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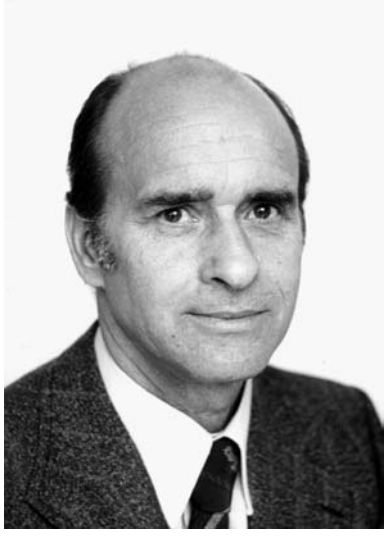
Virology Division News

Obituary

In Memoriam
Rudolf Rott (1926–2003)



Where do new virus infections come from that attract the attention of the public and the scientific community with ever increasing intensity? What role do animals play as reservoirs of these viruses? What are the mechanisms of adaptation when a virus crosses the species barrier between animals and man? Why do infections cause disease in one host species, but not in another? Fundamental contributions to a better understanding of these problems were made by Rudolf Rott who died on April 28. He was 76 years old.

Born in 1926, Rudi belonged to the generation whose youth was traumatically marked by the second World War and the post-war period. He left high school in 1943 to join the German army as a volunteer. Still at the age of 17, he became a commissioned officer. After the war and after finishing high school, he studied veterinary medicine in Gießen, where he subsequently became a research assistant in the Department of Microbiology and Hygiene with Elmar Roots. It was here that his life-long passion for virology originated. Rudi always considered meeting Werner Schäfer at Gießen one of his greatest fortunes in life. Werner Schäfer quickly recognized the extraordinary scientific talent of the young veterinarian, and offered Rudi a position at the Max Planck-Institut für Virusforschung in Tübingen. In the fifties and sixties of the last century this was one of the world's leading virus research centers, and when Rudi went there it was in its hey-day. Gierer, Schramm, and Wecker had discovered RNA genomes with plant and animal viruses. Anderer had elucidated the amino acid sequence of the TMV coat protein and was able to reconstitute the virus from RNA and coat protein. Schäfer had discovered that fowl plague virus was an influenza virus and thus laid the foundation for the paradigm role of this virus in influenza virus research. He had also shown that fowl plague virus was an excellent model for studying the architecture and replication of enveloped viruses, in general. The hemagglutinin, the nucleocapsid protein and other viral components had been recognized as different structural and functional entities, and Rudi became heavily engaged in their biochemical and immunological characterization. He was very successful in his research and was soon recognized as one of the most promising young scientists in his field.

In 1964 Rudi returned to his alma mater in Gießen as chairman of the new Department of Virology. Apart from at the Max Planck-Institut in Tübingen, virology was not well developed in Germany at that time. Rudi felt that the field could be promoted best by scientific excellence in an academic environment. The new institute was therefore conceived as a research institute.

From the beginning the focus was on influenza viruses, and they remained the central issue for the three decades of Rudi's chairmanship, although the spectrum of viruses under investigation increased significantly later.

It soon became clear that influenza virus research at the new institute would follow two major tracks: (1) the elucidation of the structure of the virus genome and of the replication mechanisms, and (2) the analysis of the biosynthesis and function of the envelope constituents. Studies on molecular epidemiology and pathogenesis would follow and prevail in later years. The finding that influenza viruses have segmented genomes provided an explanation for their high genetic variability. In a classic study on the origin of human influenza virus subtypes H2N2 and H3N2 published 1978 in Virology, Rudi and Christoph Scholtissek showed that gene exchange was the mechanism underlying the emergence of new pandemic viruses.

Reassortants obtained in the laboratory became invaluable tools to address many important problems in influenza virology on a genetically well defined basis. Thus, it was shown that some of the reassortants derived from two apathogenic parent viruses had acquired pathogenicity. Comparisons among many reassortants revealed that pathogenicity was associated with quite different gene sets. This led to the concept that pathogenicity depends on an optimum gene constellation rather than being defined by a single gene.

Among the viral glycoproteins investigated, the influenza virus hemagglutinin always played a prominent role. The observation that influenza virus infectivity depends on proteolytic activation of the hemagglutinin revealed that receptor binding is not the only function of this protein, it also mediates virus entry by membrane fusion. Equally important was the finding that hemagglutinin activation is a prime determinant of pathogenicity. In a series of studies that extended almost to the end of his scientific career, Rudi demonstrated how structural changes of the cleavage site altered pathogenicity, with heterologous RNA recombination as one of the most interesting mechanisms involved. Among the activating enzymes were also bacterial proteases, which proved to have a decisive effect on the development of pneumonia in co-infected animals.

Numerous other viruses interested Rudi. These included coronaviruses, infectious bursitis virus, papilloma viruses of rodents and birds, *Borna disease virus* (BDV), and paramyxoviruses. In fact, Rudi's observation that cleavage activation of a viral glycoprotein determines pathogenicity was first demonstrated with *Newcastle disease virus* and was later confirmed and extended by studies on *Sendai virus*, another paramyxovirus.

BDV was a particular challenge for him. This virus, which causes infections of the central nervous system (CNS), is endemic in horses and sheep in Central Europe and can be experimentally transmitted to other hosts. Rudi showed that the disease was the result of a T cell-mediated immuno-pathological reaction in the CNS. Disease symptoms vary depending on the host species and immune status, and Rudi was excited when he found that infection of tree shrews caused behavioural disorder. This prompted collaborative studies with clinical groups which showed that seroprevalence for BDV-specific antibodies was significantly higher in neuro-psychiatric patients than in controls. Whether BDV is indeed responsible for human neuro-psychiatric disorders is a matter of ongoing research in many laboratories.

Such a large scientific programme could only be successful with a clear conceptual framework. Rudi realized at a very early stage that elucidation of the pathogenetic mechanisms he was so much interested in would require a multidisciplinary approach combining virological, cell biological, molecular biological, biochemical and immunological expertise. This went well beyond the limits of his own Department, but with his enthusiasm, his charisma, and his scientific stature he was able to convince other groups that it was worthwhile to collaborate with him. Therefore Gießen was soon recognized internationally as a center of virology that over the years became the scientific home of numerous German virologists and the host of guest investigators from all over the world, many of whom were going to be Rudi's

life-long friends. Highly ranked academic appointments and prestigious awards, such as the Robert Koch Prize, are documents of his extraordinary scientific reputation. However, despite all of this Rudi continued to be a dedicated researcher working at the bench until the end of his professional career. And he was never distracted from what he considered to be his prime mission, to work for the benefit of his Institute and his field.

Many of Rudi's former collaborators and friends met him last at a reunion on the occasion of his 75th birthday. He was marked by the disease which he had already fought then for some time, finding all the loving care he needed so much with his wife Renate, to whom he was married for almost 50 years. Those who were there and all of his other friends and colleagues will sorely miss him and remember him as a great scientist whose contributions to virology will live on.

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