

ROLAND HERBERT THORP: HIS CONTRIBUTION TO AUSTRALIAN PHARMACOLOGY*

Roland Thorp joined the Wellcome Physiological Research Laboratories in 1936 as an assistant to the then Chief Pharmacologist, John William Trevan, who introduced the concept of the LD₅₀ as an index of toxicity and founded the statistical basis of biological standardization. Trevan stimulated Thorp's interest in pharmacology, and encouraged his development as a pharmacologist. Pharmacological research in Universities and pharmaceutical companies was very much in its infancy in the 1930s, but the Wellcome Laboratories was one of the great pharmacological research institutes, for Sir Henry Dale had been director before taking over at the National Institute for Medical Research, and it was at the Wellcome Laboratories that he worked with Barger, Carr, Ewins and Laidlaw on the sympathomimetic amines, histamine and ergot, and with J. H. Burn on the ganglion blocking drug tetraethylammonium. Two of Roland Thorp's junior colleagues at the Wellcome Laboratories later achieved prominence in their own fields: Tom Sears as Professor of Neurology at Queen's Square, and Otto Hutter as the Regius Professor of Physiology at Glasgow.

At the Wellcome Laboratories, Roland Thorp worked with Eric Walton and Peter Offner in developing and testing many new analgesics and helped to study their clinical pharmacology with Frederick Prescott at University College and Queen Charlotte's hospitals. He was also concerned with the pharmacological aspects of production-control, in the biological assay and standardization of insulin, vitamin D, and organic arsenicals for the treatment of syphilis. When Charles Kellaway came from the Walter and Eliza Hall Institute in Melbourne to join the Wellcome Institute as Director in 1946, he recommended that pharmacological research and production-control by biological assay should be separated. Over the period 1946-1949, Roland Thorp had the task of establishing a laboratory at Dartford for biological assays of all types: this is now a recognized laboratory for postgraduate studies in London University in such methods.

In the immediate post-war years, opportunities for pharmacologists to move from industry to university work were few, but Roland Thorp applied for the Chair of Pharmacology in Baghdad, and named Kellaway as a referee. This led Kellaway to suggest that Thorp should apply for the newly advertised Chair of Pharmacology in the University of Sydney, which he did, after further encouragement from John Gaddum. There had been a nominal Chair of Pharmacology in the University of Sydney in the years 1918-1921 which was held by Henry George Chapman, but the position taken up by Roland Thorp was generally regarded as the Foundation Chair of Pharmacology.

When he arrived in Sydney, Thorp became responsible for the teaching of pharmacology to some 460 students in the medical course; lectures in pharmacology had been given previously by the very capable Dr Hales Wilson, in his capacity as a part-time lecturer. Thorp's appointment was also as Director of Pharmacy. There were about 180 pharmacy students pursuing a part-university, part-apprenticeship course with only one full-time lecturer, Miss

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Dorothy Large, and there were some 600 students who had passed the University course in pharmacy but had not succeeded in becoming registered pharmacists by passing the examination of the Pharmacy Board. Thorp's first task was to expand and upgrade the teaching in pharmacology, and this remained as a continuing challenge until his retirement. Training in pharmacy was soon elevated to a full-time degree course, with pharmacology as a major component. Service courses in pharmacology were also introduced in the course for dentistry and veterinary science.

One key to this early development of pharmacology in Sydney and later in other Australian universities, was to establish the subject in the Faculty of Science in its own right rather than leaving it always as a service subject for medicine, pharmacy, dentistry or veterinary science. This move encouraged the study of pharmacology as a career subject, and a steady stream of science-trained pharmacologists has emerged ever since. Many of these have taken higher degrees. Prominent doctorate alumni from the Department of Pharmacology of the University of Sydney include the late Professor S. E. Wright, Professors L. B. Cobbin, F. Michal, M. J. Rand and T. R. Watson.

The University of Sydney has justifiably prided itself on its B.Sc. (Med.) degree in which selected students devote an additional year during the medical course to a project in one of the basic sciences. With the development of the Department of Pharmacology, this provided a means of creating a pharmacologically informed section of the medical profession. In most years, a number of students spent the year of their B.Sc. (Med.) course in pharmacology, and the majority of them reached distinction in their subsequent careers. Notable among these, and worthy of special mention, are Professor B. L. Firkin, Dr W. A. Barclay, Dr G. D. Thorburn and Dr Victor Chang.

In addition to the development of teaching, Roland Thorp provided a great stimulus to the research activities of his new Department of Pharmacology by fostering the establishment of Fellowships. Even before he arrived, Burroughs Wellcome (Australasia) established a Fellowship in Experimental Pharmacology: the first appointee, F. E. Peters, is now Australian Government analyst. Within a couple of years Drug Houses of Australia also established a Fellowship, and later Nicholas Laboratories provided similar support. Such support was vital to Australian pharmacology because most holders of such a Fellowship have found a senior place in pharmacology in Australia or overseas.

When Roland Thorp arrived in Australia, he had to develop quite different lines of research to those in which he was previously engaged as a pharmacologist in the pharmaceutical industry in Britain. As a suitable topic to study in Australia, and yet one which could involve a small group with diverse interests in the field of pharmaceutical science, Roland Thorp chose the cardiac glycosides and, together with the late Sydney Wright, T. R. Watson and H. Silberman, a study was made of the methods of analysis and separation of cardiac glycosides in *Digitalis* species. Mrs Dorothy Thorp made a study of the genus *Digitalis* from a botanists's standpoint. She collected all species and varieties, reported their differential pharmacognosy and cultivated many of them on a pilot scale for glycoside analysis. Watson and Thorp screened Australian plants for cardiac stimulant activity, and S. E. Wright and some of the graduate students made extensive studies of cardiac glycoside metabolism. This project enabled a wide variety of students with a diverse scientific training to become involved in original research without dependence on overseas supplies or chemical syntheses.

Research in the pharmaceutical industry was something which was sadly lacking in Australia, but already in the early 1950s it was becoming harder for companies to produce useful new drugs without vast financial resources and a measure of good luck. Australia

simply did not have the markets sufficient to support units of a viable size. In the early 1950s, Drug Houses of Australia established a small research unit, and a few years later a much more ambitious project was launched in the old home of the Nicholas family in the Dandenong Mountains near Melbourne: the Nicholas family established a successful pharmaceutical business in Australia during the first world war, and had spread to the U.K. in the 1940s. More recently, a research institute was established by Riker Laboratories Pty. Ltd at Thornleigh, a suburb of Sydney. These endeavours in industrial pharmacological research started off with great intentions and hopes, but the chances of producing wonder-drugs were fast becoming more remote. Their lack of success was due to several factors; the timing of their establishment, the lack of developed research in academic pharmacology and gross underestimates of the difficulty of developing new therapeutic agents without comprehensive synthetic chemical facilities.

A different venture in research was attempted with the establishment of the Smith, Kline and French Institute in the Department of Pharmacology in the University of Sydney. This development was the result of discussions relating to the proposed establishment of a research division in the Australian branch of the Company and it was suggested that this should be done in two stages rather than as one major creative step. First an Institute was set up in the University; it was proposed that this would gradually, and 3-5 years were envisaged, be transplanted piece by piece to the Company's own premises, but that contact between the two partners should be ongoing so that the facilities of each could be used for research and teaching in the widest possible way. The venture started in 1960 and two research projects were supported; a study of possible cardiac stimulant autacoids and the pharmacology of substituted adenyly nucleosides and nucleotides. The project was generously supported, and could have been more richly funded if the University then had more accommodation available. The scheme was part of a larger view held by the Company at that time, of surveying and supporting research in universities on a world-wide basis. It became apparent after the initial 3 years that the climate of the pharmaceutical industry was not suitable for the second stage to prosper, hence the Institute continued under the original arrangements until it was gradually brought to a conclusion in 1969. A total of some \$500,000 had been donated for research and much new information had been published, particularly on the mechanisms of platelet aggregation, on the relationship between structure and pharmacological activity of adenyly nucleosides and nucleotides, and on cardiac stimulant substances. A number of patents were filed, but the areas of study were of greater academic than commercial interest and were unlikely to lead to a viable production of new drugs which could be used in more than very restricted applications in unusual clinical conditions; that is, the circumstances did not warrant the vast expense of the toxicological investigations which would have been required for governmental approvals.

Until well into the 1960s, the Australian Government had no laboratories for the testing of pharmaceutical products, and all such work was done under contract either in Thorp's Department or in the corresponding one in Melbourne to which the late Professor F. H. Shaw had been promoted in the early 1950s. In addition, these Departments became engaged in work which had been initiated in about 1948 by the veterinary scientist Professor Stewart on the analytical control of doping in the great Australian racing industry. The Australian Jockey Club were quick to take advantage of the opportunity for doping control that was offered by the new Department of Pharmacology in Sydney, and later established their own laboratories at Randwick Racecourse, under Mr Peter Ashelford who had begun his expert career in the Department of Pharmacology.

One very difficult feature in the establishment of pharmacology in Australia is that of contact with the leaders of teaching and research in the larger, well developed centres and it was in this respect that the pharmaceutical industry in Australia came to Roland Thorp's assistance in a generous and continuing way. In 1956, he suggested the creation of a fund to serve two purposes: to invite a Visiting Professor of Pharmacology to Australia, and secondly to help young graduates of the University of Sydney to travel overseas to continue their studies. The cost to some thirty participating companies was small, but the rewards were immense. Professor F. R. Winton started the series of Visiting Professors, and he was followed by Professors C. A. Keele, J. M. Robson, J. H. Gaddum and Dr Marthe Vogt. In addition to their time in the University of Sydney, they visited other universities where some pharmacological or physiological research was in progress, and they all helped our Australian graduates who later took up postgraduate opportunities in Great Britain. Roland Thorp's initiative in introducing the scheme for Visiting Professors of Pharmacology was an important factor to the development of pharmacology in Australia.

In his 25 years as Professor of Pharmacology in the University of Sydney, Roland Thorp made a number of major contributions in areas outside his special subject to Australian universities and the community. In particular, he was instrumental in the establishment of the Australian Consumers Association, and is still the Chairman of the Association.