Lepr Rev (1982) **53**, 243–247

Retirement of Dr R J W Rees

In September this year, Dr R J W Rees retired from his position as Head of the Laboratory for Leprosy and Mycobacterial Research at the National Institute for Medical Research (NIMR), Mill Hill, London. He will be succeeded by Dr J Colston at the NIMR, but will retain his long-standing association with LEPRA as Chairman of its Medical Advisory Board and Vice-Chairman of the Editorial Board of this Journal.

Difficult though it will be to pay realistic tribute to the extraordinarily high quality of Dick Rees's contribution to the subject of leprosy over several decades, we shall nevertheless be making an attempt to do this in a future number of *Leprosy Review*. Around mid-1983, it is hoped to devote an issue of the Journal to articles by leading authorities on the most important aspects of leprosy, which will summarize the present state of knowledge and reflect his outstanding participation over a long period of time. Meanwhile, to mark his formal retirement from Mill Hill, we print the following personal tributes.

From 'Close colleagues in London'

In the early fifties Dr James Doull, then the distinguished head of the Leonard Wood Memorial Foundation, suggested to a small informal meeting in London that it was time that leprosy research emerged from the descriptive stage into a subject more susceptible to scientific discipline and more attractive to medical scientists. A few years later the young Dick Rees, who was initially taken on to the staff of the NIMR to assist Dr Philip D'Arcy Hart in laboratory tuberculosis research, made his first successful venture into leprosy research by adopting a suggestion of Dr John Hanks that he take up tissue culture to try to grow the then uncultivated 'rat leprosy bacillus' (*Mycobacterium lepraemurium*). With Garbutt, Wong and Barr (1958–62) he demonstrated unequivocal growth of this organism in an established line of cells (rat fibroblasts). Since then he has exercised enormous and world-wide influence in transforming the study of leprosy into an important and intriguing immunological and chemotherapeutic area of research.

The centre of Rees's work has been, throughout, NIMR; an important stage was when (1969) he was given the task of developing there his own Laboratory for Leprosy and Mycobacterial Research. Besides being engaged in basic investigations, and in the questions thrown up from field work, the Laboratory

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has been the co-ordinating centre for Medical Research Council-participating projects in Malaya, Ethiopia, India and elsewhere. Of these the first and most important was the Leprosy Research Unit, Sungei Buloh, set up in 1957 by Rees, under his direction and sponsored by the MRC and the Malaysian Ministry of Health. He visited India a few years ago, at the invitation of the Indian government, to advise on many aspects of leprosy. A continuing connection with leprosy research in India is the link scheme between the NIMR and the Central JALMA Institute for Leprosy in Agra. This scheme (sponsored in the UK by The Overseas Development Administration) is run jointly by Rees and the Director of JALMA, Dr K V Desikan, and encourages collaborative research and exchange of personnel between the two Institutes.

Rees has advised upon and stimulated work in numerous other projects, including some in the USSR and China. Many leprosy research workers from overseas, scientists and technicians, owe part at least of their expertise to the training facilities provided at Mill Hill. Many researchers have been encouraged in their projects. The international aspect of Rees's work is recognized by the Laboratory being also a World Health Organisation Collaborating Centre for Reference and Research on *M. leprae*. He has participated as a 'founder member' in two of the Steering Committees of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, IMMLEP and THELEP, dedicated, respectively, to the development of a leprosy vaccine and to the improvement of leprosy chemotherapy. A further involvement in leprosy research has been his chairmanship of the LEPRA Medical Advisory Board, which sponsors research programmes in Britain and elsewhe

Rees has also acted on Doull's plea for drawing in many young scientists of different backgrounds into leprosy research: one should mention particularly Philip Draper, Michael Waters, John Pearson and Gordon Ellard. Students, too, have been a source of new blood, fired by his introduction to the subject. To all these international and national activities Rees has brought his remarkable organizing ability; characteristic determination, patience, sound judgment and modesty; as well as scientific astuteness. One of his extraordinary talents is the ability rapidly to switch attention and memory from one to another of the very varied topics raised by the stream of visitors (and telephone callers!) to Mill Hill, and then immediately to concentrate on detailed technical problems of his own laboratory colleagues.

With all this stimulatory and administrative leadership, Rees has never abandoned bench work. The early tissue-culture contribution has been mentioned. Space permits mention of only a few of the subsequent investigations in leprosy which he has carried out, or in which he has played a prominent part. Partial immunosuppression produced by thymectomy plus irradiation of mice was observed to increase their susceptibility and to allow dissemination of infection when *M. leprae* was administered by the Shepard footpad technique (1966); in normal mice infection remains local and limited. This new model has proved of

great value. Thus the enhanced infection makes it possible to detect small numbers of live *M. leprae* among large numbers of dead organisms (valuable for following the progress of chemotherapy). It also provides a somewhat better model for studying the pathology of the infection than does the earlier model in normal mice.

A technique was introduced for following the progress of treatment of leprosy, using the staining morphology of sampled bacilli (1966); the Morphological Index is now widely used as a quantitative measure of viability of *M. leprae* suspensions. Proof was obtained that *M. leprae* could develop resistance to dapsone during treatment (1964), thus establishing a requirement for combined chemotherapy (as with tuberculosis); later, the existence of primary resistance was observed (1977). *M. leprae* was seen to reside free in striated muscle of patients (1970). An enhancement of macrophage resistance to *M. lepraemurium* and *M. microti* by lymphokine treatment of cell cultures was achieved (1971). New evidence for the airborne transmission of leprosy from the nose, and its risks, were studied (1974).

In recent years the Mill Hill laboratory's activities have included further exploitation of the thymectomized-irradiated mouse model to study pathogenesis (e.g. at the ultrastructural level), as well as immunology and chemotherapy of the disease, including the efficacy of new drugs. The relative profusion of yield from the nine-banded armadillo, compared with man or mouse, has redirected attention to the bacillus itself, permitting new discoveries about the organism and its antigens and their immunogenicity; these studies have been facilitated by the armadillo colony set up by Rees at Porton Down, Salisbury. Thus a refined product for the 'lepromin' skin test has been obtained and successfully tested. *M. leprae* has been shown to have a more lively intermediary metabolism *in vitro* than thought; such studies may offer clues to its normal survival *in vivo* and even the hope of cultivation. Purification and fractionation have made progress towards characterization of specific antigens and constituents, and – perhaps more important – towards the production of a safe and protective vaccine.

While leprosy has been Rees's prime field of activity, he has never lost his earlier interest in tuberculosis. Among his notable contributions are the discovery (1951) of the antituberculous effect in mice (later found also in cultured macrophages) of the well-known nonionic surfactant 'Triton WR-1339'; this led to the synthesis by Sir John Cornforth and his colleagues of a large series of analogues (including Macrocyclon) whose varied effects on tuberculous infection correlated with their structural differences. Another important observation was to draw attention to the aggravation of experimental tuberculosis by cortisone, and to its human implications (1950).

The important service of Rees to medicine and to the community was officially acknowledged by the award of CMG in 1979. One hopes that his retirement, at a time when his vigour is undiminished, will leave him free to

pursue some of his research interests, but will not free him from at least some of his international commitments. His successor, Dr M J Colston, should find the Mill Hill laboratory in excellent shape for developing leprosy research further and in new directions.

From Dr Tore Godal in Norway

I spent the winter of 1969–70 at the NIMR. After lunch, coffee was served in a separate room with soft chairs and a lovely view of the 'green belt'. This peaceful atmosphere, with the smell from a humble cigar, provided the opportunity to ask questions from my daily dose of leprosy scientific literature. On almost every topic, Dr Rees could fill in and present views based on direct personal experience or indirectly via one of his collaborators.

In the international community of leprosy, there has been a continuous discussion on whether leprosy is a disease that follows the same ground rules as other infectious diseases or whether it is a unique, singular disease. This discussion includes almost all aspects of the disease, including whether it is infectious and whether it is caused by a mycobacterium. Together with Shepard, Rees has made outstanding contributions to the creation of a sound scientific basis for the study of leprosy.

The establishment of the morphological index as a measure of bacillary disintegration, the discovery of secondary DDS resistance in 1964, of persisters in the mid-70s and the detection of primary DDS resistance in the late 70s, are all fundamental steps towards the development of rational combined chemotherapy in leprosy. Likewise, studies showing that high-dose DDS did not precipitate reactions more often than low-dose DDS were instrumental in eliminating the low-dose DDS dogma. These clinically orientated projects were made possible by the network of MRC field stations. At AHRI and ALERT in Addis Ababa we benefited greatly when Dr Rees responded positively to our invitation to establish such a unit there.

Nevertheless, to an immunologist the most significant contribution so far by Rees to the science of leprosy at the conceptual level was his discovery of a lepromatous-like disease in mice immunosuppressed by thymectomy and X-ray irradiation and reconstituted by bone-marrow cells, providing for the first time unequivocal evidence that T cells are of key importance in protective immunity to intracellular parasites. The model could also be used to study the pathogenesis of nerve damage in lepromatous leprosy, reversal reactions and detection of persisters.

These contributions, in combination with his continuous wholehearted commitment to the training of scientists from all over the world, both in his own laboratory and at courses abroad, have paved the way to the establishment of leprosy on a respectable scientific base. This has in turn created positive

feedbacks in the scientific community by and large, and no doubt has facilitated the development of international research endeavours such as IMMLEP and THELEP. Together with Dr Shepard, Dr Rees from the very beginning agreed to serve on the Steering Committee of both IMMLEP and THELEP – both of which are very demanding tasks. Moreover, to both scientific working groups, Dr Rees has provided key services, such as screening for persisters in thymectomized mice for THELEP drug trials, supplying *M. leprae* from the armadillo and running the *M. leprae* bank.

We wish him a happy and active retirement, in which his resources both at the bench and in an international context will be available for many years to come.