Ronald James Linden
3rd April 1920–11th April 2010

At the time of him joining Leeds Medical School, it already had a reputation for cardiovascular work in physiology, medicine and surgery and he was soon involved in this exciting and developing field. After his PhD he had a stimulating year as a research fellow at the National Heart Institute in Washington DC, teaming up with several of the best American workers on the heart. This year was to prove seminal. On his return to Leeds, Ron set out to create something similar at Leeds. The Cardiovascular Unit was formed, within the Department of Physiology, which combined responsibilities for clinical cardiac investigations with fundamental ‘blue skies’ research of the highest quality. In 1966 he was appointed to a Personal Chair and in 1977 to the headship of a separate Department of Cardiovascular Studies, his chair being endowed by the British Heart Foundation, one of the first to be endowed by the Foundation.

Loyal to his colleagues, and commanding loyalty in return, he founded a dynasty of Leeds-trained cardiovascular physiologists who have spread far and wide. The reputation of his department as a centre of excellence was due to his persistence and also from his collaborators. He enthused his departmental staff by his style of work. The duration of the meticulously monitored experiments done in his laboratories was legendary, even among students.

He served on the editorial boards of several prestigious journals and was a member or chairman of several committees giving advice to government departments on physiological topics. He rendered valuable service to a number of high powered UK committees, notably the University Grants Committee, the British Heart Foundation and the Ministry of Defence.

Following retirement in 1985, he took up two six-month appointments at the newly formed medical school of the Chinese University of Hong Kong and also continued research collaboration with Gianni Losano at the University of Turin. He was awarded an honorary degree in Medicine and Surgery by the University of Turin in 1993.

Ron Linden was 90 years and 8 days old when he died suddenly and unexpectedly from a heart attack on 11th April. Only a week before, he had enjoyed his 90th birthday party with his three sons and their wives, eight grandchildren and five great grandchildren present.

Ron was the epitome of rugged individualism and Yorkshire bluntness. He was born in Scriven, Knaresborough, the second son of a Master Grocer, Alfred Linden. He won a scholarship to Knaresborough Grammar School (of which he later became a Governor) and left there to study Medicine in 1939. However, he left in 1940 to join the Royal Navy and served throughout the war, culminating in being promoted to first lieutenant on T and U class submarines most notably on HMS Unseen, patrolling the Mediterranean whilst based in Malta (1943–1944).

Returning to the Medical School at Leeds in 1946 he graduated MB CHB in 1951 with honours, PhD in 1958 and was awarded the DSc in 1965. His lifelong commitment to his speciality was seen from his first appointment – as house officer in cardiology at Leeds General Infirmary and throughout his posts from demonstrator to professor. He sought to exploit the clinical applications and relevance of basic physiological sciences.

Ron was a true Yorkshire man. He played cricket for Leeds University in his early years at Leeds and supported Yorkshire cricket, Leeds United and Leeds Rhinos. He was an amateur photographer, taking pictures mostly of his family and was very proud that he once won a prize for a photograph of his eldest granddaughter and her puppy awarded by the magazine, Amateur Photographer. He was an enthusiastic gardener and took particular pleasure in growing an immaculate lawn, camellias, roses and vegetables.

Ron Linden married Isobel Hendry in 1944 when stationed in Campbeltown, on the west coast of Scotland. They had only known each other for three weeks when they got married. Isobel died in 2007. They had three sons.

Roger Linden

Cecil Kidd writes:
Following the award of his PhD at Leeds, Ron spent a seminal year as a research fellow at the National Heart Institute at Bethesda, Washington DC, working with some of the best US workers in cardiovascular physiology, led by Sarnoff examining mechanisms of cardiac ‘contractility’ in the whole heart. On his return to Leeds he decided to set up a similar model there, initially funded by the Wellcome Trust.

The Cardiovascular Unit in the Department of Physiology was the result and it initially comprised three laboratories working on different aspects of cardiovascular physiology led by Ronald, John Ledsome and myself: Roger Hainsworth replaced John when he went to Vancouver. Roger focused on the physiology of the peripheral vascular system and I worked on the various cardiac receptor and central nervous mechanisms. Over time the Unit evolved, became a Department and eventually also had clinical staff and responsibilities: the overall aim was to pursue basic physiological science and to exploit their relevance to cardiac clinical applications.

Ron and his group of students produced a substantial series of studies that rigorously examined the influence of the various factors
affecting the force of contraction of cardiac ventricular muscle. Using the rate of change of left ventricular pressure ($dP/dt$) as an index, they were able to identify effects of autonomic nerves, heart rate and length etc. on the inotropic state of the left ventricle. The work introduced a significant rationalization of knowledge at the time which was bedevilled by non-specific terms such as ‘contractility’ and ‘vigour’ of contraction. The papers were published in *The Journal of Physiology* and the overall conclusions were adumbrated in a chapter he wrote with Mike Snow in *Recent Advances in Physiology*. He introduced new rigorous approaches and techniques in acute mammalian work including the maintenance of an appropriate acid–base balance, using the then new techniques for acute measurements in blood and gas chemistry such as $pH$, $P_{O_2}$ and $P_{CO_2}$.

Ron then took up the topic that occupied him for the major part of his research career. He started an investigation into the role of right and left atrial receptors in control of blood volume. Several workers, including Henry and Gauer, had previously suggested that atrial receptors were involved in blood volume control but the provoking stimuli were unclear. Work with John Coleridge and Albert Hemingway in Leeds before he went to the States had examined the pattern of distribution of these mechanoreceptors in the canine heart following their initial description by Paintal. Ron and his group devised preparations in which the left atrial receptors could be selectively and discretely stimulated by inflation of small balloons, without affecting return of blood to the heart. They measured heart rate and urine flow. Each inflation was followed by an increase in heart rate and urine flow. Over a period, they examined the characteristics of the responses including the alterations in receptor activity following their specific stimuli. Later, he and his group, now including Kappagoda and Snow, devised preparations that could examine responses evoked by selective stimulation of right atrial receptors. Again, the responses included a similar increase in heart rate and urine flow to that evoked by the left atrial receptors. Overall there was little doubt that the evidence clearly indicated that the afferent sensory side of the responses involved vagal afferent fibres from receptors in the right and left atria.

They were also able to show that the increase in heart rate was due to increased activity in sympathetic efferent fibres to the heart but was without effect on cardiac vagal motor fibres. However, the nature of the efferent pathways involved in the increased urine flow following stimulation of the receptors was more controversial.

Direct recording of activity in sympathetic nerve fibres during left atrial receptor stimulation by the Leeds group demonstrated that there was an effect on activity in renal sympathetic fibres. This was decreased at a time when activity in efferent sympathetic fibres to the hind limbs and visceral abdominal areas was unaffected. In neural terms, the pattern of these efferent responses was very different from any other described at that time. However, there was also strong evidence from other labs that a humoral pathway, probably including antidiuretic hormone (ADH), was involved. Ron and his group followed this up with a series of studies. They devised an assay for plasma ADH and learnt how to destroy the pituitary gland, acutely, thus removing the source of ADH. An increase in urine flow still occurred when the receptors were stimulated when there was no increase in plasma ADH. For a time these experiments appeared to falsify the hypothesis that ADH was involved and the Leeds group examined the nature of a possible diuretic agent. An assay was then devised, using the malphigian tubule of the bed bug (*Rhodnius prolixus*) to show the presence of such a diuretic and that was unaffected by ADH. Further experiments were carried out and the conclusion was that atrial receptor stimulation resulted in release of a blood-borne diuretic agent in addition to ADH. At present, its nature is unknown as are the relative contributions of the reduction in neural traffic in renal sympathetic nerve fibres, the increase in the postulated diuretic agent and the reduction in plasma ADH to the increase in urine flow which follows stimulation of the atrial receptors. That is how the picture currently remains: many disagree with the idea of a diuretic agent but the experimental evidence says otherwise!

Throughout his career, Ron was interested in exercise and was a strong informal advocate of the Canadian Air Force Programme; indeed over a beer (or two), he persuaded many of us to take it up. This exercise theme comes out in another of his projects but now in patients. This examined the relationship between changes in the electrocardiogram during exercise in patients with coronary heart disease and attempted to define the extent of the problem.

A novel exercise test was developed and was shown to provide an accurate index of myocardial ischaemia and its severity. It avoided maximal or excessive exercise, which could limit performance by means other than the onset of cardiac symptoms. Instead, a sub-maximal test was used to derive an index based on the progressive ST segment depression of the electrocardiogram, relative to an exercise-induced increase in heart rate. The steepest slope obtained in 13 electrocardiography leads was labelled as the maximal ST/HR slope. It was shown to be an accurate index of the presence and severity of myocardial ischaemia resulting from coronary heart disease and left ventricular enlargement.

This again demonstrates Ron’s primary commitment throughout his career to the exploitation of the relevance of basic physiological science to clinical situations.

The Department of Cardiovascular Studies was unique in the UK at the time and was totally funded by the British Heart Foundation, Wellcome Trust and MRC.
Ron published many scientific papers and reviews in journals of the highest quality, including The Journal of Physiology. The Department hosted a number of very successful international conferences and took a leading part in the periodic visits of The Physiological Society to Leeds. With Tissa Kappagoda, he published a Physiological Society monograph entitled Atrial Receptors.

Ron served on the Editorial Board – and became Chairman – of The Journal of Physiology as well as other prestigious journals. He was Chairman of the Cardiovascular Commission of the International Union of Physiological Sciences for a number of years.

He became a Member of The Physiological Society in 1956, serving on the Committee from 1968–73. Following his great friend Robert Comline, he became Treasurer, the Senior Officer of The Society at the time, from 1980–86, after which he was elected Honorary Member.

In the Department and in every aspect of his career, Ron created an atmosphere characterised by a rigorous attention to detail and positive vigorous discussions with everyone: he generated a very relaxed atmosphere with frequent highly enjoyable and bibulous get-togethers and parties. There was constant positive critical debate and analysis allied to experimental confirmation: in the early days, ideas of Karl Popper were frequently invoked. He stimulated many young scientists from a wide range of backgrounds and countries to pursue high-flying careers in laboratory experimental work in physiology and its related areas of anaesthesia, surgery and cardiology, and the pharmaceutical industry.

We all owe him a huge debt. He had a remarkable ability to enthuse individuals of whatever background and to gain their trust and loyalty which he richly rewarded.

Note: in preparing this account, I had help from Roger Linden, Michael Snow, Peter Mcwilliam, David Mary and Ann Silver. I am very grateful for their assistance. Any omissions, errors or misinterpretations are solely my responsibility.