The ITP Support Association Platelet Reprint Series

No. 1 – The History of ITP

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Title: **The History of ITP**

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The cause of ITP is assumed to be the development of antibodies that destroy the patient's own platelets. Antibodies are normal protein molecules produced against anything the body recognizes as foreign, such as an infectious bacteria or viruses as, or transplanted organ. Occasionally the body's ability to distinguish foreign from self makes an error, and antibodies are formed that react with and damage the patient's normal cells. When the antibodies react against a person's own cells, they are termed autoantibodies. When they react against platelets, the disease is ITP. When they react against red blood cells, the disorder is autoimmune hemolytic anemia. In other disorders, antibodies can react with skin cells, joint tissue, kidney cells, or multiple or organs. In a sense, a person with ITP is "allergic" to his or her own platelets as a result of making the abnormal antibody.

In spite of our knowledge for merely 50 years that autoantibodies are the cause of ITP, there are no routine laboratory tests that can demonstrate these antibodies and assist in the diagnosis. This is different from autoimmune hemolytic anemia, where autoantibodies against red blood cells can easily be demonstrated, using a test devised by Professor Robert Coombs at Cambridge University in England 60 years ago. There has been much research on techniques for demonstrating anti-platelet autoantibodies, and much has been learned about how ITP occurs, but a readily available and reproducible laboratory test remains an elusive goal.

The history of ITP is closely tied to the story of the first demonstration of a blood plasma factor which causes platelet destruction. It was this blood plasma factor that was subsequently identified as an autoantibody. This initial dramatic experiment is part of the legend of ITP, and it is graphically described in a book by Lawrence K. Altman, the medical writer for the New York Times. He described the story of Dr. William Harrington, whose career research on ITP began when he was a medical student in Boston in 1945 and cared for a young woman with ITP who died from hemorrhage. Five years later, when he was receiving his hematology training at Washington University in St. Louis, he was caring for another woman with severe bleeding, whose platelet count had not increased after splenectomy. Dr. Harrington developed a theory that platelets were destroyed by a plasma factor, because he had also read reports that some mothers with ITP had given birth to babies with severe thrombocytopenia. To prove his theory, he worked with a young colleague on a summer Sunday afternoon in 1950. They removed a pint of blood from the patient and infused it into Dr. Harrington. The results were dramatic, as Dr. Harrington's platelet count fell to nearly 0 and he developed purpura and petechiae. At that time, his colleagues insisted he remain in the hospital. It was 5 days before his platelet count recovered to normal. In spite of the clear dangers, these studies were repeated with 9 other ITP patients and several other volunteer physicians.

Harrington's work is a milestone not only for ITP, but it was the first evidence for antibodies against one's own tissues and formed the initial basis for our theories of autoimmune disease. These experiments could be described as heroic, and in the tradition of other scientists of many years ago who infected themselves with yellow fever, malaria, scarlet fever, and other dangerous diseases. However, these self-experiments may also be described as being foolish with unnecessary risks, according to current rules of clinical research. In the past 50 years, each experiment using human subjects must be reviewed by an impartial board of scientists. Each hospital and medical school has such a board, and they are all (in the U.S.) supervised by the National Institutes of Health. Dr. Harrington's self-experimentation would not be allowed today. We can say that we are wiser in 1999 than he was in 1950, but his results still stand as landmark and legend in the story of ITP.