blood sampling/IUT as needed → prolong pregnancy safely → deliver at 37–38+6 weeks if no IUT required.
- **Caveat:** Despite precise-sounding thresholds, most recommendations rest on very low-certainty evidence, given how rare severe alloimmunization is and how hard trials are to run. These recommendations should guide, not replace, specialist fetal-medicine judgment.
- **Bottom line:** Identify the antibody, determine if the fetus is actually at risk via cffDNA, treat Kell with extra caution, use MCA-PSV as the core surveillance tool, reserve IVIG for severe/early cases, extend IUT to 35 weeks when feasible, and avoid over-early delivery—all within multidisciplinary care.

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HER story.. HER Words..
A Rare Rh Pregnancy, An Extraordinary Journey

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Anti-Rh17 alloimmunisation is exceptionally rare, associated with severe fetal anaemia and significant challenges in pregnancy, particularly because compatible blood is extremely difficult to source. For this mother, the journey was made even more difficult by two previous pregnancy losses with significant challenges with blood availability. Her next pregnancy was therefore planned even before conception, with close coordination between the fetal medicine, haematology and transfusion teams. What followed was a journey of careful planning, uncertainty, courage and extraordinary teamwork.

Q1. After experiencing two previous pregnancy losses, what made you decide to try again?

After everything I had been through, trying again was not an easy decision. There was always a fear in the back of my mind that history might repeat itself. But I wanted to complete my family. This time, I decided that if I was going to try again, I wanted to do it with proper planning and with the best care possible. So, even before I became pregnant, I came to AIIMS and discussed everything with the doctors. Knowing that we were planning the pregnancy together gave me a sense of hope.

Q2. How did you feel knowing that this pregnancy was being planned and monitored so carefully from the very beginning?

It gave me a lot of confidence. After my previous experiences, I was naturally very scared. But this time, I felt that there was a plan for every step. The doctors were involved even before I conceived, and throughout the pregnancy I was closely followed. I always knew what was happening and why. That made me feel that I was not facing this pregnancy alone.

Q3. Till around 26 weeks, things were going well. What went through your mind when you were told that your baby now needed treatment?

That was probably one of the most frightening phases for me. Until then, everything had been going well, and suddenly I realised that we had reached a stage where my baby might need a transfusion. My biggest worry was whether the right blood would be available when we needed it. I kept wondering, *"How long will it take to arrange the blood? What if it is not available in time? Will everything be ready when my baby needs it?"*

Q4. During your pregnancy, what do you remember about the process of arranging everything you needed for your treatment?

It was overwhelming. I knew that finding compatible blood for my baby was going to be difficult, and I was aware that blood was being arranged from different places, including Lucknow and Japan. I also knew that another patient with the same rare blood group had come forward and donated blood for my baby. That was very emotional for me. Knowing that someone who understood what I was going through was willing to help my baby is something I will always remember. There were many people involved, and I could see how carefully everything was being planned. Knowing that the team was preparing in advance and keeping me informed gave me a lot of confidence, even during the most anxious moments.

Q5. You had to go through repeated admissions, scans and procedures. What helped you keep going during those difficult weeks?

I think it was the trust I had developed in my doctors. Of course, I was scared before every procedure and every admission. But I was always told what was happening and what the next step would be. I also kept reminding myself why I was doing all of this—I wanted to meet my baby. So I just took it one day at a time.

Q6. Your baby is now one year old. How has the journey been for you, looking back?

It is difficult to put it into words. After two losses, there were times when I wondered if I would ever get to bring my baby home. Today, my baby is one year old. When I look back at everything—the fear, the uncertainty, the long admissions, the procedures and all the effort that went into this pregnancy—it all feels worth it. I finally have my baby, and my family feels complete.

CONCLUSION

This story is a reminder that behind every high-risk pregnancy is a patient carrying not only a medical diagnosis, but also her own history of fear, loss and hope. For this mother, the journey from previous pregnancy losses to a carefully planned pregnancy was filled with uncertainty, but also with trust and extraordinary human support. Her experience also highlights the power of multidisciplinary care and collaboration. From preconception planning to repeated fetal interventions and the search for rare compatible blood, many people worked together towards one shared goal.

Patient Information Sheet : Rh Alloimmunisation In Pregnancy

Saloni Kamboj[1], Anubhuti Rana[2]
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What is Rh alloimmunisation?

When your blood group is Rh-negative, while your baby's blood group may be Rh-positive, it can result in Rh alloimmunization. It rarely happens in first pregnancy but your body may form antibodies against the baby's red blood cells and can affect future pregnancies. These antibodies can cross the placenta and destroy the red blood cells of an Rh-positive baby and cause anaemia.

Why is it important?

If the antibodies report shows critical titre, the baby may develop:

- Moderate to severe anaemia
- Swelling of the baby due to accumulation of fluid (hydrops)
- Heart failure
- Jaundice and anaemia after birth
- In severe untreated cases, fetal death

However, it is preventable and regular monitoring with timely treatment can significantly improve the outcome.

How will my pregnancy be monitored?

Your doctor may advise:

1. Blood tests
    - o Blood group and antibody testing
    - o Measurement of antibody levels/titre at regular intervals
2. Ultrasound examination
    - o To assess the baby's growth and wellbeing
    - o To look for any signs of anaemia (by MCA Doppler) or fluid accumulation

What happens if the baby develops severe anaemia?

If significant anaemia is suspected, you will be referred to a fetal medicine specialist, who upon further evaluation may advice Intrauterine blood transfusion (IUT). The goal of intrauterine transfusion are to prevent or treat fetal heart failure (hydrops), which can be caused by anemia, and to allow the pregnancy to continue so the baby can be more developed when it is born.In an intrauterine transfusion, specially prepared compatible blood is given directly to the baby, usually through the umbilical cord, under continuous ultrasound guidance.

Some babies may require more than one transfusion during pregnancy.

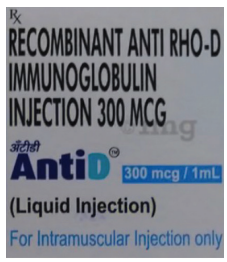
What are risks associated with the procedure?

Fetal bradycardia and bleeding from the puncture site are the most common complications of IUT, but usually resolve. Procedure related fetal loss is around 1.6 % and procedure related complications like preterm rupture of membranes, infections, emergency cesarean delivery is around 3%

What are outcomes in alloimmunized pregnancies?

Survival after IUT is over 90 percent in most centres. Survival is less when severe anemia develops before 20 weeks of gestation. During your evaluation, you will be provided with a detailed review of your baby's condition and treatment options in order to help you and your family decide what the best treatment plan may be.

What is Anti-D injection?



Anti-D immunoglobulin is given to eligible Rh-negative mothers to prevent the formation of Rh antibodies.

It may be advised:

- Routinely during pregnancy, according to protocol
- After delivery of an Rh-positive baby
- After events where fetal blood may enter the mother's

circulation, such as bleeding during pregnancy, miscarriage, ectopic pregnancy, invasive procedures, or abdominal trauma

Important: Once significant Rh antibodies have already developed, Anti-D injection cannot remove these antibodies. Your pregnancy will then require appropriate monitoring by your obstetrician/foetal medicine specialist.

Please discuss any questions or concerns with your obstetrician or fetal medicine specialist.

What can you do?

- Attend all scheduled antenatal and ultrasound appointments.
- Carry your blood group and antibody reports with you.
- Inform your doctor immediately if you have vaginal bleeding, abdominal trauma, or any procedure during pregnancy.
- Do not miss recommended blood tests or Doppler examinations.
- Discuss the plan for delivery and newborn care with your treating team.

Know your Drug: Anti- D Immunoglobulin

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WHAT IS ANTI D?

Anti-D immunoglobulin (RhIg) is a passive Antibody used to prevent alloimmunization in an unsensitized RhD-negative pregnant person after exposure to RhD-positive fetal red cells. This aids in preventing the consequent hemolytic disease of the newborn. However, it does not treat established alloimmunization. Postpartum prophylaxis reduced sensitisation from about 13–16% to 0.5–1.8%; with routine antenatal prophylaxis this risk is reduced further to 0.2%.[1]

DRUG CLASS

It is a human immunoglobulin. It is available in both monoclonal and polyclonal preparations. Monoclonal Antibodies are derived from lab grown hybridoma cells capable of unlimited supply; however, it may not cover various epitopes including weak D Antigens. Polyclonal Anti-D immunoglobulin is derived by the pooled plasma of donors with high titers and includes wide variety of epitopes. The half-life of Anti-D is about 23 days.

INDICATIONS

It is offered toan unsensitised RhD-negative patient when the fetus or newborn is RhD-positive or RhD status is unknown:

- As Asroutine antenatal prophylaxis at 28 weeks
- After a potentially sensitising event. Events include antepartum haemorrhage, abdominal trauma, invasive prenatal procedures, external cephalic version, fetal intervention, late miscarriage or termination, stillbirth and delivery.
- Within 72 hours of birth of an RhD-positive infant.

It is not to begiven to a to pregnant mother who is already sensitized to RhD Antigen.[1–4]

MECHANISM OF ACTION

Anti-D binds RhD-positive fetal erythrocytes in the maternal circulation and facilitates their clearance before a maternal immune response develops. It cannot reverse an established immune Anti-D response.

DOSE AND ROUTE OF ADMINISTRATION

A common regimen followed in India is to administer 300 micrograms (1,500 IU) intramuscularly at approximately 28 weeks, and after indicated sensitizing events later in pregnancy, and postpartum. This covers approximately 30 mL fetal whole blood (15 mL fetal red cells). An additional 10ug of Anti-D is required for every 0.5ml of fetal RBCs. International protocols, commonly use 250 IU before 20 weeks and at least 500 IU after 20 weeks, with further doses guided by feto maternal hemorrhage (FMH) testing. Intra-muscular injection into the deltoid is the preferred route, since gluteal injection may lead to the drug reaching only into the subcutaneous layer with consequent delayed absorption and action. The common side effects include redness, myalgia, slight fever, pain or swelling at injection site. Most are mild and self-limiting. Contra-indication includes previous allergic reaction to Anti-D formulation. Intra-venous formulations also exist, but they should be verified before administration.[2–4]

TIMING OF ADMINISTRATION

The ABO/RhD type and the Antibody screen is to be done at booking and repeated at around 28 weeks before routine prophylaxis. Routine prophylaxis of Anti-D should be administered independent of previous use of Anti-D for a sensitizing event earlier in the pregnancy. As per FOGSI GCPR guidelines, routine antenatal prophylaxis should be offered after assessing Indirect Coombs Test (ICT), with a single dose of 300ug of Anti-D immunoglobulin. RCOG also recommends similar schedule and reports that single dose between 28-30 weeks consisting of 300ug of Anti-D is more cost effective, enabling better compliance and logistical benefits. Prophylaxis should be given as soon as possible, ideally within 72 hours of a sensitizing event and after delivery. If delayed, it should be administered promptly rather than being omitted. In the event of repeated uterine bleeding which is clinically judged to represent the same sensitizing event, a minimum dose of 100ug Anti-D Ig should be given at 6 weekly intervals. Feto-maternal hemorrhage (FMH) screening should be performed every 2 weeks from 20 weeks onwards for further management. [1–4]

CONTRAINDICATIONS

It is not to be used prophylactically in RhD-immunized patients, or when the fetus/newborn is reliably RhD-negative. A serious prior hypersensitivity reaction to the specific preparation requires specialist assessment. A positive Antibody screen after recent prophylaxis may reflect passive Anti-D which is reflected usually in titer values of up to 1:4.[2,4]

PRECAUTIONS

Before administering, maternal blood group with RhD type should be verified, antibody history, indication, dose, batch and administration time should be elicited. FMH should be

quantified when indicated after 20 weeks, especially after major trauma, persistent or severe bleeding, intra-operative cell salvage or post-delivery with major hemorrhage. If FMH > 4ml, follow up maternal sample should be taken after 72 hr of intramuscular administration, to assess for clearance of fetal cells.[2–4]

ADVERSE EFFECTS

Injection-site soreness, headache or mild fever can occur. Hypersensitivity and anaphylaxis are rare; Intravenous haemolysis is a concern with inappropriate administration to an RhD-positive recipient. Maternal blood group and results of ICT should be checked before administering.

STORAGE AND HANDLING

The injection should be refrigerated at 2–8 °C; not frozen and protected from light Expiry, appearance and cold-chain integrity must be confirmed before use.

PATIENT COUNSELLING

The patient should be explained thatthat Anti-D prevents sensitization in the current and future pregnancies. After the administration the patient should be asked regardingany fever or adverse local reaction. The dose and date on the antenatal record should be noted. Anti-D is compatible with breastfeeding.[1–3]

KEY TAKEAWAYS

- Confirm maternal blood group and ICT status and then administer Anti-D Ig.
- Give routine prophylaxis at about 28 weeks and postpartum after an RhD-positive birth, with separate doses after indicated events.
- Check FMH when indicated so large bleeds receive adequate coverage.

	ACOG (2024 update)	NICE (2026)	SOGC (2024)	FOGSI GCPR (2022)
POG < 12 weeks	Forgoing Rh testing and Anti-D prophylaxis < 12 weeks	Do not offer Anti-D < 12 weeks	Recommend against Anti-D < 8 week Suggest against Anti-D <12 weeks	150ug of Ant-D
Sensitizing events 12-20 weeks	300ug of anti-D > 12 weeks	At least 50ug (No FMH testing)	300ug of anti-D	150ug of Ant-D
Sensitizing events >20 weeks	FMH testing and anti-D accordingly	Minimum of 100ug + FMH testing (where indicated)	FMH testing and anti-D accordingly	300ug of Ant-D
Routine antenatal Anti-D prophylaxis (RAADP)	Single (300ug) at 28 weeks	Single (300ug) at 28 weeks OR Two doses (100ug) at 28 and 34 weeks	Single (300ug) at 28 weeks OR Two doses (120ug) at 28 and 34 weeks	Single (300ug) at 28 weeks OR Two doses (100ug) at 28 and 34 weeks
Post Delivery	300ug single dose within 72hr + FMH testing for additional dose	At least 100ug + FMH testing for additional dose	120/300ug single dose within 72hr (if missed give till 28 days)	300ug single dose within 72hr (if missed give till 10-28 days)

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Brain Boost Zone

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1. **A 28-year-old G2P1L1 woman with blood group O Rh-negative is referred at 18 weeks of gestation. Her first pregnancy was complicated by an Rh-positive baby. She has an anti-D antibody titre of 1:32. Her husband is Rh-positive. Ultrasound shows no evidence of hydrops.**

   What is the next best step in management?

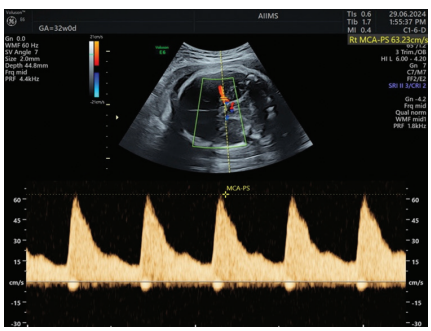
   A. Administer anti-D immunoglobulin immediately
   B. Repeat indirect Coombs test at 28 weeks
   C. Perform serial middle cerebral artery peak systolic velocity (MCA-PSV) Doppler surveillance
   D. Immediate cordocentesis
   E. Plan delivery at 34 weeks

2. **A 30-year-old Rh-negative woman with known anti-D alloimmunisation is at 26 weeks of gestation. MCA-PSV is 1.65 multiples of median (MoM). Ultrasound shows mild ascites.**

   What is the most appropriate next step?

   A. Repeat MCA Doppler after 4 weeks
   B. Administer anti-D immunoglobulin
   C. Perform fetal blood sampling and consider intrauterine transfusion
   D. Deliver immediately
   E. Start maternal corticosteroids only

3. **Which of the following is the correct technique for measuring MCA-PSV?**



   A. Sample the distal MCA near the skull vault
   B. Use an angle of insonation as close to 0° as possible
   C. Measure during fetal breathing movements
   D. Use an angle of insonation greater than 60°
   E. Sample the posterior cerebral artery

4. **Which of the following is the most appropriate packed red-cell preparation for intrauterine transfusion?**

   A. Whole blood, RhD-positive, non-irradiated
   B. O RhD-negative, leukoreduced, irradiated packed red cells with high haematocrit
   C. Maternal blood collected immediately before the procedure
   D. O RhD-positive, leukoreduced packed cells
   E. Standard cross-matched adult packed cells without additional processing

5. **Name of largest study till date investigating neurodevelopmental outcomes in children treated with IUT for hemolytic disease of the fetus/ newborn?**

   A. Magpie study
   B. LOTUS study
   C. ORACLE study
   D. CLASP Study

6. **Dose required of Anti D for additional FMH?**

   A. 10 ug of anti-D should be given for every additional 0.5 mL of fetal RBCs in maternal circulation.
   B. 15 ug ug of anti-D should be given for every additional 0.5 mL of fetal RBCs in maternal circulation.
   C. 10 ug ug of anti-D should be given for every additional 1 mL of fetal RBCs in maternal circulation.
   D. 15 ug ug of anti-D should be given for every additional 1 mL of fetal RBCs in maternal circulation.

7. **Antepartum and Post partum anti D reduces risk of alloimmunisation to:**

   A. 0.14 - 2%
   B. 2-8%
   C. 1-6%
   D. 8-10%

8. Which of the following is NOT CORRECT about the risk of fetal–maternal hemorrhage associated with the following procedures?

A. External cephalic version is not associated with risk of fetal–maternal hemorrhage

B. 14% risk of fetal–maternal hemorrhage with chorionic villous sampling

C. 2-6% rate of fetal–maternal hemorrhage with amniocentesis

D. Cordocentesis can cause fetal–maternal hemorrhage and warrant anti-D immune globulin prophylaxis

9. Which of the following is NOT TRUE regarding anti-D immune globulin?

A. Median half-life of anti-D immune globulin is about 23 days in the third trimester

B. If delivery occurs within 3 weeks of the standard antenatal anti-D immune globulin administration, the postnatal dose may be withheld in the absence of excessive fetal–maternal hemorrhage

C. If delivery occurs within 3 weeks of anti-D immune globulin administration for antenatal procedures, such as external cephalic version or amniocentesis, or for third-trimester bleeding, the postnatal dose may be withheld in the absence of excessive fetal–maternal hemorrhage

D. If delivery occurs within 3 weeks of anti-D immune globulin administration and the Kleihauer–Betke test is positive, the postnatal dose should be withheld.

10. In patients with antenatal hemorrhage after 20 weeks of gestation, which of the following is NOT TRUE?

A. Anti-D immune globulin is recommended for Rh D-negative women who experience antenatal hemorrhage after 20 weeks of gestation

B. Volume of fetal–maternal hemorrhage can be assessed by Kleihauer–Betke test and an appropriate amount of Rh D immune globulin then can be administered to cover the estimated volume of fetal–maternal hemorrhage

C. In cases of chronic or episodic bleeding, a negative serial indirect Coombs testing indicates persistence of anti-D immune globulin and theoretically no additional treatment with anti-D immune globulin is necessary

D. Cell-free DNA testing can be used to ascertain the fetal Rh D status to avoid repeated administration of doses of anti-D immune globulin with an Rh D-negative fetus

ANSWER KEY

1.C 2.C 3.B 4.B 5.B 6.A 7.A 8.A 9.D 10.C

From the Resident Desk
When a Mother's Blood Remembers
The Unseen Journey of Rh Alloimmunisation

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We have seen many mothers enter our door,
With hope for the child they are waiting for.
Some after miscarriages, some fetal demise,
Yet carrying another dream in their anxious eyes.

They come with old reports held close to their chest,
With questions medicine alone cannot put to rest.
A pregnancy once lost, a heartbeat once gone,
Yet somehow they gather the courage to carry on.

Then comes the diagnosis, unfamiliar and strange
Rh alloimmunisation and suddenly worlds change.
We speak of antibodies, antigens and blood,
While behind those words rises an emotional flood.

"Doctor, is my own body making my baby sick?
Why can't my immunity simply learn a new trick?
How can the blood that keeps my baby alive
Be the reason my little one struggles to survive?"

And there lies a paradox difficult to explain:
A system meant to protect may unknowingly cause pain.
The immune system remembers what it encountered before,
And when exposed once again, it remembers even more.

Yet antibodies can cross the placental line,
While a mother keeps praying, "Please let my baby be fine."
They target fetal red cells, unseen in their flight,
And anemia may deepen despite her hope and might.

Then begins the surveillance the waiting, the fear,
The question before every scan: "Is my baby safe here?"
We measure the MCA and watch the waveform rise,
While she searches for reassurance within the doctor's eyes.

The Doppler fills the room with a heartbeat strong,
And for a few precious moments, nothing feels wrong.
Then silence while measurements appear on the screen
Perhaps the longest few seconds a mother has ever seen.

And when fetal anemia demands that we intervene,
Another unfamiliar world enters the scene.
Intrauterine transfusion words difficult to hear,
Carrying both possibility and fear.

As we explain the procedure and consent must be signed,
A hundred frightening questions race through her mind:
"Will the needle hurt my baby? Will everything be fine?
Can you really transfuse blood through that tiny cord inside mine?"

We calculate donor blood, hematocrit and flow,
But beneath every calculation is one thing we know:
For us it may be a procedure carefully planned
For her, it is her child's life placed in another's hand.

Then follow admissions, transfusions and scans,
Hospital corridors replacing ordinary pregnancy plans.
Weeks are no longer counted toward celebrations alone,
But toward the next transfusion and the hope of going home.

Still, these mothers learn a language never sought
Titres and hydrops become part of every thought.
MCA Doppler, fetal anemia, transfusion once more,
Terms no mother imagined she would know before.

Yet through every needle, every scan, every night,
They carry their fear and continue to fight.
Fragile perhaps ,but remarkably strong,
Holding on to hope when the road feels long.

And sometimes there comes an even heavier thought:
"The Anti-D injection was missed or not sought."
Suddenly yesterday returns with merciless might
"If I had received it then, would today be all right?"

And slowly prevention transforms into guilt,
Around one missed moment, an entire sorrow is built.
But medicine must never allow knowledge to blame,
Nor let a missed opportunity become lifelong shame.

Because no mother commands her antibodies to rise,
No mother chooses sensitisation or fetal demise.
She did not instruct her immunity what to see
Her body simply followed its biological memory.

Perhaps this is where science and spirituality meet:
Where mechanisms are clear, yet answers incomplete.
Science may explain how antibodies arise,
But not every why behind a mother's tear-filled eyes.

The same placenta through which nourishment flows
May become the path an antibody knows.
Yet if blood can cross that invisible line,
So can medicine with knowledge refined.

A needle enters where once we could only observe,
Donor cells restore what anemia would otherwise disturb.
Drop after drop, through a vessel so small!

AOGD Clinical Meeting from VMMC &Safdarjung Hospital held on 25.09.2026

THE BLUE GESTATION: CONGENITAL HAEMOGLOBIN M DISEASE - A RARE CAUSE OF METHEMOGLOBINEMIA IN PREGNANCY

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Introduction

Methemoglobinemia is a rare disorder characterised by methemoglobin >1%, leading to impaired oxygen delivery and functional anaemia. It presents with central cyanosis and a classical saturation gap - low SpO2 with normal PaO2 despite normal cardiorespiratory examination. Congenital Hemoglobin M disease due to HBB gene mutation is extremely rare in pregnancy with limited literature and poses diagnostic dilemma.

Case details

A Primigravida at 14 weeks gestation presented with breathlessness, headache, cyanosis and clubbing. SpO2 was 41% on room air, and 88% with support. Systemic examination was normal. 2D Echo showed normal LVEF, no RWMA, IVC 1.3cm collapsible. G6PD normal, DCT negative. ABG showed high PaO2 170 mmHg with low saturation - saturation gap. Co-oximetry revealed MetHb 13.5%, FO2Hb 75.9%, FCOHb 1.1%. Clinical exome sequencing identified a heterozygous missense variant in HBB gene c.190C>T p.His64Tyr, exon 2, autosomal dominant, Likely Pathogenic, suggestive of congenital Hemoglobin M disease. She was managed with high-flow oxygen, IV ascorbic acid and IV methylene blue 1-2 mg/kg. Maintenance oral ascorbic acid 1g TDS was given. She improved in 24 hours.

Discussion and Conclusion

High index of suspicion for methemoglobinemia is required in pregnancy with unexplained cyanosis and saturation gap. Genetic testing confirms congenital Hb M disease. Methylene blue and ascorbic acid are safe, effective and life-saving with good feto-maternal outcome.

BEYOND MORNING SICKNESS: PRESERVE THE MOTHER'S WELLNESS

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Introduction

Hyperemesis gravidarum (HG) is the severe end of the spectrum of nausea and vomiting in pregnancy and may rarely progress to life-threatening metabolic and multiorgan complications.

Case:

A 25-year-old G3P1L0A1 presented at 20+1 weeks with intractable vomiting (15–20 episodes/day), intolerance of oral fluids and 6-kg weight loss (PUQE 15, HELP 45). Both previous pregnancies were complicated by severe HG and ended in a missed abortion at 4 months and an intrauterine death at 7 months.

Management was escalated stepwise by a multidisciplinary team. First line: IV fluids guided by IVC collapsibility, thiamine, metoclopramide, ondansetron and pantoprazole. Second line: nasogastric feeding and IV hydrocortisone. Third line: total parenteral nutrition. Despite this, she developed severe hyponatremia (118 mEq/L), refractory hypokalemia (1.9 mEq/L), acute kidney injury (creatinine 3.71 mg/dL), hepatocellular injury with jaundice (ALT 1307 U/L, AST 748 U/L), hypoalbuminemia and recurrent acid–base disturbances. Fetal assessment showed severe growth restriction with anhydramnios. Gastrointestinal, hepatic, neurological, infectious, autoimmune, trophoblastic and psychiatric causes were excluded.

Discussion

After 25 days of high dependency care and failure of all lines of therapy, the couple was counselled and the pregnancy was terminated at 23+5 weeks. Vomiting stopped within 24 hours, oral feeds were established and biochemical parameters improved progressively. Recurrence of HG in all three pregnancies suggests strong maternal susceptibility, warranting preconception counselling and early aggressive treatment in future pregnancies.

Conclusion

Severe refractory HG can be life-threatening. When stepwise medical therapy fails, timely termination may be necessary to prevent irreversible maternal morbidity.

DISSEMINATED HYDATOSIS WITH RIGHT VENTRICULAR INVOLVEMENT IN PREGNANCY: A RARE CASE REPORT

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Introduction

Cardiac hydatid disease being a rare entity, poses unique diagnostic and therapeutic challenges during pregnancy. Symptoms may overlap with physiological changes of

pregnancy, resulting in delayed recognition.

Case Details

A 32-year-old primigravida at 27 weeks 2 days, presented with progressive NYHA class II-III dyspnoea, cough, palpitations, pedal oedema and paroxysmal nocturnal dyspnoea. She was being treated for respiratory tract infection and bronchial asthma since one month outside. Echocardiography and cardiac MRI demonstrated a 19 x 29-mm cystic lesion in right ventricle with daughter cysts. Further evaluation revealed an elevated NT-pro BNP, peripheral mild eosinophilia and positive Echinococcus IgG serology. Additional imaging confirmed presence of pulmonary, pleural, pericardial and hepatic cysts, consistent with disseminated hydatosis. She was put on continued feto-maternal surveillance with multidisciplinary approach. Foetal growth restriction with absent end-diastolic flow developed at 34 weeks, necessitating caesarean delivery with a live born 1450-g male neonate. Patient refused for cardiac surgery, albendazole was initiated postpartum in a dose of 400mg twice daily, and patient is following up in cardio-obstetric OPD of the institute showing regression in cyst size.

Discussion

Disseminated hydatosis with right ventricular involvement carries risks of cyst rupture, embolization and haemodynamic compromise. Diagnosis requires a high index of suspicion, particularly when cardiopulmonary symptoms are disproportionate. Cardiac MRI differentiates it from other causes of right heart failure. Management of women remote from delivery presents a dilemma with both medical and surgical options feasible.

Conclusion

Unexplained progressive dyspnoea in pregnancy warrants comprehensive cardiac evaluation. Early multimodality imaging and coordinated multidisciplinary management are crucial for optimising foeto-maternal outcomes.

Previous Events, September, 2026

AOGD Pre-Conference Workshop on "Menopause and Ageing Skills Lab: Beyond the Lecture," conducted by Menopause subcommittee on 10th September 2026 at EROS Hotel. It was conducted successfully attended by 60 delegates







AOGD pre-conference workshop on "Precision Prenatal Care in the Second Trimester: Early Risk Prediction Integrating Fetal Anatomy, Doppler and Genetics for Adverse Pregnancy Outcomes" conducted by Fetal Medicine and Genetics sub-committee on 10th Sep 2026 at VMMC & Safdarjung Hospital, New Delhi which was attended by 58 delegates.







AOGD pre-conference workshop on "Vision 2026: Building an ethos of Quality and Precision Care in OB/GYN" conducted by QI Obst & Gynae Practice sub-committee on 10th Sep 2026 at The Park Hotel. It was attended by 90 delegates and faculties.



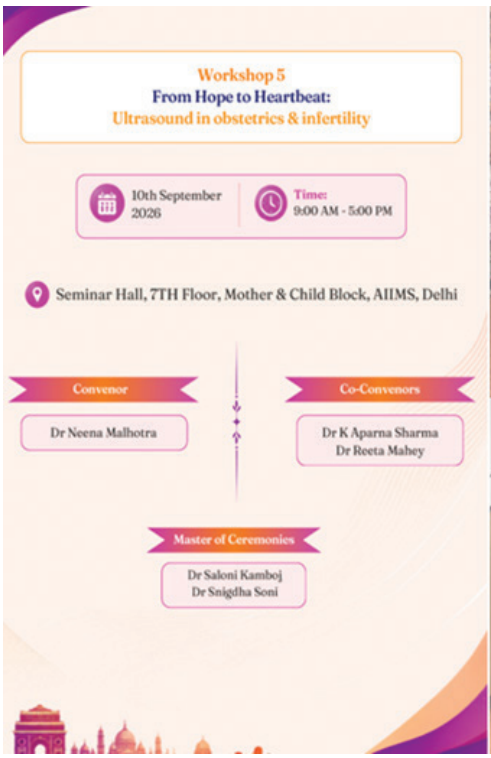


AOGD pre-conference workshop on "Life-Saving Obstetric Interventions and Best Practices Across All Stages of Labour – A Video- Workshop" conducted by Safe motherhood Subcommittee on 10th Sep 2026 at LHMC & SSK Hospital which was attended by 45 Delegates.





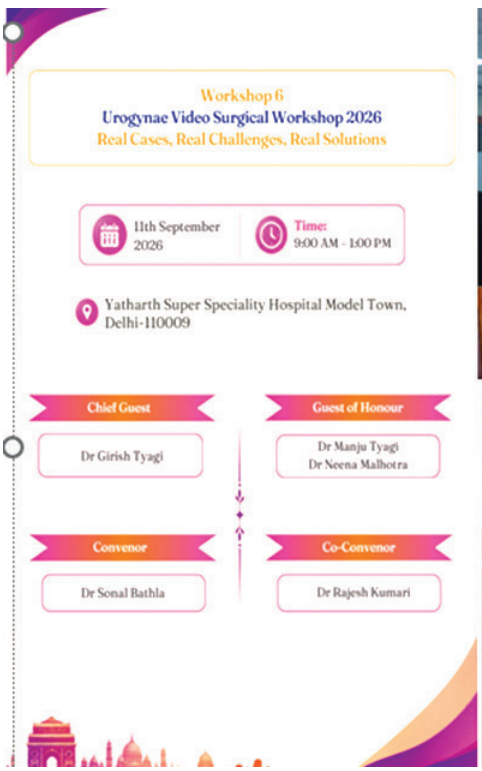
AOGD pre-conference workshop on “From Hope to Heartbeat: Ultrasound in Obstetrics & Infertility” conducted by Department of Obst & Gyane , AIIMS, New Delhi on 10th Sep 2026. It was attended by 50 delegates







AOGD pre-conference workshop on “Urogynaecology Video Surgical” conducted by Urogynae Subcommittee on 11th Sep 2026 at Yatharth Super speciality Hospital, Model Town, Delhi. Attended by 56 delegates.







AOGD pre-conference workshop on “Bridging clinical excellence and legal safety: protecting patients, protecting practice “conducted by Medicolegal Subcommittee on 11 Sept ,2026 at Fortis Hospital, Shalimar Bagh. Attended by 55 Delegates.



AOGD pre-conference workshop on "Adolescent Mental Health " conducted by Adolescent Health Subcommittee and Public Awareness Committee on 11th Sep 2026 at Kailash Deepak Hospital. Interactive session with 40 adolescent schoolgirls.



AOGD pre-conference workshop on "Surgical Precision Through Camera Vision" conducted by Endoscopy & Endometriosis subcommittee on 11th Sep 2026 at Sir Ganga Ram Hospital. Attended by 85 Delegates.



AOGD Pre Conference on "INCISE: Shaping Skills in Gynae Oncology" conducted by Oncology Subcommittee on 11th Sep 2026 at UCMS & GTB Hospital. Attended by 82 Delegates.



AOGD Pre-Conference Workshop on Infertility & ART, " IVF Decoded: From Basics to Breakthroughs," conducted by AOGD Infertility & Reproductive Endocrinology Sub-Committee, as part of AOGD 2026 on 11th Sep, 2026 at VMMC & Safdarjung Hospital. attended by over 100 delegates and senior faculty members.









48th Annual Conference of AOGD 2026 was organized by Department of Obstetrics & Gynae, AIIMS, New Delhi on 12th & 13th September 2026 at India Habitat Centre. It was a successful academic event and attended by 540 Delegates & Faculty members.














48th Annual Conference
WITH HER
Empower • Respect


Organized by: Department of Obstetrics and Gynaecology, AIIMS, New Delhi, India


CTG at 31+5 weeks


Theme: With HER (Heal, Empower, Respect)...
....Every Step of the way!!!




48th Annual Conference
Theme: With HER (Heal, Empower, Respect)...
....Every Step of the way!!!
India Habitat Centre, New Delhi

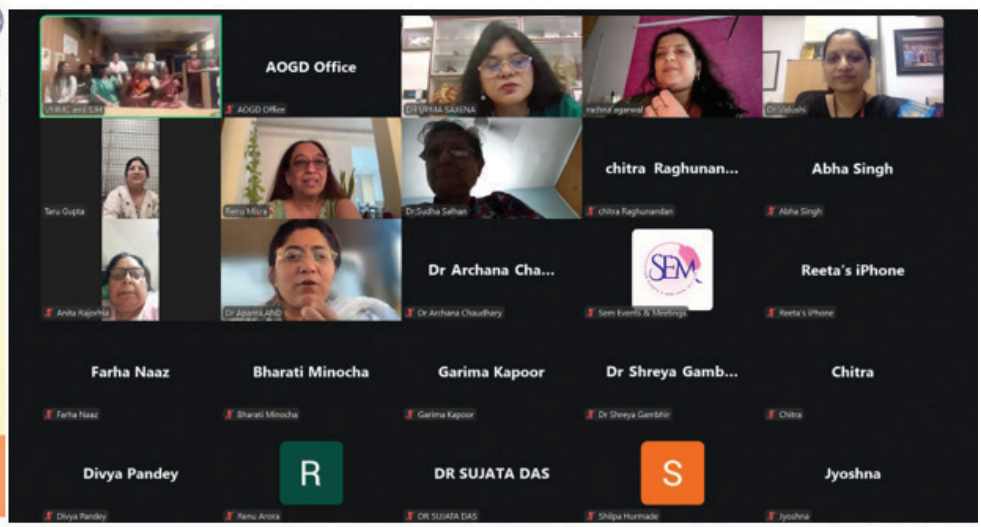

AOGD 2026
THE MATERNAL MEDICINE OLYMPIAD
- BOLLYWOOD EDITION QUIZ
SIKANDARS
BAAZIGARS
KHILADIS
DABANGGS

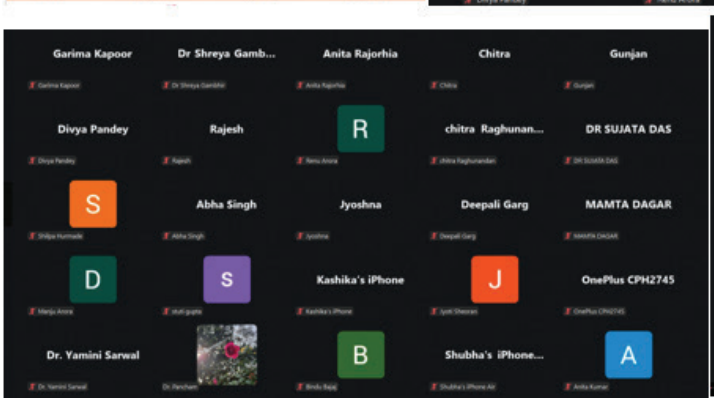
Cultural program (AOGD Conference , 2026)

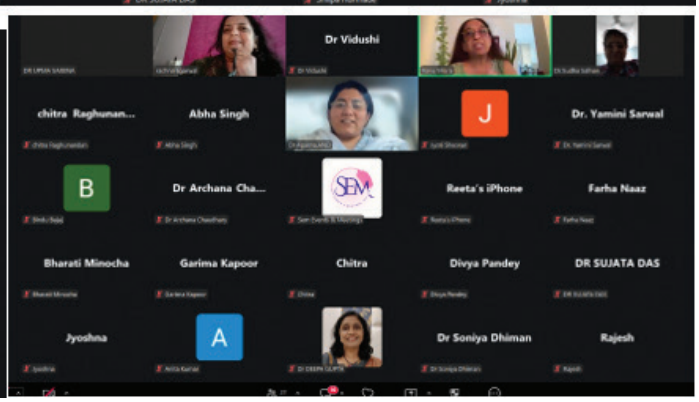


The AOGD Monthly Clinical Meeting (Virtual) was conducted by the Department of Obst & Gynae, VMMC & Safdarjung Hospital on 25th September 2026 and attended by around 56 participants.









CME on Advancing Women's Health was conducted by Endometriosis subcommittee on 30.09.26 at Hotel Park and was attended by 80 delegates.







Association of Obstetricians & Gynaecologists of Delhi

MEMBERSHIP FORM

Name:.....

Surname: .....

Qualification (with year): .....

Postal Address: .....

City:..... **State:** ..... **Pin code:** .....

Place of Working: .....

Residence Ph. No. ..... **Clinical / Hospital Ph. No.** .....

Mobile No:..... **Email:** .....

Gender: Male:..... **Female:**.....

Date of Birth: Date.....**Month** ..... **Year**.....

Member of Any Society:.....

Cheque/DD / No: .....

PHOTO

Cheque/Demand Draft should be drawn in favour of: AOGD 2026

FOR ONLINE TRANSFER THROUGH NEFT/RTGS

Name of Account: AOGD 2026

Account no: 45142130513

Name of Bank: State Bank of India

Branch: AIIMS, New Delhi

IFSC code: SBIN0001536

MICR code: 110002005



For Life Membership	: Rs. 11,000 + Rs. 1,980 (18% GST applicable) = Rs. 12,980/-
For New Annual Membership*	: Rs. 2,000 + Rs. 360 (18% GST applicable) = Rs. 2,360/-
For Old Renewal Membership+	: Rs. 1,200 + Rs. 216 (18% GST applicable) = Rs. 1,416
Entrance Fees (Payable once)	**: Rs. 400/-**

Encl.: Attach Two Photocopies of All Degrees, DMC Certificate and Two Photographs (Self attested)

*** Annual Membership is for the calendar year January to December.**

*** In case of renewal, mention old membership number.**

*** Life membership on or after 1st January, 2022 shall have to renew the life membership after 20 years. The minimum renewal amount will be 25% of the prevailing subscription fee at time of renewal.**

Note: 18% GST will be applicable as FOGSI requires it.

Send Complete Membership Form Along with Cheque / DD and Photocopy of required documents to the secretariat.
For online transaction send scan copy of all documents with payment slip on given mail id

Secretariat

AOGD Office, Room No. 714, 7th Floor, Mother & Child Block, Department of Obstetric and Gynaecology, All India Institute of Medical Science (AIIMS), New Delhi- 110029

Tel.: 011-29576771, (M): 9717392924 | Email Id: aogdaiims2026@gmail.com

AOGD SECRETARIAT
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