IN MEMORIAM

A Tribute to Eberhard F. Mammen, M.D. (1930–2008)

It was with profound sadness we learned that the world had lost a pioneer in the field of blood coagulation with the passing of Eberhard F. Mammen (Fig. 1) on July 1, 2008. He was born in 1930 in Carolinesiel, East Friesland, Germany, a quaint town by the North Sea. He is survived by his wife, Hanna, his children, Hens Heinrich, Dirk Steffen, Rolf Eberhard, and Susanne Marie, and by his grandchildren, Erich, Steffen, Erika, Alyssa, Sean, Claire, and Deirdre.

Eberhard studied medicine at the University of Munich and obtained his M.D. at the University of Giessen in 1956. He started his research in blood coagulation and coauthored his first article with Fritz Beller on thromboplastin formation while still an undergraduate.[1] After completing his postgraduate training in the Department of Internal Medicine, University of Marburg, he joined the faculty of the University of Vienna in 1957. As a Fulbright Scholar, he went to Wayne State University in Detroit and joined the world-renowned laboratory of Walter Seegers. There he made several discoveries in the field of hemostasis, among which was the discovery of Fibrinogen Detroit.[2]

One of us (A.P.) had the great fortune of collaborating with Eberhard in the discovery of Fibrinogen Detroit. During 1966, I (A.P.) was taking care of a 17-year-old girl who used to bleed severely every month during her menses. All the clotting factors were normal, including the fibrinogen level as determined by turbidometric and immunologic techniques. Although Eberhard was in the Department of Physiology, he had a great interest in clinical hematology, and very often I used to send him blood samples from patients who had clotting problems. I sent the blood from my patient to Eberhard, and he reported that he could not demonstrate clottability of plasma fibrinogen by addition of thrombin during the 30-minute test period. Other coagulation factors were present in normal amounts, and prothrombin activation was normal. Family studies showed that the defect in this fibrinogen had an autosomal dominant pattern of heredity, and immunologic studies revealed some differences from patients with two other known dysfibrinogenemia cases, Fibrinogen Baltimore and Fibrinogen Cleveland.

During those days, my (A.P.) laboratory was involved with studies related to gamma globulins, and I decided to undertake detailed physicochemical studies of Fibrinogen Detroit. Native and cleaved Fibrinogen Detroit had the same sedimentation constants and molecular weights as those of normal fibrinogen. In fresh samples, the free SH groups/mole of fibrinogen were similar in both normal fibrinogen and Fibrinogen Detroit. The amino acid composition revealed a decreased content of lysine, glucosamine, and galactosamine in the abnormal fibrinogen. Total carbohydrates, protein-bound hexose, sialic acid, and hexosamine were also decreased in the abnormal fibrinogen.

At the end of these extensive studies, both Eberhard and I (A.P.) were totally frustrated. What caused Fibrinogen Detroit not to clot when treated with thrombin remained a puzzle. One day, during a Walter Seegers symposium, Eberhard and I were having lunch with Birger and Margarita Blomback (Karolinska Institute, Sweden; see Fig. 2). We related our studies and frustration with Fibrinogen Detroit to the Blombacks who were very much interested in the fibrinogen molecule from an evolutionary point of view. They asked if we could spare pure Fibrinogen Detroit and normal fibrinogen for further studies in their laboratory. I immediately went to my laboratory and brought both abnormal fibrinogen and normal fibrinogen (which we had purified from Eberhard's blood) and gave this to the Blombacks. Four weeks later, I got a call from Birger who wanted to meet with Eberhard and I at the Detroit Metropolitan Airport on a certain day when he was planning to arrive in Detroit. Thus we met. It was truly an exciting day of our lives. Birger was able to decipher a specific molecular defect in the N-terminal disulfide knot of the α (A) chain in which the arginine at the 19th position was replaced by serine. We wrote the manuscript at the airport, which was then hand delivered to the editor of *Nature* in London by Birger and published promptly within 3 months. This was the first demonstration of a molecular defect in an abnormal fibrinogen.[3]

Eberhard participated regularly in the teaching of our hematology fellows, who truly admired his clarity and simplicity of presentation of topics dealing

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A Tribute to Eberhard F. Mammen, M.D. (1930–2008); Guest Editor, Emmanuel J. Favaloro, Ph.D., M.A.I.M.S.

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Figure 1 Eberhard F. Mammen (1930–2008).

with the area of "complicated clotting." Eberhard worked with me (A.P.) as an associate editor of the *American Journal of Hematology* for 30 years. He was very fair and prompt in his reviews and was truly a great supporter of the journal, and I enjoyed his association immensely. He contributed to the *American Journal of Hematology* enormously both as a teacher and as a scientist. Over a span of five decades, he published more than 300 articles on various topics in thrombosis and hemostasis.

Perhaps as a result of the influence of his country-doctor father, who had intended his son to follow his footsteps, Eberhard had always tried to excel in a broad area of medicine rather than confine himself in any single discipline. Thus, it was not surprising to see him working with the distinguished German obstetrician Fritz Beller in his earlier career, laying the groundwork for his later joining the Department of Obstetrics and Gynecology. Only a few people would ever possess the talent and experience of Eberhard's, being also on the faculty of the Department of Physiology and Pharmacology, the Department of Pathology, and of the Department of Surgery, Wayne State University School of Medicine, Detroit, Michigan. But his first and true research love was blood coagulation. Mentored by the pioneer of mechanisms of coagulation, Walter Seegers, he engaged in extensive studies in a wide variety of disorders of hemostasis. His published work covers both basic investigations of clotting proteins and the scientific basis of clinical complications ranging from disseminated intravascular coagulation to thrombosis in preeclampsia.

Figure 2 Left to right: unknown scientist, Birger Blomback, Margarita Blomback, Ananda Prasad, and Eberhard F. Mammen. Photo taken in 1968 in Detroit, Michigan, at the time of the discovery of Fibrinogen Detroit (see Ref. 3).

Eberhard could not be happier when he founded the journal *Seminars in Thrombosis and Hemostasis*, becoming the editor in chief and remaining so until the time of his death. Under his guidance, this journal has blossomed into a publication that embraces education and research of the highest caliber, treasured by both basic scientists and clinicians. One of us (H.C.K.) was most privileged to be the guest editor of this journal for eight issues on subjects ranging from thrombosis to fibrinolysis to hyperviscosity. On each occasion, Eberhard was most attentive to my needs and generously gave me valuable advice.

We shall all be missing Eberhard's enthusiasm, his cheerful smile, and, most of all, his unique sense of humor.

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