



Manfred Martin Mayer, 1916–1984

OBITUARY

MANFRED MARTIN MAYER

June 15, 1916–September 18, 1984

I met Manfred Mayer for the first time in September of 1938 when I went to Columbia to visit Michael Heidelberger, having just returned from a Rockefeller Fellowship at Upsala, Sweden, and having begun to work at Cornell University Medical School. The time and place are recorded because Pierre Grabar had just finished a year in Michael's laboratory; because this was his last day, a photograph was taken showing Michael, Pierre Grabar, Pete Treffers, Sulo Karjala, Mary O'Neill, Manfred, and myself. Thus began a scientific association and close personal friendship that was to last for 46 years.

Manfred had received his B.S. degree from City College in June of 1938 and had joined Michael's group as Laboratory Assistant in Immunochemistry, a position I had held from 1933 to 1937; I was Michael's first Ph.D. and Manfred was his third. He and his family had lived in Frankfurt but, fortunately, had left in December 1933 when Hitler took power. His college education had been entirely in the United States. He had inherited my three linear feet of laboratory bench space, which was at a 90° angle and adjacent to a bench on which the microKjeldahl distillation apparatus, then the *sine qua non* of quantitative immunochemistry, was located. "Micro" had a very different meaning in those days; the usual quantitative precipitin reaction required 100 μg to 1.0 mg antibody nitrogen (N) and digestion was carried out in 100 ml Kjeldahl flasks. Improvements over the subsequent years have increased the operating range to about 1 to 8 μg of antibody N, and Kjeldahls are almost never used. It was part of the duties of the laboratory assistant to digest and often to distill the Kjeldahls of the senior investigators, and to wash glassware if Mary O'Neill was ill, in addition to working on his own research problems.

Because I was at Cornell, Manfred and I saw one another only occasionally until June 1941, when I returned to Columbia to work in the Neurological Institute. From then on we met several times a week, because I frequently dropped in at Michael's lab around lunch time to talk to him and to the others in the group, and especially to Manfred. He was beginning to work on the precipitin reaction and on complement, and these were the subjects of his early papers. He also continued work on the cross-reaction of types III and VIII pneumococcal capsular polysaccharides with horse and rabbit antisera, a problem on which Michael, D. L. Shrivastava, and I had previously published. We spent considerable time discussing and analyzing the data, and I was clearly able to see a kindred spirit who wanted first of all to know the truth. When a question was raised, he would purse his lips (in a characteristic manner difficult to describe exactly) while de-

cidating on a proper explanation—one could almost feel the synapses operating—and would come out with a critical appraisal of the point. No doubt, our seeing eye to eye on the issues and ways to resolve them led to increased closeness; when we frequently saw things differently, our vigorous discussions usually led us to effectively solve the problem by setting up a few more experiments.

After a second paper on the type III-VIII cross-reactions by Heidelberger, Kabat, and Mayer had appeared in the *Journal of Experimental Medicine* in 1942, Manfred continued working on the problem with Michael, doing competition studies displacing the cross-reacting polysaccharide with the homologous polysaccharide. These areas provided him with crucial insights into his major field of activity, for which he became the outstanding authority—the study of complement as a series of successive enzymatic reactions. His doctoral dissertation was a study of the chemical and immunologic properties of phosphorylated serum albumin. He had a good background in physical chemistry from City College, which complemented the laboratory's expertise in organic chemistry.

Sometime in 1942, we began to discuss the need for a textbook of quantitative immunochemistry that could broaden the field. At that time, everyone who was carrying out quantitative precipitin or agglutinin determinations by a technique acceptable to the Heidelberger School had been instructed personally by Michael or by one of his disciples, and a book that could serve as a laboratory manual was essential if quantitative immunochemistry was to realize its destiny. We decided to collaborate on a book which we called *Experimental Immunochemistry*. After a survey by John Wiley and Sons, which concluded that it would never sell 1000 copies, Charles C Thomas came to visit Michael and gave us a contract, and Michael agreed to write an introduction. We made an outline of the book, divided the chapters to correspond to our interests and laboratory experience, and began to write. For several years we met on Saturdays and Sundays at one or another's apartment, reading aloud every written word and revising it until we both agreed. Michael also read most of it and made many suggestions.

We had both married, I at the end of 1942 and Manfred in 1943. These were trying times for our wives, who heroically had to amuse themselves together for most of the weekend in addition to preparing meals. We completed the book in 1945, but the first edition did not appear until 1948, allegedly due to paper shortages after the war; fortunately, we were able to revise it extensively

in galley proof. It went through three printings in the next 10 years. The second edition, with Manfred continuing to write about complement, appeared in 1962, went through four printings, and was translated into Czech, Russian, and Spanish. It did not go out of print until 1984.

Prior to 1938, Michael had introduced a quantitative analytical method for measuring complement, and he and Manfred, together with A. G. Osler and Otto Bier, continued to work extensively on the complement fixation reaction. Also, the malaria problem had become of crucial importance to the Armed Forces in World War II, and Manfred and Michael began a study of the feasibility of active immunization against relapsing vivax malaria with formalinized sporozoites; it was Elinor who actually suggested that one might attempt to vaccinate between relapses. Manfred also began, with Michael and Otto Bier, an evaluation of the role of Ca^{++} and Mg^{++} in the reactions of complement components, and this naturally led to his consideration of complement components as enzymes. I remember well his telling me before leaving for Hopkins that this was the area in which he would continue to work intensively.

From this outline of his accomplishments as a graduate student and as a member of the Scientific Staff of the Division of War Research at Columbia with Michael, his subsequent brilliant accomplishments and promise as an independent investigator are clearly evident. In 1946 he took an independent position as Assistant Professor of Bacteriology at Johns Hopkins, where he was to spend the rest of his life, rising to Associate Professor of Microbiology in 1948 and to Professor in 1960. He served as Acting Chairman in 1957. He was a fine teacher and lecturer and devoted to his students.

While at Johns Hopkins, he delineated the sequence of enzymatic reactions of the 14 complement components leading to the hemolysis of the red cell through the recognition and use of hemolytic intermediates. These intermediates were reagents for assays of the various components and made their purification possible. He established that each step leading to hemolysis involved "one hit" in which the activated next component reacted with a previously created receptor on the red cell and the successive series of interactions created holes in the red cell membrane rather than destroying its structure completely. His studies indicated the complex nature of the third component of complement, which was ultimately shown by Robert Nelson's group to be composed of six different proteins (C3 to C9) in the guinea pig system, and by Hans Müller-Eberhard and co-workers in the human system. Manfred also was the first to recognize that C2 had a binding site and a catalytic site and that decay of activated C2 was a consequence of its interaction with water rather than with a receptor on the activated fragment of C4. He demonstrated that lysis of the red cell was due to the creation of a pentamolecular complex of

the terminal five components forming a transmembrane channel, beautifully seen as doughnuts in the electron microscope. This is now the accepted model for the hemolysis of the red cell by complement.

Apart from his first love, complement, he worked on malaria, the purification of polio virus at the time the vaccine was being developed, and on lymphotoxins. With R. A. Nelson he developed the *T. pallidum* immobilization test for syphilis, which is important for the elimination of false positives which occur in the usual less-specific serologic tests.

Manfred continued to emphasize the rigorous methods of physical chemistry. He had many students and founded a school in the area of complement research. Many of his Ph.D. students and postdoctorals became important creative scientists. Those that I recognize include the late Herbert Rapp, Lawrence Levine, Keith Cowan, A. A. Marucci, L. G. Hoffman, Frank Austen, Tibor Borsos, R. M. Stroud, H. S. Shin, M. L. Shin, M. Gately, C. Gately, and Teruko Ishizaka. Manfred and Abraham Osler had been in Michael's laboratory at the same time, and when Osler came to Hopkins they again collaborated.

Manfred received numerous awards, including a citation from Columbia for his malaria work during World War II, the Kimble Award for Methodology in 1953, the Selman Waksman Lectureship Award in 1957, an honorary Doctor of Medical Sciences from Johannes Gutenberg University, Mainz, Germany, in 1969, the Karl Landsteiner Award from the American Association of Blood Banks in 1974, the Albion O. Bernstein Award from the Medical Society of the State of New York in 1976, and the Gairdner Foundation International Award in 1982. He was a Harvey Lecturer in 1976-1977, was President of the American Association of Immunologists in 1976, was elected to the National Academy of Sciences in 1979, and served as a consultant to various government agencies and on the Editorial Board of the *Journal of Immunology* and other immunologic journals.

I knew Manfred as a superb scientist and a great human being. His own background and struggles as a refugee led him to help those who came to him under similarly tragic circumstances. He was completely free of racial prejudice, and I understand he had the first two black graduate students at Hopkins. He and Elinor shared a great love for music; he played the viola in a community orchestra until bursitis made it too difficult. In recent years, he and Elinor traveled during the summer, taking courses in archeology, fifth century B.C. Greek history, anthropology, and studied Northwestern Indian Art in Alaska shortly before his death.

Manfred will live on not only for his own scientific contributions but also through his four sons and his scientific children and grandchildren. He will be missed by all who knew him.

Elvin A. Kabat