

OBITUARY

Richard John William Rees,
C.M.G., F.R.C.P., F.R.C.Path.
1917–1998



Richard John William "Dick" Rees died on 3 October 1998 aged 81. He was one of the most influential leaders in the fight against leprosy, a fight which has seen remarkable advances in recent years. During a research career spanning more than four decades, he dedicated himself to bringing the benefits

of modern medical science to some of the poorest and most ostracized people in the world.

Dick was educated at Sheen County Secondary School, before studying medicine at Guy's Hospital. After qualifying from Guy's in 1942, he served as a captain in the Army Blood Transfusion Service in the North Africa and Italian campaign. At the end of World War II, he returned to Guy's and started what was to become a remarkable career in experimental pathology. In 1949 he made the defining move in his career; Philip D'Arcy Hart was establishing the Medical Research Council's new Tuberculosis Research Unit in London, and Dick Rees was recruited to the National Institute for Medical Research at Mill Hill to carry out laboratory-based research on tuberculosis (TB), research which was to underpin the Unit's activities.

The study of tuberculosis was changing rapidly; the discovery of streptomycin in 1944 was to be the start of a new era of successful chemotherapy. Other drugs against TB quickly followed, and the TB Research Unit became the major focus of research on the use of these new compounds for treating

TB. Dick's early work, in collaboration with Philip D'Arcy Hart and Sir John Cornforth, involved an investigation of the anti-tuberculous activity of a group of compounds which appeared to act through a host cell-mediated mechanism. These compounds, now called "calixarenes," are the source of renewed interest since they represent a novel approach to understanding how macrophages can inhibit mycobacterial multiplication.

Although research in TB was creating much excitement in the early 1950s, Dick Rees made another important change of direction. He heard of a lecture, ostensibly about TB, in which the speaker drew the audience's attention to the fact that the related disease of leprosy had attracted virtually no interest from medical researchers and, like many of its sufferers, was isolated from the mainstream of medicine. Dick gradually started to shift his focus, drawing on the TB Unit's experience in successfully bringing together high-quality laboratory-based research and clinical research carried out under difficult field conditions; he turned his attention to leprosy. Meticulous observation enabled him to establish the relationship between viability of the leprosy bacillus and its staining properties. This enabled him to establish the concept of the morphological index, or MI, as a measure of therapeutic progress, thus providing the first laboratory correlate of successful chemotherapy.

Although useful, the MI lacked the precision and sensitivity required to carry out precise comparisons of therapeutic regimens. However, Dick instantly recognized the importance of the research being carried out by Charles Shepard at the Centers for Disease Control in Atlanta, Georgia, U.S.A. If *Mycobacterium leprae* could be reproducibly grown in the foot pads of mice,

then here at last was a method for reliably monitoring the viability of the bacteria isolated from patient tissue. Dick confirmed Shepard's findings and extended them by using immunosuppressed mice which permitted greater bacterial multiplication. From his base at Mill Hill he began to establish an international network of collaborators in leprosy research. Field units were set up, first in Sungei Buloh in Malaysia and later in Addis Ababa, Ethiopia, and then in Hyderabad, South India. It was these interactions in particular, with discoveries made in the Rees laboratory at Mill Hill underpinning the clinical research of Dr. Michael Waters in Malaysia and Dr. John Pearson in Addis Ababa, which transformed the way in which leprosy was studied, and ultimately how leprosy patients are treated.

Using the mouse foot pad technique Rees and his colleagues demonstrated the emergence of secondary drug resistance, then primary drug resistance. By utilizing the greater sensitivity of thymectomized-irradiated mice they were able to demonstrate the presence of a population of drug-sensitive bacteria which remained viable for several years following treatment, the so-called persisters. It was these findings which provided the impetus for the recommendation of multiple drug therapy by the World Health Organization in the early 1980s.

In the same way that he had instantly appreciated the importance of the mouse foot pad work, Dick also recognized the potential of using the armadillo as a source of large numbers of *M. leprae*. The mouse had provided a tool to support his clinical research, now the work of Dr. Eleanor Storrs in the U.S.A. at last offered the possibility of carrying out basic studies on the immunology, physiology and ultimately the molecular biology of *M. leprae*. A colony of infected armadillos was established in the U.K. and, with the support of the World

Health Organization, the "IMMLEP Bank" was set up with Dick providing a range of *M. leprae* "products" to the research community. We can anticipate that within the next 12 months we will have the complete genome sequence of the leprosy bacillus. How fitting that the material supplied by Dick's IMMLEP Bank should ultimately reveal the most fundamental secrets of the organism which he spent his life trying to understand.

Even before he was officially appointed Head of the Medical Research Council's Laboratory for Leprosy Research at Mill Hill in 1969, Dick Rees' remarkable scientific abilities and commitment to the cause of leprosy had become widely recognized. In 1963 he became Chairman of the Medical Advisory Board of the charity LEPRO (The Leprosy Relief Association); he was a central figure in leading the research and disease control activities of LEPRO for more than a quarter of a century and remained closely associated with the charity until shortly before his death. He also played a leading role in the World Health Organization's leprosy program. Although Dick officially retired in 1982, he continued to work both for LEPRO and WHO, and was a profound influence on the leprosy work of both organizations long into his retirement years.

Dick Rees was a modest man, communicating his ideas in a quiet but forceful way to his colleagues and students all over the world. There are few people working in leprosy today, be it in the scientific laboratory or in the remotest part of the world where leprosy remains an important health problem, who have not been influenced by his enthusiasm and devotion. A world without leprosy was a dream which inspired his research career; it is a dream which he more than most has helped to bring within our grasp.—M. J. Colston—Leprosy. Rev. 69 (1998) 403–405.