ITP Support Association Platelet Reprint Series

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Title: **Intravenous Anti-D: Another Treatment for ITP**
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In previous issues of "The Platelet", we discussed the benefits and risks of steroids and IVIG as treatments for ITP. A newer product, anti-D immunoglobin, is increasingly used for ITP.

Anti-D is a fraction of the gamma globuli antibodies that are derived from blood plasma (the clear part of the blood). Therefore anti-D is a minute component of a product we previously discussed, IVIG. The development of anti-D was based on ideas about how IVIG may work in ITP. Since IVIG is a mixture of many antibodies produced from large pools of plasma donated by thousands of volunteers, it contains antibodies against many different things, not only infectious germs (viruses and bacteria) but also different types of human cells, including red blood cells. Antibodies against red blood cells can develop in any person who has received a previous blood transfusion or in women following pregnancy when their fetus had a different blood type. One way that IVIG works is by antibody binding to red cells, causing these antibody-coated red cells to be destroyed in the spleen. This may then serve to "distract" the spleen from destroying platelets in patients with ITP. It is a clever idea. While the spleen is busy destroying the red blood cells, it may not notice the smaller platelets. You could describe this as the spleen having lunch on the anti-D coated red cells and becoming so full that it doesn't have to have platelets for desert. Since our blood has 20 to 30 times more red cells than platelets, destruction of some red cells may not be noticed.

Therefore studies were done to test the effectiveness of specific components of IVIG. The first fraction to be studied were antibodies specific for red cells that are "D-positive". D is one of the factors of the Rh system. These Rh factors are called "antigens", the cell surface structures recognized by antibodies. D is the strongest antigen on the red cell surface and many years ago it was a cause of major problems for newborn infants. If the fetus blood type was positive for D (called "Rh-positive") and the mother was negative for D (called "Rh negative"), the mother could make antibodies against the fetal red cells and the baby could be born with severe anemia. This problem was solved 30 years ago by the use of anti-D (a product commonly known as Rhogam) given to mothers to remove the baby's red blood cells from her circulation before she can make the dangerous antibodies. Then 10 years ago, a new anti-D preparation was studied in patients with ITP.

Anti-D is effective for treatment of ITP. When it was introduced for treatment of patients in the U.S. in 1995 (a product named WinRho), it had promise because it was simpler to administer and somewhat less expensive than IVIG. Whereas an infusion of IVIG takes many hours, the intravenous infusion of anti-D takes less than 15 minutes. Whereas an infusion of anti-D may cause severe headaches, nausea, and vomiting, these reactions are less common than with IVIG. Whereas a full treatment of IVIG in an adult may cost over $10,000, the cost of anti-D is "only" about $6,000. Therefore some doctors who used IVIG for treatment of patients with ITP have changed their practice to use anti-D. In our survey of pediatric hematologists in the U.S. in 2001, we found that anti-D was the most commonly used initial treatment for children with severe and symptomatic ITP. In the past year, anti-D is beginning to be sold in the U.K.

The specific role of anti-D for treatment of ITP remains uncertain and controversial. Although most patients respond with an increased platelet count, the increase usually lasts only several weeks. Therefore, it is used for only temporary treatment. It has been said that repeated treatments with anti-D may postpone or prevent the need for splenectomy, but this did not happen in a study of adults with ITP that we recently completed in the U.S. The frequency of splenectomy was the same in patients who were either treated or not treated with anti-D.

A limitation of anti-D is that can only be used in patients who are Rh(D)- positive – about 85% of the population. Also anti-D is not effective after splenectomy. The risks of anti-D are similar to IVIG, since it is derived from blood. In our study, 22% of patients had moderate or severe side effects from anti-D that included headache, chills, fever, nausea, vomiting, and muscle aches. More severe reactions can occur, though they are rare. Patients may develop severe anemia and even kidney failure related to the destruction of the Rh(D)-positive red blood cells.

When the doctor feels that it is important to increase the platelet count rapidly, either IVIG or anti-D can be used. But, like IVIG, its expense, the need for intravenous infusion, and the side effects make it far from an ideal treatment. Like all other drug treatments for ITP, anti-D should not be administered just because the platelet count is low. As we have said before, we physicians should be treating patients, not platelet counts.