American Perspective reprinted from: **Sept 05**

Title: **Rituximab for ITP**

Author: **James N. George, M.D., George R. Buchanan, M.D.**

In a previous issue of The Platelet we discussed the options for treatment of ITP following failure of splenectomy. We emphasized that splenectomy is successful treatment for most patients with ITP who continue to have bleeding problems. Two-thirds of TTP patients will achieve normal platelet counts following splenectomy, which will remain normal without further treatment. About half of the remaining patients have improvement of their platelet count so as to require no further treatment. About 15% of patients exhibit no response to splenectomy and have persistent severe thrombocytopenia with platelet counts less than 20,000-30,000. Even low platelet counts in this range may be safe. If patients have no significant bruising or bleeding, no further treatment may be needed. If bleeding symptoms occur, a wide variety of drugs has been used to raise the platelet count but none with very good results and all with some toxicity.

Rituximab is one of the newest treatments used for patients who have persistent severe and symptomatic thrombocytopenia following splenectomy. Rituximab is one of a new class of treatments defined as "biologic agents" or "targeted treatments". The term, "biologic agent", refers to the structure of rituximab. It is not a chemical synthesized in a laboratory. It is an antibody originally developed in mice against human cells. The mouse cells are then transformed so that the antibody can continually be produced in laboratory cell cultures. These types of antibodies are very specific for a single target, and are called monoclonal antibodies. The "mab" in the generic name rituximab and the brand name Mabthera indicates that this is such a monoclonal antibody. Rituximab is directed against a single target molecule on human lymphocytes, the cells that produce antibodies in our system. Thus it is described as "targeted treatment". Rituximab hones in is on the specific cells which make the antibody against platelets in patients with ITP. Different from other treatments that are more general in their that suppression of the immune system, such as azathioprine (Imuran) and cyclophosphamide (Cytoxan), rituximab does not suppress bone marrow function and platelet production. Therefore it may be safer than other immune suppressive drugs. Patients who have taken rituximab do not appear to be at serious risk for having infections, as may occur with other immune suppressing treatments. The major side effect of rituximab is that patients can have allergic reactions, particularly to the first dose. The other major concern about rituximab is that it is extremely expensive, similar to other new biologic agents. Rituximab is usually given as a series of four intravenous infusions (each lasting up to 6 hours) one week apart. An estimated cost for these four infusions (in an average size adult) is 15,000 dollars.

Rituximab was originally developed for malignant disorders of lymphocytes, called lymphomas. It has been approved by the drug regulatory agencies in the U.S., U.K. and Europe in 1997-1998 for use in lymphoma. Since lymphocytes are the body's antibody-producing cells, rituximab has also been tried in many different autoimmune disorders, including ITP. A number of studies have demonstrated that 30-40% of ITP patients who receive rituximab respond with a normal platelet count and need no further treatment. This is similar to previous treatments for severe persistent ITP following splenectomy, or maybe even a little better. But since rituximab is a new drug, the duration of follow-up observation has been short – only a few years. Therefore we do not yet know the durability of responses to rituximab.

Is rituximab currently the best treatment for patients who fail splenectomy? This is not certain. Perhaps rituximab is gaining popularity mainly because it is new. Some doctors are even suggesting that rituximab should be used sooner in the course of treatment for patients with ITP, perhaps even before splenectomy. Whether this is right is also uncertain. Splenectomy has a consistent record of success for over 60 years; rituximab has only been used for ITP for only 4 years.

The good news is that rituximab is an effective treatment for many people with ITP, and we are always glad to have more drugs to choose from. The uncertainty is whether rituximab is better or as good as the other existing treatments that we have previously used. Further studies may give us the answer.