



Hemolytic Disease of the Fetus and Newborn (HDFN)

A GUIDE FOR PARENTS OF
INFANTS AT RISK FOR HDFN



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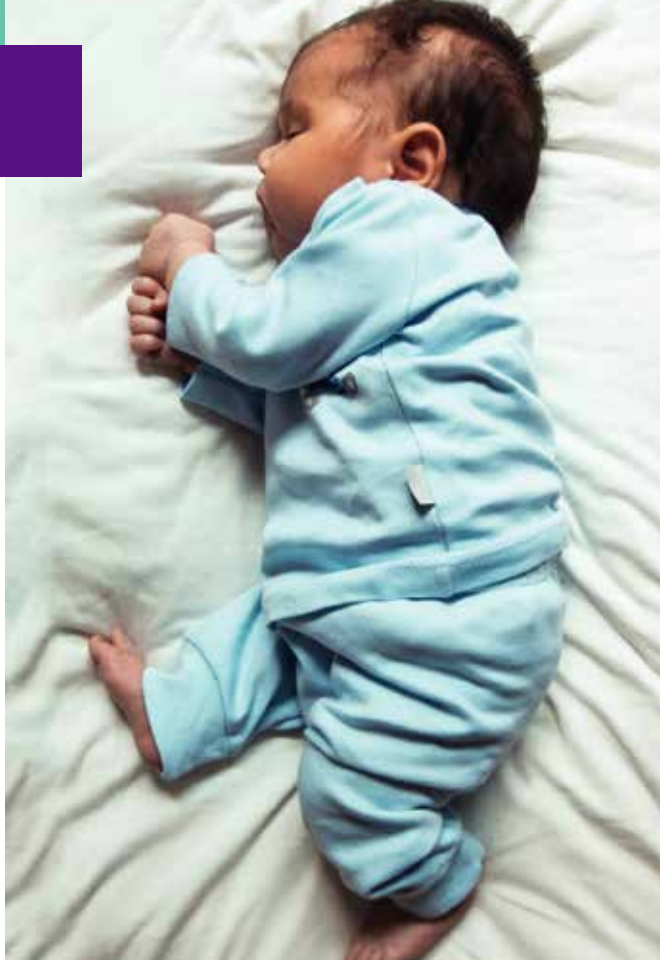
Welcome.

Dear Families,

Congratulations on the birth of your new baby! If you have been diagnosed with red blood cell antibodies during your pregnancy (alloimmunization), or your baby has been diagnosed with HDFN, you may have a lot of questions. This booklet reviews common questions and concerns about blood incompatibilities and how they may affect your baby. With close monitoring and timely treatment, babies with HDFN have a very high survival rate. Unfortunately, due to the rarity of alloimmunization and the variation in care practices around the world, well managed pregnancies and ideal outcomes are not universal- but they can be.

You are a vital part of your baby's care team. Parents who learn about the condition and understand the monitoring and treatment options are better able to advocate for their babies. Please discuss the available treatment options with your baby's provider.

This pamphlet provides the most recent evidence-based management guidelines for HDFN.



What is HDFN?

Maternal alloimmunization occurs when a woman makes red blood cell antibodies after being exposed to a blood type that is different from her own. This exposure usually occurs during a previous pregnancy, childbirth or a blood transfusion. These antibodies can cross the placenta during pregnancy and attack the unborn child's red blood cells, a disease called **Hemolytic Disease of the Fetus and Newborn (HDFN)**. Destruction of red blood cells results in fetal anemia.

Maternal antibodies remain in the infant's circulation and can continue to attack the baby's red blood cells up to twelve weeks after birth. If too many red blood cells are destroyed, the baby can become anemic. Additionally, destroyed blood cells release bilirubin, which can build up to toxic levels in the infant's system, known as hyperbilirubinemia. Close monitoring and regular lab work are vital to ensure that your infant's bilirubin levels stay in a safe range and that he or she is not becoming anemic.

HOW IS HDFN DIAGNOSED?

Some babies are diagnosed with HDFN before birth via MCA Doppler scans or percutaneous umbilical cord blood sampling (PUBS) and some are diagnosed after birth. A blood sample can be taken from your baby after birth to test hemoglobin/hematocrit, blood group, bilirubin and for a **Direct Coombs' Test or a Direct Agglutination Test (DAT)**. If the infant's DAT is positive, it means the mother's antibodies are bound to the baby's blood cells. Infants who are DAT positive need further monitoring for HDFN.



Complications of HDFN:

HYPERBILIRUBINEMIA

Complications of HDFN after birth can range from very mild to severe, but they are all treatable. The biggest risks to your baby are **high bilirubin and anemia**.

BILIRUBIN

- Bilirubin forms when your baby's red blood cells break down. If too much bilirubin builds up in your baby's body it can be dangerous. This is called **hyperbilirubinemia**. Hyperbilirubinemia is one of the most common issues that newborns with HDFN have. High levels of bilirubin can cause your baby's skin and eyes to turn yellow. This is called **jaundice**.
- Hyperbilirubinemia can last up to 3 weeks, or longer in severe cases. For most babies with HDFN, bilirubin levels peak on days 4-6 after birth. Bilirubin levels are measured with a Total Serum Bilirubin (TSB).
- If your child's bilirubin levels get too high, your child could develop a severe form of hyperbilirubinemia called **kernicterus**. Kernicterus is caused by bilirubin build up in the baby's brain and can cause brain damage, hearing loss, seizures and even death.

Complications of HDFN: HYPERBILIRUBINEMIA



Thankfully, severe hyperbilirubinemia and kernicterus are preventable.

TREATMENT OPTIONS FOR HYPERBILIRUBINEMIA INCLUDE:

- Phototherapy is provided in a hospital and is not painful or invasive. Your child will be placed in a special bed under a bank of blue lights. In some cases, a blanket of blue light, called a biliblanket, is added under the baby. This blue light lowers your baby's bilirubin levels through a process called photo-oxydation. Photo-oxydation works by breaking down the bilirubin into byproducts that are removed from the baby's body through urination.
- Intravenous Immunoglobulin (IVIG): This medication is given to babies with high bilirubin levels and those whose levels are not responding to phototherapy. The goal of this medication is to prevent the need for an exchange transfusion.
- Exchange Transfusion: If infant still has high levels of bilirubin an exchange transfusion is done. During an exchange transfusion the baby's blood that contains high levels of bilirubin is removed and replaced with compatible donor blood.

Warning signs for severe hyperbilirubinemia/kernicterus include: limpness, excessive tiredness, arching of the head/neck/back, a high-pitched cry, and fever. If your infant develops any of these symptoms, it is considered a medical emergency and he must be seen by a physician immediately.

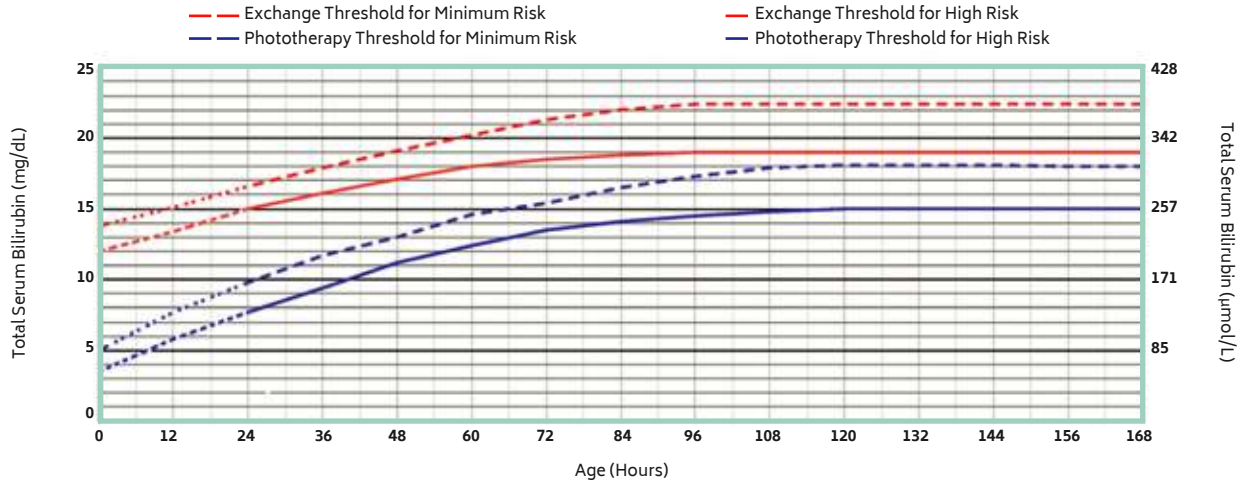
HOW YOU CAN KEEP YOUR BABY SAFE:

Talk to your doctor about your child's bilirubin levels and any treatment that may be required. Having a care plan in place before your child needs treatment is key. Ask for your baby's bilirubin levels and plot them on the TSB graph on the next page. Infants with HDFN will be in the medium or high risk category depending on gestation. If you feel uncomfortable with your baby's bilirubin levels or rate of rise, talk to your baby's doctor about more proactive treatment options.

Total Serum Bilirubin (TSB)

Guidelines for phototherapy and exchange transfusion in infants 35 or more weeks' gestation.

Modified from management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation, Pediatrics 2004, 114:297



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors=isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured.)
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50 µmol/L) below those shown but home phototherapy should not be used on any infant with risk factors.
- The dashed lines for the first 24 hours indicate uncertainty due to wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or TSB is ≥ 5 mg/dL (85 µmol/L) above these lines.

Complications of HDFN: Anemia

WHAT IS HEMOLYTIC ANEMIA?

Hemolytic anemia is also a common complication of HDFN. Hemolytic anemia occurs when the maternal antibodies destroy too many of the baby's red blood cells. Some babies with HDFN are born anemic and some don't develop anemia until several weeks after birth. Untreated anemia can be fatal, so regular lab work is essential if your infant was DAT positive. If your baby has undergone a series of intrauterine blood transfusions before birth, the majority of your baby's blood cells will be the donor blood cells from the transfusions. In this case, your baby's bone marrow will be suppressed and will not be making new red blood cells. As your baby grows, he or she will need more blood. Since the bone marrow is not making new blood, your baby can become anemic weeks after birth.

HOW IS ANEMIA DIAGNOSED?

Your baby will have regular blood tests to check the hemoglobin and/or hematocrit. This will show if your baby is getting low on red blood cells. In general, the hemoglobin or hematocrit is checked every 1-2 weeks until it is rising for 2 weeks in a row without treatment.

As part of your child's assessment for anemia, the doctor will also check the reticulocyte count. This test shows how many reticulocytes (young red blood cells) are in the baby's bloodstream and gives an idea of how quickly the baby is making new blood. This may also be used to help decide if a blood transfusion is needed or if you should wait and test again.



Complications of HDFN: Anemia

HOW IS ANEMIA TREATED?

Blood Transfusion: If your baby's hematocrit/hemoglobin drop too low, the doctor will perform a blood transfusion to resolve the anemia. The doctor will give your baby antigen negative donor blood through a needle into his or her vein.

Folic Acid: Infants who are mildly anemic or who may become anemic might be given folic acid. Folic acid is the synthetic version of folate, which is used up when infants make new red blood cells. Giving folic acid helps to ensure that the baby has everything he or she needs to produce new red blood cells.

Erythropoietin: Erythropoietin stimulates the bone marrow to produce more red blood cells. This medication may be used for infants with a low reticulocyte count, but most hematologists simply wait for the reticulocyte count to come up on its own.

Please know that **BABIES WITH HDFN HAVE HEMOLYTIC ANEMIA, NOT IRON DEFICIENCY ANEMIA.**

Multiple studies have shown that infants with HDFN are at high risk for iron overload, especially if they have undergone a series of intrauterine transfusions. Iron supplements should not be given to infants with HDFN without first checking their ferritin levels.



Complications of HDFN: Anemia

HOW YOU CAN KEEP YOUR BABY SAFE:

- Some babies become anemic with no visible warning signs. Other babies develop noticeable symptoms such as: difficulty breathing, excessive tiredness or fussiness, pale skin, bluish/pale coloration of the lips or fingernails, and fast breathing. Let your physician know if your baby has any of these symptoms.
- Set up necessary follow up appointments for your child after hospital discharge. Most pediatricians are not familiar with late onset anemia, so a pediatric hematologist is recommended.
- If your baby had intrauterine blood transfusions before birth, the routine newborn screening test might not be accurate. Ask your pediatrician to repeat the test after your baby has been cleared of HDFN.
- Remember that your baby could become anemic up to 12 weeks after birth.
- Talk to your doctor about your child's levels and any treatment options that may be required. Having a care plan in place before your child needs treatment will help you understand the care and testing needed.

GOOD QUESTIONS TO ASK:

- How often will your child have blood draws to check for anemia?
- What will happen if your baby's hemoglobin/hematocrit are dropping?
- If the baby's reticulocyte count is low, what are the treatment options?
- Who should you contact if your child's results won't be back until after hours or over the weekend?
- What is the procedure like if your baby needs a blood transfusion?

Keep track of your baby's hgb/hct levels and let your doctor know if you are concerned.

Complications of HDFN: Neutropenia & Thrombocytopenia

NEUTROPHIL COUNT

A neutrophil count is used to detect **neutropenia**, a complication of HDFN. Neutropenia occurs in about 45% of infants with HDFN, and can last up to one year. Infants with neutropenia may become sick more easily, and get worse more quickly than usual. These babies may need antibiotics and other medications when they become sick. Talk with your doctor about things that you can do to reduce your child's risk of contracting illnesses. Common precautions include frequent hand washing, limiting visitors and the number of people who have close contact with your child, covering the car seat or stroller to prevent strangers from touching your baby, and avoiding crowds. **Call your child's doctor if he or she develops a fever of 100.4°F (38°C) or higher.**

My child's neutrophil count is: _____

THROMBOCYTE COUNT aka PLATELET COUNT

Thrombocytopenia occurs in about 26% of infants with HDFN. Infants who are thrombocytopenic have a reduced number of platelets which causes them to bruise or bleed easily. Ask your doctor about things that you can do to keep your child safe if he or she is thrombocytopenic. **If your child experiences any of the following, see your physician: bruising easily, nose bleeds, prolonged bleeding from small cuts, and black or tarry stools.**

My child's thrombocyte count is: _____

What You Can Do For Your Child After Birth

- Talk to your child's birth team to confirm that the DAT, bilirubin and hemoglobin/hematocrit will be collected from the cord blood immediately after birth.
- After birth, closely monitor your baby's bilirubin levels to check for hyperbilirubinemia and plot them on the graph provided in this booklet. Typical testing frequency is every 4 to 6 hours in the first 24 hours of life, then every 12 to 24 hours for the first week and until bilirubin is consistently trending downward below treatment levels.
- Monitor your baby's hemoglobin and hematocrit to check for anemia. This is typically checked in the cord blood at birth, at least one additional time before discharge and then weekly after discharge from the hospital.
- After discharge from the hospital, weekly hematocrit and reticulocyte counts may be needed to monitor for delayed onset anemia.



What Every Parent Should Understand



- The biggest risks to your baby are: hyperbilirubinemia, kernicterus and anemia (including delayed-onset anemia that can happen after your baby is discharged from the hospital.)
- Regular blood work is essential for infants with HDFN. The most important blood tests are: DAT, hemoglobin/hematocrit, bilirubin, reticulocyte count.
- You are your baby's biggest advocate. You will likely be responsible for setting up your child's appointments with specialists after discharge from the hospital. Most infants will need weekly or biweekly lab tests to monitor for delayed onset anemia until 8-12 weeks old. Keep all of your child's appointments.
- Iron should not be given to babies with HDFN unless the ferritin level has been checked and is low.
- With the right monitoring and care, babies with HDFN recover and have no lasting effects.

Emotional Support

Having a baby with HDFN can be a traumatic experience. Stress caused by a high risk pregnancy and delivery, post partum recovery, and a newborn with medical needs can make it harder to cope emotionally. This can lead to complications such as anxiety, depression and post traumatic stress disorder (PTSD.) Women with high-risk pregnancies are 5.2 times more likely to experience anxiety compared to women with low-risk pregnancies. 25-50% of women with prenatal or postpartum anxiety will develop postpartum depression.



WE WANT YOU TO KNOW:

- Being a good parent means taking care of YOURSELF as well as your baby.
- Both you and your baby need attention, care and rest in order to recover.
- Ask your partner, family, friends, medical team and faith community for help in the days, weeks and months after having your baby.
- Be patient. It takes time for your baby to recover from HDFN. It takes time for you to heal from the stress and trauma you might have experienced.
- Anxiety, depression and PTSD are treatable. Reach out to your doctor or a mental health professional for more information about treatment options.
- Remember, you are not alone; this is extremely common among women dealing with alloimmunization and HDFN.

Glossary & Abbreviations

Alloimmunization - Maternal alloimmunization occurs when a woman makes red blood cell antibodies after being exposed to a blood type that is different from her own. This exposure usually occurs during a previous pregnancy, childbirth or a blood transfusion.

Anemia - An inadequate amount of red blood cells. Untreated anemia may result in organ damage, heart failure or death.

Antibody - Antibodies are free-floating proteins in the blood plasma that bind to foreign antigens in order to destroy cells that have the foreign antigens.

Antigen - Antigens are protein surface markers located on red blood cells. The term antigen comes from "antibody generating". Everyone has antigens on their red blood cells.

Bilirubin - A product that is produced when red blood cells are broken down. Excess bilirubin can cause jaundice, hearing loss, tooth enamel problems, permanent brain damage or even death if left untreated.

Direct Antiglobulin Test (DAT) - This test is sometimes called the Direct Coomb's Test. DAT looks for antibodies that are bound to red blood cells and is typically done on infants. With certain antibodies, this test can be negative even when the baby is still affected and needing treatment.

Delayed onset anemia - Anemia that is not present at birth, but happens between 2 and 12 weeks old.

Exchange Transfusion - Blood from the infant is removed and replaced 1-2 times with donor blood. Exchange transfusions are given if phototherapy and IVIG do not bring bilirubin levels down to a safe level.

Ferritin - A blood protein that contains iron. A ferritin test shows how much iron is being stored in the body. Normal ferritin range for newborns is 25-200 ng/mL. The normal range for infants from 1-5 months old is 50-200 ng/mL.

Glossary & Abbreviations

Hematocrit - The percentage of the volume of whole blood that is made up of red blood cells. The normal hematocrit range for infants 0-6 months is 37.4 - 55.9% for females, and 43.4 - 56.1% for males.

Hemoglobin - A protein in red blood cells that carries oxygen. The normal pediatric hemoglobin range for infants age 0-6 months is 12.7 - 18.3 g/dL for females and 14.7 - 18.6 g/dL for males.

Hemolytic Anemia - When the maternal antibodies destroy too many of the baby's red blood cells

Hemolytic Disease of the Fetus and Newborn (HDFN) - A blood disorder that occurs when the blood types of a mother and a baby are incompatible. The mother's antibodies cross the placenta during pregnancy and destroy the baby's red blood cells.

Hyperbilirubinemia - High levels of bilirubin.

Intravenous immunoglobulin (IVIG) - An infusion that is given to newborns to treat hyperbilirubinemia.

Kernicterus - A yellow staining of the brain as a result of high levels of bilirubin. Signs of Kernicterus are considered a medical emergency and include: a high pitched cry, arched back, and an inconsolable infant.

Neutropenia - This is a reduced level of neutrophils, a specialized kind of white blood cell. Approximately 45% of babies with HDFN develop neutropenia

Phototherapy - A special blue light that is used to lower the baby's bilirubin levels through a process called photo-oxidation.

Reticulocyte Count - A measure of how many immature blood cells are in the bloodstream. These are young RBCs and can give an idea of how quickly a baby is making new blood to replace what the antibodies are destroying

Thrombocytopenia - Thrombocytopenia is defined as a platelet count of less than $150 \times 10^9/L$. Approximately 25% of babies with HDFN develop thrombocytopenia.

Total Serum Bilirubin - A blood test that measures the amount of bilirubin

This resource is for informational purposes only. It is not a substitute for advice from an experienced medical professional who is familiar with your child's specific treatment plan and condition. If you are unsatisfied with the quality of your child's care, please feel empowered to reach out to another provider for a second opinion or transfer your child's care. In an emergency, call 911 or go to the nearest emergency room.

For additional resources visit:
AlloHopeFoundation.org



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Protecting babies, supporting families.

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To find out how your antibody can help others, please contact Southern Blood Services, Inc.
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