



Rh-Factor and Prophylactic RhoGAM

The Rh or Rhesus blood group system is one of thirty current human blood group systems. Clinically, it is the most important blood group system after ABO. Together, the two blood systems make up what we call “blood type”. At present, the Rh blood group system consists of 50 defined blood-group antigens, but the most important one is the D antigen. The terms *Rh-factor*, *Rh-positive* and *Rh-negative* refer to the *D antigen* only. Besides being important for blood transfusions, your Rh-factor becomes important in pregnancy if you are Rh-negative and the baby’s father is Rh-positive. Approximately 85% of Caucasian people have Rh-positive blood, with even higher percentages for other ethnicities. Therefore, if you do have an Rh-negative blood type, it is likely that the father of the baby is Rh-positive, and in that case you have a 60% chance that you are carrying an Rh-positive baby. If this is the case, then you and your baby’s blood types are incompatible.

This potential incompatibility is usually not a problem. Under normal circumstances, the placenta makes sure that maternal and fetal blood cells do not mix. However, a traumatic event, such as a heavy fall or a car accident can sometimes cause a small fetal-maternal hemorrhage where a small portion of mother’s and baby’s blood mixes at the placenta. The other obvious chance for mom and baby’s blood to mix is during childbirth, particularly with a high-intervention birth such as a c-section or forceps delivery.

Hemolytic Disease of the Newborn

So what happens if an Rh-negative mom is exposed to some of her Rh-positive baby’s blood? Her body mounts an immune-response to that blood, seeing it as a foreign invader and producing antibodies, called “Immunoglobulin G anti-D” (IgG anti-D) which kill the fetal red blood cells that have passed over into the mother’s blood stream. Because IgG anti-D can cross the placenta, there is a potential for the mother’s body to start attacking the baby. This results in Hemolytic Disease of the Newborn (HDN), which usually presents as either severe edema leading to heart failure (hydrops fetalis) or a type of brain damage caused by extreme levels of bilirubin (kernicterus). Both conditions are a result of the baby’s body producing far more blood than usual in an effort to combat the maternal antibodies’ breakdown of red blood cells. It is important to note that almost always, when the mother’s body first detects her baby’s foreign blood type, her immune response is just enough to deal with the blood in her own system. This is called sensitization. If, however, she goes on to have another baby with Rh-positive blood, her body, having already been sensitized, will mount a much more vigorous attack and it is this baby that is at risk of developing HDN.

Rh₀(D) Immune Globulin (RhoGAM) was developed in the 1960s and was approved by the FDA in 1968. RhoGAM is a concentrated dose of IgG anti-D, the antibodies that attack Rh-positive blood cells, collected from the blood plasma of carefully screened Rh-negative people. It works by attacking and killing any Rh-positive blood in the mother before her own body can detect its presence and mount an immune response. It is given by intramuscular injection as a precautionary measure within 72 hours of an event where there was potential for a fetal-maternal hemorrhage, and is given to mothers of Rh-positive babies within 72 hours after birth. Currently both the American College of Obstetricians and Gynecologists and its UK counterpart, the Royal College of Obstetricians and Gynecologists, both support giving all Rh-negative mothers a prophylactic dose of RhoGAM at 28 weeks pregnancy to cover the “silent” sensitizations that occur. That is, the mother has had no traumatic event, but a fetal-maternal hemorrhage still occurs and the mother develops antibodies as an immune response. We know that this occurs because about 1% of Rh-negative mothers will become sensitized for no apparent reason. Studies show that if all Rh-negative women receive a prophylactic dose of RhoGAM at 28 weeks gestation, the rate of “silent” sensitization drops to about 0.35%.

Benefits

There is no doubt that the introduction of RhoGAM has made a dramatic reduction in the rates of HDN. What used to be a 1 in 2,000 chance has now dropped to a 1 in 62,000 chance. There is no debate about the benefit of the Rh-

negative mother receiving RhoGAM in the case of a traumatic event or after the birth of her Rh-positive child. The only controversy is centered around the prophylactic 28-week dose. Even though there is an absolute drop of “silent” sensitizations, it takes 278 women receiving a prophylactic dose of RhoGAM to prevent 1 sensitization.

Risks

RhoGAM is made from human plasma. Since all plasma-derived products are made from human blood, they may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent. The strict safety protocols and modern filtration techniques surrounding the harvesting of plasma and isolation of the antibodies make these risks incredibly small.

The second concern is the effect of the IgG anti-D on the unborn baby. There has been no systematic study that looks at the short and long-term side effects of IgG anti-D in babies. We do know that up to 10% of the antibodies injected pass through the placenta and into the child. They may test positive for the antibodies, and may be slightly anemic at birth, though not to the point where treatment is needed.

Another objection is that giving RhoGAM at 28 weeks is not needed in up to 40% of cases, since the baby is already Rh-negative. Indeed, if both the baby’s parents are Rh-negative, this whole discussion becomes moot.

Fetal Blood-typing

Since 2010, Sequenom Center for Molecular Medicine has offered a revolutionary series of tests including finding the blood type of an unborn baby by analyzing the circulating cell-free fetal-DNA that can be found in the mother’s blood. This blood test costs \$250, but is covered by many insurance companies.

References:

- RCOG Guideline No. 22, March 2011 *The Use of Anti-D Immunoglobulin for Rhesus D Prophylaxis*
- [en.wikipedia.org/wiki/Rho\(D\)_immune_globulin](http://en.wikipedia.org/wiki/Rho(D)_immune_globulin)
- www.rhogam.com/
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