

Patient information

Hemolytic disease of the newborn (HDN): Rhesus (Rh) disease and other non-ABO antibodies

Context

The ICTMG's mission is to optimize patient outcomes through evidence-based international transfusion guidance development and relevant local implementation. In 2022, the ICTMG published a guideline of evidence-based recommendations for health-care professionals on the use of intravenous immunoglobulin in the management of Rh- and ABO-mediated HDN. To learn more about ICTMG, visit [ICTMG.org](https://www.ictmg.org).

This patient pamphlet is provided as an additional resource for patients and families. This pamphlet has been adapted with permission from the Hospital for Sick Children. To view this source material, please visit [AboutKidsHealth](https://www.aboutkidshealth.ca).

About HDN

What is HDN?

Hemolytic disease of the newborn (HDN) is a blood disorder in which the baby's red blood cells break down quickly, known as hemolysis.

This causes the release of a breakdown product, bilirubin, into the baby's bloodstream as well as the destruction of the red blood cells in the baby's body.

HDN causes a newborn baby's red blood cells to break down more quickly than they should. This occurs due to differences in blood type between mother and baby.

When there is a difference between the mother's blood type and the baby's blood type, the mother's immune system can react and can cause the baby's red blood cells to break down.

The breakdown of red blood cells causes anemia, too little blood (also known as low hemoglobin) and an increase in bilirubin, which causes jaundice, often seen as a yellow discoloration of the skin.

HDN due to Rhesus (Rh) disease

Often the most serious type of HDN is Rhesus (Rh) disease. This usually occurs when the mother is RhD negative and the baby is RhD positive, and the mother has developed an antibody to RhD from a previous exposure to RhD positive blood.

Rh disease does not typically occur in the first pregnancy. However, exposure during the first pregnancy can create significant risk for the next pregnancy and baby.

Sometimes there has been an unidentified previous miscarriage which caused exposure, and thus the first known pregnancy is affected. See below for details of how to prevent Rh disease in future pregnancies.

HDN due to other non-ABO antibodies

Antibodies can develop less commonly against many other red cell antigens, which can also cause HDN. In addition to RhD, more severe disease can occur due to Kell and c antibodies. HDN has been described due to at least 40 other red blood cell antibodies that occur less commonly.

Patient information

Hemolytic disease of the newborn (HDN): Rhesus (Rh) disease and other non-ABO antibodies

About HDN

What causes HDN?

HDN can occur when the baby and the mother's blood group do not match. The mother's immune system then develops antibodies against the baby's blood group.

A mother's bloodstream has many circulating antibodies. Antibodies are proteins which act in the immune system. Many antibodies are used to fight infection, while others can target other parts of the body including the antigens on red blood cells.

If a mother has specific antibodies against the baby's blood group, the antibodies can travel across the placenta into the baby's bloodstream. These antibodies can still be active in the baby's blood stream for weeks to several months after birth. The antibody can attach to the baby's red blood cells and destroy them, which leads to HDN.

In types of HDN caused by non-ABO antibodies, this red blood cell destruction can happen before delivery, after delivery, or both.

A mother can develop new blood type antibodies when there is mixing of the baby's and the mother's blood during pregnancy, or when the mother has been exposed previously to the part of the baby's red blood cell that does not match.

This can be a previous blood transfusion, a previous miscarriage or a previous pregnancy, amongst other things. As there needs to be previous exposure, this type of HDN rarely occurs in the first pregnancy.

A person's blood group (or blood type) is classified based on special antigens on the surface of the red blood cell. The antigens are made of proteins, carbohydrates and/or lipids and vary from person to person. These antigens are inherited by our genes.

There are many different antigens on a person's red blood cells. A small number of these can cause HDN if they do not match between mother and baby.

There are four major blood groups: A, B, AB, and O. A person's red blood cells may also contain a protein called the Rhesus (Rh) factor.

- If a person has the Rh factor, they are RhD positive (Rh+). This is sometimes referred to as a 'positive blood group'.
- If they do not have the Rh factor, they are RhD negative (Rh-), or a 'negative blood group'.

There are many more blood groups beyond the "ABO system" or the "Rh +/- system", however these are the most commonly discussed blood groups.

All babies inherit their blood group from both parents. Sometimes, the baby will have a blood group from their father which is different from their mother.

If the baby's blood group is different from the mother's, the mother's immune system may then develop antibodies targeting the different blood group that is on her baby's red blood cells, but not hers.

Patient information

Hemolytic disease of the newborn (HDN): Rhesus (Rh) disease and other non-ABO antibodies

About HDN

What are the risks to my newborn?

Often babies affected by this condition need monitoring before they are born, as they are at risk of anemia. If the antibody is identified during the pregnancy, and is of a high level, you will be referred to a health-care team to monitor the baby and potentially treat any anemia. Your team will talk to you about this.

Newborn babies are at risk of developing anemia from the destruction of their red blood cells. Anemia is when a person has too few red blood cells, also known as low hemoglobin. People need red blood cells to carry oxygen and provide energy to parts of their body, including their heart and brain. Anemia is life threatening if the red blood cells are too low. Anemia can develop before birth in severe cases.

Newborn babies can also develop jaundice, which is caused by the breakdown product of red blood cells (bilirubin). Jaundice does not develop in babies before birth as the mother's blood circulation clears the bilirubin quickly.

Jaundice is often seen as yellowing of the skin and eyes in the newborn baby.

Very high levels of bilirubin are toxic to the developing brain and can cause a condition known as kernicterus. Kernicterus is damage to the brain's nerve cells and can cause neurological consequences such as hearing loss and cerebral palsy. This is why treatment is initiated quickly to lower bilirubin levels. Kernicterus is very rare, due to early recognition of risk factors and bilirubin testing.

Can HDN be prevented?

Blood tests performed on the mother during pregnancy can detect whether the baby is at risk of developing HDN. Blood tests determine the mother's blood group and screen for antibodies in her blood that may cause HDN. Ultrasounds during pregnancy can also look for evidence of anaemia in the developing baby. If anemia is detected early, the health-care team can begin to manage the problem before the baby is born.

Rh disease is the only type of HDN that can be prevented. If a pregnant mother is Rhesus D negative, she will routinely be given an injection of a protein known as RhD immunoglobulin, called RhIg (also known as Rhogam, Winrho, Rhig, anti-D). This injection prevents the mother from developing antibodies towards the RhD antigen thereby preventing Rh disease.

RhIg is typically given at 28 weeks (3rd trimester), and again within three days after birth if the newborn baby has a Rh-positive blood group. It is also given during any procedure or trauma when the RhD negative mother is potentially exposed to the fetus' blood which can cause development of antibodies, for example during a miscarriage.

In severe cases during pregnancy, specialized blood sampling of the fetus or blood transfusions in the baby before they are born at a specialized hospital, are sometimes required to prevent bad outcomes for the baby.

Seek medical attention if your baby:

- develops more jaundice or is very pale
- is very sleepy
- is not feeding well
- develops a high-pitched cry
- has any other concerns

Patient information

Hemolytic disease of the newborn (HDN): Rhesus (Rh) disease and other non-ABO antibodies

HDN treatment

How is HDN treated?

After the baby is born, symptoms can range from mild jaundice to severe jaundice and severe anaemia. The baby will have blood tests repeated over several days to determine how the hemolysis is progressing (assessing bilirubin levels and hemoglobin levels if necessary).

Depending on the severity of the jaundice, determined by how elevated the bilirubin levels are, there are a few different treatment options.

- Phototherapy is the most common treatment required and uses a special lamp and/or blanket of blue light to help the baby's body to get rid of the bilirubin. Phototherapy makes the molecules of bilirubin come together, allowing the kidneys to excrete them out of the body through urine. Usually, babies require this treatment for hours to days.
- If jaundice is severe and phototherapy is not enough to treat it quickly, an exchange transfusion may rarely be needed. Exchange transfusions remove the blood with critically high bilirubin levels and replaces it with donated red blood cells.
- If anaemia is severe, red blood cell transfusions are required.
- Other therapies, including intravenous immunoglobulin (IVIG), a plasma-based blood product, can also be considered to dampen the immune process in some instances.

What happens next?

The antibodies that cause hemolysis are present in the baby for several months; however, initial treatment is usually only in the first few weeks, with ongoing monitoring in case further treatment is needed. Over time, the amount of antibodies is reduced and they become less active. This may take several months.

Even if the jaundice and/or anemia was not severe at birth, it can sometimes worsen over time and your baby can become anemic in these first few months. It is important babies are seen by their health-care provider regularly for at least 6-8 weeks to watch for signs of anemia, and potentially have blood tests during this time. After this time, the antibody is too weak to cause problems.

Babies need to be monitored regularly for at least 6-8 weeks, even if no active treatment was initially required when the baby was born.

Some cases of HDN are mild and might not need any treatment, while others can be severe and need a lot of monitoring and treatment. Most babies with this condition will have no long-term problems, if recognized and treated early.

Your health-care team will discuss treatment options with you if they are needed for your baby.

Health-care professionals:

Share this pamphlet with your patients and scan the QR code to access the ICTMG's HDN guideline on [ictmg.org](https://www.ictmg.org).

