

For the Society for Maternal-Fetal Medicine (SMFM) with the assistance of Stephen Bacak, DO, MPH, from the University of Rochester Medical Center Division of Maternal-Fetal Medicine, and T. Flint Porter, MD, from the University of Utah Division of Maternal Fetal Medicine.

What is fetal anemia?

Fetal anemia occurs when there is a decrease in the baby's red blood cell (RBC) count before delivery. RBCs are necessary to carry oxygen to the organs of the developing baby, and the baby may not get enough oxygen if the RBC level is too low. Severe fetal anemia is rare, but it can be dangerous for the baby, and may lead to heart failure, abnormal fluid buildup in multiple body areas, and even death.

What causes fetal anemia?

Many conditions can lead to fetal anemia. The most common causes in the United States are maternal RBC alloimmunization (see below) and infections such as a parvovirus. Other causes include abnormalities in the way the baby makes RBCs, genetic or metabolic syndromes, and vascular tumors of the baby or placenta.

Maternal RBC alloimmunization occurs when the mother's and the baby's RBC are not compatible. When the baby's RBCs cross into the mother's blood, the mother's immune system makes proteins called antibodies that can cross the placenta and attack the baby's RBCs. This process is known as hemolytic disease of the fetus and newborn (HDFN). The most common causes of maternal alloimmunization are blood transfusions prior to or during pregnancy; feto-maternal hemorrhage associated with delivery, trauma, spontaneous or induced abortion; and

ectopic pregnancy. Obstetric procedures such as chorionic villus sampling (CVS) and amniocentesis can also lead to maternal alloimmunization.

In the past, Rhesus group D incompatibility between the mother and baby (also known as Rh (D) alloimmunization) was the most common cause of HDFN. Rh (D) immune globulin prevents a mother from making harmful antibodies, and its use has made fetal anemia due to Rh incompatibility less common. Unfortunately, other RBC incompatibility groups can still lead to fetal anemia.

Fetal anemia can also be caused by parvovirus infection. Also known as "fifth disease," parvovirus is a common childhood viral infection that causes a rash on the face, trunk, arms, and legs. The virus attacks developing RBCs in a baby's bone marrow. If the baby is not monitored closely, the result can be severe fetal anemia and death, especially if the infection occurs before the 20th week of pregnancy. Other viral, bacterial, and parasitic infections (such as toxoplasmosis, cytomegalovirus [CMV], coxsackie virus, and syphilis) can also cause fetal anemia. Fortunately, these infections are rare.

Fetal anemia may occur in certain genetic and metabolic disorders including Down syndrome, alpha-thalassemia, G-6-PD deficiency, Fanconi anemia, Gaucher disease, and Niemann-Pick disease. Finally, some twin pregnancies that

share a placenta (monochorionic twins) are also at risk of fetal anemia.

What is the treatment for patients at risk of fetal anemia?

Treatment for women at risk of fetal anemia varies, depending on the suspected cause of the disease. In women with suspected RBC alloimmunization (based on the presence of antibodies in their blood), a key step is determining the blood type of the father of the baby in order to determine whether the baby is at risk. If that is not possible, the baby's blood type can be evaluated using amniocentesis, or in some cases by examining the mother's blood (using cell-free DNA technology).

Women who develop antibodies against their baby's blood are then tested during pregnancy to determine their antibody levels. This testing should be repeated at least every 4 weeks. If a pregnant woman had a prior pregnancy complicated by fetal anemia, antibody levels are not helpful in the current pregnancy. Additional tests should be performed including ultrasound or direct assessment of the baby's RBC levels to diagnose fetal anemia. These tests are also necessary when the antibody level is elevated and the baby is at risk for anemia.

Pregnant women who have been exposed to parvovirus should be tested to see if they previously had a parvovirus infection. If parvovirus infection is confirmed in a pregnant woman who has not previously been exposed to the virus, she should undergo close ultrasound monitoring to identify signs of fetal anemia.

How is fetal anemia diagnosed?

A true diagnosis of fetal anemia can be made only by sampling blood from the umbilical cord. However that procedure is invasive, can be difficult to perform, and may result in loss of the pregnancy or early delivery. Stillbirth is reported in 1%–2% of women undergoing cordocentesis. Fortunately, there are less risky ways to determine whether a baby is anemic. The Society for Maternal-Fetal Medicine (SMFM) recommends using ultrasound to measure the blood flow in one of the arteries in the baby's brain (called the middle cerebral artery or MCA). One of the fetal responses to anemia is to speed up the blood flow to the brain. This test has been shown to be useful in screening for fetal anemia in several conditions, including RBC alloimmunization and parvovirus. Measurement of MCA blood flow using ultrasound should be performed by ultrasonographers, maternal-fetal medicine physicians, or others with special training in the proper technique.

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