

Sidney Montague Hilton

17 March 1921–28 January 2011

Sidney Montague Hilton who died recently had been Bowman Professor and Head of the Department of Physiology at the Medical School in Birmingham from 1965 to 1983. He was a distinguished physiologist who made leading contributions to understanding brain control of cardiovascular changes accompanying behavioural reactions associated with sudden emergencies like the fear-flight-fight reaction. These have relevance to psychosomatic disease and to chronic hypertension. Hilton was in the vanguard of thinkers who provided experimental evidence against the long-held view that there is a single brain centre controlling blood pressure. He was an excellent lecturer and travelled widely.

Sidney Hilton was educated at St Paul's School, London from where he won a place to study medicine at Cambridge having gained an exhibition at Jesus College. During the second World War he was allowed time to take the Part II Honours Tripos course in Physiology following which he did his clinical training at Guy's Hospital, London where he subsequently held several house appointments. He then was required to do National Service and for this he served in the RAF at the Institute of Aviation Medicine, Farnborough. Here he assisted in developmental work on the design of flying equipment and with Professor J Beattie at the Royal College of Surgeons carried out studies on ways to accurately measure oxygen levels in the blood, non-invasively. On leaving the RAF in 1950, Sidney returned to Cambridge to the lab of Professor Adrian (a Nobel Laureate, later to become Lord) who had done ground-breaking work on the generation of vasomotor nerve activity by the brain, a key element in the control of blood pressure. It was here that he decided on a career in physiological research and possibly the seeds were sown for his later major contributions. He then joined the scientific staff of the Medical Research Council



Sidney Hilton on his arrival in Birmingham in 1963.

(MRC) at Mill Hill, London, where he worked in the division led by another great figure in biomedical science, Professor Feldberg, who had made major discoveries concerning chemical transmission between nerves. Hilton's major interest at the time was the local mechanical and chemical control of blood vessels. He found that the widespread dilatation in the large arteries supplying skeletal muscles during contraction depended on transmission by smooth muscle conducting elements in the walls of the arteries. This conducting system turned out to be functionally important for ensuring that a local stimulus caused a widespread opening up of the arteries supplying an organ. This was probably the earliest evidence pointing to a chemical mediator that we now know is nitric oxide, a major dilator in all vascular beds although Hilton concluded at the time it was a mechanically driven mechanism. There followed studies on blood flow and secretion in salivary glands which in collaboration with Dr Graham Lewis provided the first evidence that the increase in blood flow essential for secretion was not solely dependent on nerve-mediated release of acetylcholine but also on the simultaneous release of polypeptides. Subsequently the polypeptides became recognized by others as important agents for ensuring blood flow in organs such as the heart and other vascular beds, and were later targeted in clinical treatments for

cardiovascular disease. At the end of the 1950s his attention began to move to the regulation of the heart and vascular system by the brain, and it was here that arguably he made his biggest contribution. He had become fascinated by the hypothesis of Cannon concerning the fright-flight-fight response (defence response) so fundamental to survival in wild animals but when over-expressed in humans can lead to chronic hypertension. At the time little was known as to how the brain initiated the defence response. Hilton realized that a key feature of this response is a selective vasodilatation in the skeletal muscle vascular bed and this could possibly be used as a marker to locate relevant brain regions in experimental animals. To study this he needed to gain experience of behavioural methods and for this there was no better place than the laboratory of Professor Kornoski (a former pupil of Pavlov) at the renowned Nencki Institute of Experimental Biology of the Polish Academy of Sciences in Warsaw. Thus, he returned to the land of his grandfather, a Polish Jew who had emigrated to London from Lodz in the early part of the 20th century. It was at the Institute in Warsaw that he was fortunate to team up with Andrzej Zbrożyna, a brilliant young behavioural physiologist who later joined Hilton at the MRC Institute in England. The two were then joined by Viv Abrahams and together they used the muscle vasodilatation in anaesthetized animals as an identifying feature when electrically stimulating at sites throughout the brain. Subsequently repeating these experiments in conscious animals it was shown these were the same regions that evoked defence responses. These studies provided the first description of brain regions that are essential for initiating the typical pattern of cardiovascular, respiratory and skeletal muscle changes that comprise defensive behaviour. More recently modern brain imaging techniques and deep brain stimulation, which is primarily used to treat a variety of brain-based disorders, has confirmed that similar brain regions are involved in aggressive behaviour in humans. From these studies it was clear to

Hilton that no longer could a single localized area in the hind brain be considered responsible for blood pressure regulation, a concept that had stood for 50 years and appeared in every textbook. It was now necessary to define a model based around discrete reflex control of parallel pattern generators for the cardiovascular responses accompanying various types of behaviour. These studies which were started at the MRC Research Institute, continued with Andrzej Zbrożyna, who moved with Hilton on his appointment to the Bowman Chair of Physiology in Birmingham, a university where his younger brother Peter, a highly distinguished mathematician, had recently occupied the chair of mathematics. Interestingly Dr Zbrożyna had also played a significant part in helping Hilton's future second wife Gerta Vbová and her two children to accomplish a remarkable and harrowing epic escape from Soviet-occupied Czechoslovakia described in Professor Vbová's recent book *'Betrayed Generation'* (for a review of this book, see p. 41).

Hilton was a complex, perhaps egotistic, person whose measure of mischief in scientific and administrative confrontations often led to acrimony and this perhaps resulted in his not receiving the full credit for his scientific contribution. However, the move to Birmingham provided an opportunity to build up a department that had lost most of its staff. Hilton built up its teaching and its research to a state where it became not only one of the strongest departments in the University but also in the UK, whilst its research quality became recognized internationally. It was also a happy department and during this time it nurtured many 'prima donnas' providing three Heads of Departments at other universities as well as a Director of the Army Personnel Research Establishment in Farnborough. During this time Hilton also helped to establish the Physiology Department in the new Medical School in Salisbury (Harare), Southern Rhodesia (now Zimbabwe) that had been founded in 1963

with a special relationship to the University of Birmingham. The early days of Hilton's time in Birmingham were very happy ones for budding physiologists who not only enjoyed the intense 24/7 research activity but also the social events of parties in Gerta Vbová and Hilton's home as well as other social occasions. During this time Hilton served as Secretary of The Physiological Society where his irreverent sense of humour was not always enjoyed although his contributions to scholarly debate at scientific meetings of The Society were often a highlight and much missed on his retirement. In 2004 he was awarded the distinction, given to only a few, of being elected as an Honorary Member of The Society.

He retired in 1984 and moved with his third wife Mary to what up to then had been her family holiday home, a lovely rural but somewhat remote setting on a mountain side, above Lanelltyd near Dolgellau in West Wales. Despite being quite cut off from the scholarly environment he appeared to be very happy, much enjoying the attention of Mary's children and grandchildren. Recently he had renal failure but was looking forward to reaching his 90th birthday in March of this year but this sadly was not to be. He is survived by his third wife Mary and a number of children from previous marriages.

John Coote and Mike Spyer

Will Redfern (former postdoc of SMH) continues:

Sidney Hilton was the external examiner for my PhD in 1982, and after the viva he invited me to join his group as a postdoc. I was honoured to be asked, and am still proud to have been a part of the last research group he had before he retired. I was funded jointly by the MRC and ICI, and worked with him from 1982 to 1985 in the Department of Physiology at Birmingham. The bulk of my project involved a comparison of electrical stimulation of brain stem 'defence areas' (hypothalamus and periaqueductal grey) in the rat with pharmacological stimulation using an excitatory amino acid. Back then, everything was analogue,

cardiovascular and respiratory recordings were collected on a multi-channel chart recorder, all analysis was manual, manuscripts were first written out in long-hand, and there was no PubMed. He had an office adjoining our lab, and would pop in enthusiastically, puffing on a cigar, inadvertently triggering a nasopharyngeal reflex in the anaesthetised rat with the smoke.

I had read most of his published work on central cardiovascular control during the course of my PhD, and it had captured my imagination. His writing style reflected his personality, particularly in his reviews: in person he was engaging and witty, with a formidable intellect. Where most physiologists grappled with 'single issue' topics, he quite happily took on multi-functional, integrated responses that were fundamental to survival of the organism. He was very territorial in 'owning' this area, and like a gamekeeper apprehending a poacher, would tackle head-on anyone who wasn't going about it correctly! Before I joined his group I saw him doing this on more than one occasion at scientific meetings – it wasn't just what he said, but the subtly disparaging inflections in his voice – which later left me apprehensive ahead of my PhD viva, and always somewhat in awe of him. Fortunately I avoided ever being on the receiving end of this; on the contrary, he was always very encouraging and supportive. Sidney operated in a golden age of 'holistic' systems physiology (not to be confused with the current trend for 'systems biology') in the UK. He and his numerous collaborators have left a lasting legacy in our understanding of centrally co-ordinated patterns of responses to internal and external challenges and perturbations. I joined the pharmaceutical industry after my postdoc at Birmingham, and eventually moved to AstraZeneca, Alderley Park (formerly ICI), which I suppose could be considered a return on their investment. I last saw Sidney at his 80th birthday 'do' in Birmingham in 2001, where he was in fine form, and I'm so sorry he didn't make it to his 90th. It wasn't like Sid to miss a party.