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SIR HANS KREBS, F.R.S.

Obituary

SIR HANS KREBS (1900–1981)

Sir Hans Krebs, F.R.S., Nobel Laureate, who was formerly Professor of Biochemistry at Sheffield and later at Oxford, died on 22 November 1981 in Oxford. Until shortly before his death he was active in his laboratory directing work on the metabolic functions of liver glutathione. He was to have contributed on this topic to a colloquium at the London Meeting of the Biochemical Society in December 1981.

Hans Adolf Krebs, son of an ear, nose and throat surgeon, was born on 25 August 1900 in Hildesheim, a small town in northern Germany. At an early age he decided to follow in his father's footsteps, but before he could commence his medical studies he was conscripted into a Signal Regiment of the German Army. Fortunately, this was a brief interlude and he enrolled as a medical student at Göttingen in December 1918. He continued his studies at Freiburg, Munich and Berlin, obtaining his M.D. degree in 1925.

It was while still a student at Freiburg that he had his first taste of research and his first publication on the physicochemical basis of histological staining. This study impressed on him the importance of an adequate background in organic and physical chemistry, and therefore he enrolled for a course in chemistry and biochemistry under Professor P. Rona.

The crucial event in the subsequent development of his research interests was his appointment as a research assistant in the laboratory of Otto Warburg in 1926. It was here that he learnt the techniques of manometry, spectrophotometry and preparation of tissue slices which Warburg had developed and which were to form the basis of much of Krebs' experimental work in the next 50 years. Equally important, there was the daily contact with one of the greatest biochemists of the period. Towards the end of 1930 Warburg indicated that he did not retain senior scientists in his group and he advised Krebs to return to medicine to earn a proper living.

In 1931, Krebs took up a clinical post in Freiburg in the Department of Medicine headed by Professor Thannhauser. At last he was able to carry out his own ideas, namely to use tissue slices to study metabolic processes. Within 12 months he and Kurt Henseleit (a medical student) made a major discovery—the catalytic ornithine cycle for the synthesis of urea—the first metabolic cycle. Apart

from demonstrating the potential of the study of tissue metabolism *in vitro*, the work has had direct clinical relevance with the discovery of the various inborn errors of the enzymes of urea synthesis.

The work on urea synthesis gained him an international reputation and this in turn led to an invitation from Sir Frederick Gowland Hopkins to work in Cambridge when he was dismissed from his post in Freiburg in 1933 under the antisemitic legislation of the Hitler regime. Sir Hans described his reception in Cambridge in moving terms in his Hopkins Memorial Lecture in 1961. In Cambridge he continued his work on amino acid metabolism, in particular on the metabolism of glutamine and the synthesis of uric acid.

In 1935, he was appointed Lecturer in Pharmacology in Sheffield. It was here that he began to build up his 'team'; the first to join him were Leonard V. Eggleston (he died in 1974 after 38 years collaboration with Sir Hans) and a Ph.D student, W. A. Johnson. Together they studied the oxidation of di- and tricarboxylic acids by minced pigeon breast muscle. Others had established that succinate could be oxidized to oxaloacetate and that 2-oxoglutarate could be formed from citrate. The elegant demonstration by Krebs and Johnson that citrate could be formed from oxaloacetate and pyruvate made a series of reactions into a cycle and linked it with carbohydrate metabolism. Today we often regard the tricarboxylic acid cycle as a truism, but this familiarity cannot detract from the brilliance of its discovery. Sir Hans and his colleagues (including Reginald Hems who joined the team in 1940) continued to develop the area of intermediary metabolism related to the tricarboxylic acid cycle.

In 1945, the Medical Research Council established a Unit for Research in Cell Metabolism in Sheffield with Sir Hans as its Director and the University created a Chair of Biochemistry for him. The Unit and the Department rapidly expanded and gained an international reputation. He encouraged his senior colleagues to study a variety of problems, rather than remain closely associated with his own work. An indication of the wisdom of this approach was that seven members of the Unit were eventually appointed to University Chairs.

In 1954, Hans Krebs was invited to the Whitley Chair of Biochemistry at Oxford and the Unit accompanied him. Despite his load of teaching and administration, novel work continued, including the

discovery of the glyoxylate cycle with Hans Kornberg and studies on the developing area of metabolic regulation. It was this area which saw most of his contributions during the past two decades, particularly in relation to the control of ketogenesis, gluconeogenesis and the redox state of the liver cell.

At the age of 67, Sir Hans retired from the Whitley Professorship and set up a new laboratory with support from the Medical Research Council in the Radcliffe Infirmary, Oxford. He was accompanied into 'retirement' by some of his close colleagues. To many retirement means an opportunity to slow down; for Sir Hans it was an enjoyable and invigorating pastime. During the period from 1967 to his death he published over 100 papers, including a number with a clinical bias.

Despite being a modest and retiring person, Sir Hans never hesitated to defend his position, whether

it was a question of experimental evidence or University politics. In his autobiography *Reminiscences and Reflections* (published after his death) he described himself as not being an easy taskmaster and of expecting high standards of performance and attitude. Although this was undoubtedly true, he also had the ability to inspire trust, loyalty and affection in his collaborators and others he came into contact with over the years.

Sir Hans' massive contributions to metabolism and its regulation are the solid rock on which much of the future work in this area of biochemistry will be based. It is now the task of the present generation of biochemists to continue his work and in this way provide a fitting memorial.

D. H. WILLIAMSON