Martha and Hans Eibl:
MAKING THEIR MARK IN IMMUNOLOGY

BY JAN M. BULT

The names Martha and Johann Eibl and Vienna are well-known throughout the immunology world and for good reason: They are two extraordinary people who have made enormous contributions to humanity for more than 50 years.

Professor Dr. Martha Eibl was born in Székesfehérvár, Hungary, in 1931. During World War II, she personally experienced the threats upon the Jewish population. Following the war, she graduated from high school and entered Vienna University Medical School in 1949. After she obtained her medical degree, she traveled to New York to be a Research Fellow at the Department of Pathology of the New York Medical School. There she worked in the laboratory of Dr. Baruj Benacerraf (see sidebar) who would go on to win a share of the 1980 Nobel Prize in Physiology or Medicine for his part in the discovery of the major histocompatibility complex genes.

In 1958, Martha Eibl returned to Vienna to practice internal medicine as a resident and to continue her studies. She received her Specialist degree in Internal Medicine in 1965 and remained until 1970 at the Clinic of Internal Medicine of the University of Vienna. From 1970-97 she worked at the Institute of Immunology of the Vienna University. In 1973, she received the Lecturers Degree and in 1980 became Professor and Head of the Department of Pediatric Immunology and Infection and Immunity.

Professor Martha Eibl is a very impressive person. She spent 20 years as the consultant physician for clinical immunology for all municipal pediatric hospitals in Vienna and is a world renowned immunologist who has taught many specialists the intricacies of immunology. The author of 294 peer-reviewed articles, she was the head of the clinical-immunological research for Immuno AG from 1966-96. Those who are trained by her speak highly about her scientific skills and dedication to patients.

"Ever since I first met Prof. Martha and Dr. Johann Eibl, at the time enjoying the privilege of doing my Ph.D. thesis under her supervision, I cannot imagine better company for being introduced to the love of science; always with a focus on the best interest of patients," said Thomas R. Kreil, Ph.D.,

Key individuals of Immuno

When you talk about the "old days" of Immuno, you have to talk about some key individuals that made the company strong:

DR. OTTO SCHWARZ
Responsible for Manufacturing and Operations

DR. HANS EIBL
Responsible for R&D

DR. FRIEDRICH DORNER
Responsible for Biotechnology and Pathogen Safety

DR. KNUT HANSEN
Legal counsel and first Chairman of the European Association for the Plasma Protein Industry. He worked hard to establish the foundation of what has become PPTA.

Associate Professor of Virology, Senior Director, Global Pathogen Safety, Baxalta. "It's a passion that has stuck with me ever since."

It was during her medical training in 1951 that Martha Eibl met Johann "Hans" Eibl, a chemist, who was one of the founders of the company that later became Immuno AG, one of the premier biopharmaceutical companies in the world.

Dr. Hans Eibl is someone you cannot miss when you see him: tall, charismatic, with a memory like a computer; he is driven by his desire to make new and improved drugs for the treatment of patients.

During World War II, he studied chemistry at the High School for Chemistry and continued his studies at the University of Vienna and received his PhD in 1952. His professional career started in 1948 working at the Serotherapeutic Institute in Vienna with Professor Eisler-Terramare as his mentor.

One of the problems of these early times was the adverse effects caused by the use of curative horse serum against tetanus and diphtheria. The most frequent adverse effect, serum sickness, occurred in about 15 percent of treated patients while the anaphylactic shock, the most severe side effect, occurred less frequently. By partial enzyme treatment of the horse serum tetanus anti-toxin as well as diphtheria anti-toxin did no longer cause serum sickness but the danger of anaphylactic reactions remained.

During World War II and thereafter, a cold ethanol fractionation process for human plasma was developed by Cohn in the United States and taken up by several pharmaceutical manufacturers in the U.S. and Europe. In Vienna, based on the experience of salt fractionation for manufacturing of anti-diphtheria horse serum and by the most advanced electrophoretic technology, teaming up with Professor Auerswald made it possible to produce human gamma globulin and albumin by salt fractionation.

Wilhelm Auerswald, with commercially interested partners around him, masterminded the setting up of a commercial production of plasma derivatives, the "Österreichisches Institut für Haemoderivate."

After World War II, the Western World was regularly struck by polio epidemics and the solely successful treatment as proven by a large study in the US was the prophylaxis with gamma globulin. This led to an explosive increase of demand.

The virus-neutralizing potency of the gamma globulin, produced by the Oesterreichisches Institut fuer Haemoderivate (OEIH), met the requirements of the U.S. regulatory authorities and the OEIH was successful in obtaining the U.S. Establishment License 258 and the Product License for gamma globulin.

In the early 1950's, the research centered on how to produce blood products and how to characterize these fractions. Inspired by this work, in the late 1950's, Dr. Auerswald and Dr. Eibl became the leaders of the OEIH, the company that later became Immuno.

Hans and Martha were married in Greenport Long Island, N.Y., in 1958, and by 1965 were a family of six. Their four children all developed different careers in Austria, Germany, and the U.S.

Dr. Hans Eibl was, from the beginning, very interested in the biochemistry of blood products and vaccines and that has never changed. He has worked with a team, including his wife, on research and development, and there are more than 200 patents globally associated with his name.

Good examples are the development of Tetanus Immunglobulin in the 1960's and factor eight inhibitor bypassing activity (FEIBA) in the 1970's. By immunizing plasma donors with Tetanus Toxoid, tetanus immune plasma could be obtained for the manufacturing of human tetanus immune globulin. In field trials in Ontario, Canada, the efficacy of as little as 250 tetanus antitoxin units were proven to be sufficient for protection. These results made treatment with horse serum obsolete.

The introduction of concentrated Factor VIII preparations was exciting since it dramatically improved the life expectancy of persons with hemophilia. The downside was that inhibitors also emerged. This led to the effort to find a solution to overcome the hemostatic failures and focus on an "activated prothrombin complex." Dr. Eibl is very modest when he states that they were lucky. Like many scientific developments, there is a lot of trial and error. The introduction of FEIBA has helped many persons with inhibitors to lead a normal life again.

Dr. Hans Eibl

- **Co-founder, Immuno**
- **Associated with more than 200 patents**

Dr. Martha Eibl

- **Austrian Society for Immunology and Allergology, Past-President**
- **IUIS (WHO) expert group for the classification of immunodeficiency diseases, Past Member**
- **European Society for Immunodeficiencies (ESID), Past Board Member**
- **1996 Red Lilly of Florence for contributions to humanity and science**

Dr. Baruj Benacerraf

According to Dr. Baruj Benacerraf's biography[1], his foreign background—he was born in Venezuela and raised mainly in France—made it difficult from him to get into medical school in the U.S., despite completing his undergraduate studies at Columbia University. In fact, it was only because of the father of a friend that he was able to get an interview and earn one of the last two places at the Medical College of Virginia.

There was another important milestone: the introduction of plasmapheresis. Important work was done to develop the first plasmapheresis machine by Grifols in Spain, but the first plasmapheresis center was established in Austria in 1963. The development of plasmapheresis in Austria was parallel to and independent from similar developments in the U.S. This historic fact was recognized with a special symposium in Vienna in October 2013.

Most of the developments Dr. Eibl worked on were achieved with an international orientation. His professional work with his laboratory is still focused on research on blood components and vaccine antigens.

When I asked Dr. Eibl if there is anything he would do differently, his first response was "I am still constantly working on improvements in blood products and vaccine antigens."

To bring the focus back on patients, the area where Professor Martha Eibl has earned her reputation, I asked her about her present efforts. She answered by emphasizing to be a strong advocate for early diagnosis and treatment.

She stressed the importance of closing the gap between scientific developments and treatment possibilities with an ongoing dialogue "One of the most important things is to think about treatment options and to talk about it," she said. Members of advisory committees of international, national and professional healthcare agencies are responsible for recommendations in accordance with good clinical practice. These recommendations are taking the lead in improving the quality of treatment for patients worldwide.

Vienna (and Austria) can be proud to have these two eminent experts as citizens! It is indeed very stimulating to meet both of them and become "infected" with their energy! I am honored to have the privilege of knowing them personally!

JAN M. BULT, *PPTA President & CEO*

References

1. "Baruj Benacerraf - Facts". Nobelprize.org. Nobel Media AB 2014. Web. 5 Aug 2015. <http://www.nobelprize.org/nobel_prizes/medicine/laureates/1980/benacerraf-facts.html>