

# GIVING BABIES A FAIR SHOT

## Suppression of the Primary Rh Immune Response with Passive Rh IgG Immunoglobulin

Vincent J. Freda, M.D., John G. Gorman, M.D., and William Pollack, Ph.D.

N Engl J Med 1967; 277:1022-1023

November 9, 1967

**A**s a young obstetrician, Vincent Freda, M.D., too often delivered babies who were brain-damaged, ill, or even stillborn because of Rh incompatibility with their mothers. These gut-wrenching experiences gave Dr. Freda the motivation to find a way to prevent the devastating disorder that accounted for hundreds of fetal and neonatal deaths and illnesses each year.

Women who are Rh-negative – between 10 percent and 12 percent of the overall population, variable by race – make antibodies to the RhD antigen present on the red blood cells of the Rh-positive fetus. Some of these antibodies enter the mother's bloodstream at the time of delivery (or, occasionally, earlier in pregnancy). In subsequent pregnancies, the mother's antibodies cross the placenta and attack Rh-positive cells of the fetus, leading to severe anemia, possible brain damage, and even death of the fetus.

"This was a devastating problem. When you talk about something that someone did that actually made a difference, this would have to be on the list," says Ronald Wapner, M.D., professor of obstetrics & gynecology and vice chair for research in the Department of Obstetrics & Gynecology at P&S. Giving the product now called RhoGAM to all Rh-negative women within 72 hours of delivery prevented the woman from forming antibodies. "We virtually wiped out one of the most severe and devastating fetal conditions."

In most cases, sensitization of the mother's immune system increases with each subsequent delivery of an Rh-positive baby by an Rh-negative mother, and by the third or fourth pregnancies, the mother's antibodies would devastate the babies' red blood cells. "The babies would go into heart failure and develop hydrops, in

## Prevention of Rh Hemolytic Disease — Ten Years' Clinical Experience with Rh Immune Globulin

Vincent J. Freda, M.D., John G. Gorman, M.D., William Pollack, Ph.D., and Edward Bowe, M.D.

N Engl J Med 1975; 292:1014-1016

May 8, 1975

which they would just swell up and ultimately die," says Dr. Wapner.

Dr. Freda and John Gorman, M.D., director of the medical center's blood bank, set out to find a way to cure the disease. They built on the work of Sir Cyril Clarke, who first identified that an Rh antibody given at birth could protect a mother's next child, and the painstaking research of Ronald Finn, who had determined the stepwise progression that led to Rh disease. Working with William Pollack, Ph.D., of the Ortho Pharmaceutical Corporation who had developed means to fractionate human immunoglobulins, Drs. Freda and Gorman experimented with volunteer prisoners at Sing-Sing, the maximum security prison in upstate New York.

They injected Rh-negative prisoners with Rh factor then injected them with Rh(D) immune globulin (RhoGAM) to see whether it prevented sensitization. The effects were stunning: In almost all cases, sensitization did not occur. They had found a simple and stunningly effective way to prevent Rh disease. (In some cases, the prisoners would be injected on a Friday and not receive the immunoglobulin until the following Monday, leading to the still-current recommendation that RhoGAM be given within 72 hours of giving birth.)

In 1980, Drs. Freda, Gorman, and Pollack, along with Dr. Clarke and Dr. Finn, were awarded the Albert Lasker Clinical Medical Research Award for their work.

Since 1967, RhoGAM shots have become standard practice in obstetric care of Rh-negative mothers. The shots are now given at 32 weeks as well as at delivery to head off possible pre-term exposure and sensitization. But the medical knowledge is constantly being



VINCENT J. FREDA, M.D., AND  
JOHN G. GORMAN, M.D.

improved and refined. "We now have a test so that by six to 10 weeks of pregnancy we can draw blood from mother and determine the blood type of the fetus," says Dr. Wapner. "In the future one can anticipate that we will not have to give women carrying Rh-negative fetuses RhoGAM."

Columbia continues to be a major referral center for maternal-fetal blood incompatibility problems and is at the forefront of development for other tests that can determine fetal vulnerabilities, including Down syndrome, by a simple blood draw from the mother. "We're one of the most active clinical research centers in the country and are involved in a lot of NIH-funded studies, including research evaluating new genetic techniques," says Dr. Wapner.