



Emeritus Professor Derek Ashworth Denton (1924–2022)

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ABSTRACT

Derek Denton was born on 27 May 1924 in Launceston and educated at Launceston Grammar School. He studied medicine at the University of Melbourne, graduating in 1947. During his residency at Royal Melbourne Hospital he cared for critically ill post-operative patients. This experience stimulated him to question accepted medical wisdom, leading to a lifelong quest to understand physiological mechanisms regulating body fluid and electrolyte homeostasis. He joined the University of Melbourne's Department of Physiology in 1949. There, together with Dr Victor Wynn, he initiated the Ionic Research Unit, investigating renal mechanisms regulating sodium and water balance, and began a mobile emergency service working across Melbourne hospitals to rapidly assess, and provide, fluid and electrolyte therapy for patients with life-threatening conditions. In 1951, Denton moved to Cambridge, working with Professor E. Basil Verney to develop expertise in large animal physiology. While in Cambridge, he married Margaret Scott, a leading ballet dancer. On returning to the Ionic Research Unit in 1953, he elucidated many aspects of the physiological regulation of bodily sodium and potassium balance utilising sheep with a chronic parotid fistula to induce sodium depletion, and sheep with transplanted adrenal gland to make groundbreaking discoveries regarding the physiological regulation of the salt-retaining hormone aldosterone. He also pioneered studies of salt appetite. In the early 1960s, Denton played an important role in establishing the Howard Florey Laboratories in the University of Melbourne, and was appointed the first Director of the Howard Florey Institute of Experimental Physiology and Medicine in 1971, retiring from this position in 1989. He continued experimental work during the next thirty years, focusing on brain function and instinctual behaviour. Derek Denton was elected FAA in 1979, FRS in 1989 and made a Companion of the Order of Australia in 2005. He died at his home on 18 November 2022.

Keywords: aldosterone, brain function, Derek Denton, fluid and electrolytes, Howard Florey Institute, hypertension, instinctual behaviour, physiology, salt intake, University of Melbourne.

Derek Ashworth Denton (1924-2022)

Family background and school education

A Tasmanian boy, Derek Ashworth Denton was born in Launceston on 27 May 1924, the youngest of Catherine (Kitty) and Arthur Ashworth Denton's four children. Arthur Denton owned a business that built coach and car bodies in Launceston. It had been a successful business that had been started in 1895 by his father, and which Arthur Denton continued until 1941 when he retired. Arthur's business was hit hard by the depression of the 1930s. Despite the financial losses he incurred, Arthur showed great loyalty to his employees, keeping them on the payroll during this time; an act of kindness that his son Derek recounted with pride many years later. Derek Denton had an older brother, Foiley Denton, and two sisters, Freda and Kathleen. Warrant Officer Foiley Denton served in the Royal Australian Air Force as a pilot during the 1939–45 war years. During his early childhood, Derek's mother Kitty suffered from rheumatoid arthritis, severely restricting her movement. Consequently, Derek's two sisters, more than ten years his senior, played a significant role in his upbringing. The Methodist Ladies College, where Freda and Kath were educated, was just a close walk from the Denton home, so close that three-year old Derek would follow his sisters to school each day. He would be taken back home, but he

persisted in following Freda and Kath, so the teachers eventually allowed him to stay at the back of his sister's class where he would listen to the lessons. Thus commenced Derek Denton's early education.

Derek grew up in a large home at 53 Elphin Street, Launceston that had its own croquet lawn. He attended Launceston Church Grammar School from which he graduated in 1941. His father, Arthur, was well-known in sporting circles being a supporter of the Launceston Football Club for many years and a member of several Tasmanian trotting clubs, owning racehorses as well as trotters. Derek's sister Freda represented Tasmania in hockey. This family sporting ethos undoubtedly influenced Arthur's youngest son Derek, who took an avid interest in tennis, cricket, football and athletics. Arthur was also a keen fly fisherman and imparted his love of fishing to both his sons. Arthur and Kitty would have been pleased that young Derek showed more-than average ability on sporting fields during his secondary schooling. In his senior years at the Launceston Grammar he captained both tennis and cricket teams and kicked goals for Launceston Grammar in its football premiership victory over Scotch College. However, tennis was the sport that he really loved; indeed, it became a life-long pastime. Possessed of a deadly double-handed backhand that he could land on a sixpence, he used this shot to great effect so that he did not feel out of place on the tennis court with the likes of Davis Cup captain Harry Hopman or Adrian Quist, twice doubles champion at Wimbledon.

University education

Graduating from Launceston Grammar in 1941, Derek Denton—known to everyone as 'Dick'—qualified for matriculation in the University of Tasmania in 1942. There he earned distinctions in physics, chemistry and botany and a high distinction in zoology in his first year of University study. It was during this first year that he developed an intense interest in the sciences. He decided to study medicine, but this was not possible at the University of Tasmania in 1942. To do so required a move to the University of Melbourne in 1943, facilitated by Dick gaining an open scholarship to Melbourne's Trinity College where he resided for three years until his final undergraduate year. Dick participated fully in Trinity's academic and social activities and continued his sporting interests, representing the College in football, cricket and tennis. When his father died suddenly from a heart attack in 1944, his widowed mother was reassured by a local doctor who also lived in Elphin St, Launceston, that he would see that Dick was able to complete his medical degree by providing funds if any financial problems arose for Kitty, probably the first of many

philanthropic gestures that Dick would be the beneficiary of over subsequent years.

Dick embraced his medical studies wholeheartedly, being fascinated with the evolutionary aspects of mammalian anatomy and physiology. He was no 'shrinking violet' and he took the opportunity to seek out his lecturers, especially Professors Roy Douglas Wright (Physiology) and Sydney Sunderland (Anatomy) (who both later received knighthoods) and engage them in discussing broad-ranging biological questions. Friendships grew from these interactions, which would prove to be influential in his future scientific endeavours. However, at one stage, Dick's medical studies were interrupted when he was placed in an isolation ward in the Royal Melbourne Hospital for two months following the discovery of a primary tubercular focus in one of his lungs, possibly picked up from a patient during the ward rounds he made as a student. He returned to Tasmania to recuperate for three months. Dick made sure he did not waste this recovery and read voraciously, educating himself in classical literature, history and music, thereby giving him a superb background for a lifelong interest in the arts and humanities.

While Dick worked vigorously at his studies, he played hard too. Together with another senior student, he operated an 'unofficial college buttery' providing wine and beer for student social activities and revelry. The Trinity College administration decided that one of their activities that involved smuggling girlfriends into the attic of the college for a boisterous party was over the top. This resulted in Dick and his co-conspirator being sent down from Trinity in 1946.² While Dick seemed to wear this episode as a badge of honour, it did result in the necessity of finding alternative living quarters so his final year was undertaken while living in cold, less than comfortable accommodation in nearby Gatehouse Street, Parkville.

Graduation and initial appointment

For Dick Denton, the year 1947 would prove to be a turning point. Unexpected events that occurred that year would have lifelong consequences. Certainly, as expected, he graduated in medicine, doing so with the degrees MB, BS from the University of Melbourne on 7 July 1947 (Fig. 1). He gained several honours and was ranked eighteenth in a class of 108 medical students. Within a few days of graduating, he commenced a residency year at the Royal Melbourne Hospital, being assigned to assist the eminent surgeon Mr Albert Coates with the care of his patients. Coates, a colonel, was one of several hospital staff members who had recently returned from active service overseas during World War 2. He had been captured by the Japanese forces in Singapore in 1941, and remained with his unit to lead a group of surgeons in

¹Anonymous (1944).

²Hewat (1990).

³Anonymous (1947).



Fig. 1. Derek Denton (2nd from left) on graduating MB.BS in the University of Melbourne, July 6, 1947. Fellow graduate and future colleague Ian McDonald is on the left, Phillipa Carter (3rd from left) and Frank Tait complete the graduating group. Photograph courtesy of the Denton family.

caring for fellow prisoners who endured the horrors of the Thai-Burma railway. He was later knighted for his bravery and service. It was into this post-war hospital milieu that Dick Denton found himself immersed. Long hours, often with little or no sleep for days on end, were typical working conditions for those looking after acutely ill patients in those times.⁴

An unexpected, but significant, event that happened in 1947 resulted from Dick's newly found interest in ballet (and ballerinas). An English company, the Ballet Romberg, embarked on a post-war tour of Australia, giving performances in capital cities and country towns. One of the leading female dancers was Margaret (Maggie) Scott, a South African who had honed her ballet skills with the Sadler's Wells company in London during World War 2. After surviving the blitz (her house was bombed), Maggie gained a reputation as an up-and-coming ballet dancer. After the war ended, she toured Europe with her ballet troupe, bringing entertainment to occupying allied troops in war-torn Germany. In late 1947, Ballet Romberg arrived in Australia. After one of her Melbourne performances, she was introduced to Dick Denton by a fellow dancer, Sally Gilmore.⁵ She had previously noticed Dick on duty in one of the wards at the Royal Melbourne Hospital when she and Sally visited the hospital to distribute the many floral bouquets presented to them following the opening night of their ballet performance at the Princess Theatre. Maggie stated that it was not love at first sight, but a relationship did develop over time, and eventually they moved into an apartment together in Jolimont, a block away from the Melbourne Cricket Ground.⁶

Three weeks after graduating, Dick was assigned by Albert Coates to care for a seventeen-year-old boy from

the suburb of Spotswood, Ron Reynolds, who had undergone surgery for a duodenal ulcer. This case would define Dick Denton's future medical-scientific path for the next half century. Unfortunately for patient Reynolds, complications arose from the initial surgical intervention that required follow-up surgery by Mr Coates. Post-operative infection resulted in the rupture of the remaining duodenum from which gastrointestinal fluid oozed. Coates then inserted a tube through which this fluid drained. Survival of the patient depended on adequate replacement of the fluid, and the task fell to Dick Denton. While it was easy to measure the volume of fluid lost, the ability was lacking in 1947 to measure its chemical composition. Dick knew that the fluid was highly alkaline and he was able to measure its chloride content, but the concentrations of crucial ions, such as sodium, potassium and bicarbonate, were not quickly measurable in that era. Despite the around-the-clock care that Dick Denton provided for his patient, the wound enlarged, and the patient's condition inexorably worsened, with the eventual death of Ron Reynolds on 6 November, a little over three months after his initial surgery.⁷

Ron Reynold's case was perplexing for the fledgling doctor, who had realised that the metabolic changes that he had observed in his patient were not in accord with contemporaneous text-book descriptions. The high concentration of chloride ions in Reynold's urine belied the low level of chloride in plasma. Denton resolved to understand the homeostatic mechanisms that were at play in regulating the volume and concentrations of body fluid in response to losses of extracellular fluid. One of the people he sought out in this quest was his old teacher, Professor R. D. Wright (known by the nickname 'Pansy' to his friends), who happened to be a patient in the hospital early in 1948. Wright suggested some approaches, but advised Dick to finish his residency before embarking on a research path. Eventually, Dick published a brief description of the case as a singleauthored letter to the journal Nature, 7 with a more detailed account in the Medical Journal of Australia.

Commencement of Research Career

On completion of his residency year, Dick Denton accepted an invitation from Professor Macfarlane Burnet (later, Sir Macfarlane Burnet and 1961 Nobel Laureate), to come to the Walter and Eliza Hall Institute as the Haley Research Fellow, where he was assigned to work with virologist and immunologist Frank Fenner, who later was leader of the World Health Organization team that eradicated smallpox from the world in the 1980s. Dick found his time in the laboratory with Fenner to be a rewarding experience, but when a second patient with a post-gastrectomy duodenal fistula

⁴Hewat (1990).

⁵Potter (2014) p. 102.

⁶Potter (2014) p. 119.

⁷Denton (1948).

was admitted to the Royal Melbourne, he was called in to assist in the management of this patient. He was joined in this effort by Dr Victor Wynn, a young doctor just out of the Army Medical Corps, and now a member of Professor Wright's Department of Physiology. After ninety days of treatment, aided by improved techniques to monitor the patient's electrolytes and acid-base balance, the patient was discharged in a healthy state. Frank Fenner and Dr Ian Wood (deputising for Burnet in his absence) were agreeable to this arrangement. However, when Dick independently sought out funding to assist his research efforts by approaching Sir Keith Murdoch, publisher of the Herald and Weekly Times, Burnet was not amused. Denton's entrepreneurial spirit rankled with Burnet, and he decided to terminate Dick's appointment at the Hall Institute. However, Burnet recognised Dick's ability, and allowed him to maintain laboratory space at the Hall Institute until he could move to the Department of Physiology, University of Melbourne. Burnet joined with Professor Wright in gaining support from the National Health and Medical Research Council (NHMRC) for Denton to continue his research in Wright's department as a NHMRC Fellow.

Dick Denton moved to the Physiology Department in 1949. Together with Dr Victor Wynn, he set up a laboratory devoted to the study of electrolyte balance that came to be known as the Ionic Research Unit. One of the first tasks they undertook was to arrange funding for the importation of a flame photometer from the Beckman Company. This was an instrument that had until that stage been used in agricultural science for the chemical analyses of soil samples. Wynn realised that it could quickly provide information on the sodium and potassium concentrations in blood, urine and other bodily fluids. He duly obtained the instrument, allowing him and Denton to push forward with their research into fluid and electrolyte homeostasis.

An NHMRC report mentions that D. A. Denton and V. Wynn had studied the behaviour of the kidneys when sodium and chloride ions were subtracted from the body in disproportionate amounts relative to the normal extracellular pattern. The renal control seemed to operate independently of plasma sodium and chloride concentrations.⁸ Word began to circulate around Melbourne hospitals regarding the newly found expertise that Denton and Wynn had gained in measuring and treating patients with severe electrolyte disorders. They were in demand to provide this expertise for the resuscitation of patients suffering intestinal fluid losses, diabetic coma or septicemia with renal failure. To enable an effective response, they would load laboratory equipment (pH meter, centrifuge, oscilloscope) into the back of Wynn's car to enable its quick transfer to the hospital where a critically ill patient required emergency treatment.

Armed with pH and electrolyte measurements of plasma, urine and other body fluids (made back in the Department of Physiology) and electrocardiograms, Denton, Wynn, Ian McDonald (one of Dick's medical school classmates), and Shirley Simon could then supervise the administration of appropriately formulated fluid replacement for patients, thus becoming a mobile emergency unit, probably an early forerunner of today's intensive care unit.

Post-graduate studies in Cambridge

By 1949, Dick Denton realised that to advance his understanding of how body fluid and electrolyte balance was regulated, he needed a suitable experimental animal. For this, he turned to sheep, with their copious secretion of alkaline saliva that could be tapped from the body through an oesophageal fistula. In 1951, Victor Wynn was awarded a Nuffield Fellowship and moved on to St Mary's Hospital in London. Several months later Dick, on Professor Wright's advice, also moved to the United Kingdom (UK) to gain experience in experimental techniques used in animal physiology. But before that happened, he and Wynn put together a detailed two hundred page monograph describing results obtained in many of their patients (and sheep) with specific sodium, potassium, chloride or pH abnormalities, and their recommendations of the compositions of the fluid therapy needed to correct the deficits.

While Dick was busy with this research, his partner Maggie Scott was touring the country with Ballet Romberg giving performances in many regional towns and cities. Her busy stage schedule eventually had a detrimental effect on her body, and she was diagnosed with a severe back injury that required surgery early in 1951. Dick spent many hours by her bedside in the Alfred Hospital, where she lay immobilised post-operatively for several months. Her ballet company had returned to the UK. After she had recuperated following the surgery, Maggie decided to return to her home in Swaziland to visit her family in mid-1951, while Dick sailed to Europe on the cargo ship Changchow as the ship's doctor a couple of months later. He found the voyage across the Pacific, visiting Tahiti and other South Sea islands, followed by passage through the Panama Canal and across the Atlantic to Marseille over several months, a memorable experience. It was his first time abroad. On his arrival in London in December 1951, he met up with Victor Wynn at St Mary's Hospital, while Maggie sailed from Cape Town and rejoined Dick in London in mid-1952. There, they settled into a flat in Chelsea, and socialised in the evenings with Maggie's ballet associates, who included the renowned choreographer John Cranko, stage and costume designer Kenneth Rowell, actor John Pertwee and artist Donald

⁸The Commonwealth of Australia Report on Work Done Under the Medical Research Endowment Act during the Year 1949.

⁹Denton and others (1951).

¹⁰Potter (2014).

Friend. Dick attended a meeting of the Physiological Society in Oxford 18–19 July 1952. Of significance for future events and on Professor Wright's introduction, Dick met up with Oxford Professor Sir Howard Florey for lunch at the Physiological Society. Wright had worked with Florey in 1938–9 just prior to the commencement of his work on the isolation and purification of penicillin, for which Florey had received a Nobel Prize in 1945.

In addition to Florey, Professor Wright had also given Dick Denton an introduction to Sir Edward Mellanby, an influential figure in the UK Medical Research Council. Mellanby made arrangements for Dick to work in the laboratory of Professor E. B. (Basil) Verney at Cambridge, one of the foremost experimental physiologists in Britain who had worked with the renowned Professor Ernest H. Starling for three years immediately after World War 1. Dick wanted to learn how to make physiological investigations in conscious, undisturbed, untraumatised animals, of which Verney was an expert. Before he settled seriously into his experimental work in Cambridge, he and Maggie picked up a small French car in Paris, and spent time driving through France, Switzerland and Spain, sampling the local wines and joining the fun and revelry they often found at inns and bars along the way. By October 1952, Dick was back in Cambridge at work in Verney's laboratory, while Maggie was performing Cranko's ballet productions at a theatre in Henley-on-Thames. Unfortunately, Dick came down with a severe case of hepatitis before the year ended, and was admitted to hospital. He eventually regained health, and he and Maggie were married in Cambridge on 13 March 1953.¹³

Best-man at their wedding was a young Swedish scientist and veterinarian, Bengt Andersson. He, like Dick, had come to Verney's laboratory to gain experience in the classical experimental methods used in investigating animal physiology. Andersson was from Stockholm and had trained in the laboratory of Nobel Laureate W. R. Hess in Zurich. Bengt and Dick worked closely with Basil Verney for much of 1953, investigating the physiological mechanisms by which dogs excreted salt and water loads. 14 Bengt and Dick would become life-long friends. During his time at Cambridge, Dick would join such luminaries as Alan Hodgkin, Andrew Huxley, Lord Adrian and other staff members of the Physiological Laboratory for morning and afternoon tea. The free exchange of ideas within a spirit of goodwill and without rancor impressed Dick, and he was determined to foster such a spirit of cooperation back in Melbourne. By September 1953, Dick considered that he had learned as much as he needed from Verney, and despite Verney's offer of a position in his Cambridge laboratory, decided it was time to return to Melbourne and apply his newly found knowledge to the study of body fluid regulation in conscious sheep. Maggie had also been offered a position in the UK, in her case as co-director of Ballet Romberg, but declined the offer and returned to Melbourne with her husband. ¹⁵

Return to the Department of Physiology, University of Melbourne 1953

Dick and Maggie Denton, together with a young dachshund (a gift from John Cranko), returned to Melbourne in mid-October 1953. They found a house to rent and live in near the Yarra in Orrong Rd, Toorak. 16 Dick returned to the Ionic Research Unit at the Physiology Department, Melbourne University and began to organise his laboratory. Within a month he had surgically prepared a sheep with a parotid duct fistula based on the model that Pavlov had pioneered in dogs half a century earlier. Two months later, Professor Wright joined the effort and surgically constructed an improved fistula with a teat from which saliva dripped; Dick adopted this improvement. During the next two years he prepared thirty-seven of these sheep for physiological study. The parotid fistula provided a tap on the extracellular fluid that drained from the fistula. These animals proved to be a physiological treasure trove that manifested new insights into the regulation of salivary composition and secretion in conscious animals, as well as the physiological response to sodium depletion. Unexpectedly, the sheep also exhibited a behavioural drive to ingest sodium salts, thereby replacing the sodium lost in saliva. This sodium appetite would become an abiding research interest for Dick Denton in future years.

In addition to Professor Wright, Dick was joined in the investigation of these animals by Drs Jim Goding, Doug Coats and Ian McDonald, and he was assisted by Ben Dyzenhaus, John Blair-West and Attilio Guarracino, who cared for the sheep. By 1956, they were ready to produce a series of publications on the physiological regulation of saliva secretion. ¹⁷ Of special interest to Dick were the reciprocal changes in sodium and potassium concentrations of saliva and urine he observed during periods of sodium depletion and the likely role of the adrenal hormone aldosterone. ¹⁸ Thinking about how he might be able to study the secretion of aldosterone from an adrenal cortex buried deep in the abdominal cavity, Dick came up with the idea that it might be possible to transplant the adrenal of a merino sheep up to its neck because of the copious skin folds in

¹¹Letter from Howard Florey to Derek Denton, July 1952.

¹²McPhee (1999).

¹³Potter (2014).

¹⁴See figs 12–15 in Verney (1957).

¹⁵Potter (2014).

¹⁶Potter (2014).

¹⁷See Denton (1957).

¹⁸Goding and Denton (1956).

that region.¹⁹ While he thought this a longshot, Wright and Goding, both experienced and skillful surgeons, were not as pessimistic. In July 1956, they succeeded in transplanting an adrenal gland into a loop of skin in the neck of a sheep; the transplanted gland received its arterial blood supply from the carotid, and venous outflow drained into the jugular vein, which could be sampled. The other adrenal was removed and the animal survived, indicating that the transplanted adrenal was functioning adequately. Over the next few months more sheep were prepared with both a parotid fistula and an adrenal autotransplant for experimentation.

In late 1956, the Olympic Games were taking place in Melbourne. During this period, Maggie and Dick Denton's first child Matthew was born on 2 December. Their second son, Angus, was born five years later in January 1961. In 1959, they purchased the family home at Orrong Rd, Toorak where they lived for the rest of their lives. As well as raising her young family, Maggie was also engaged in establishing a national ballet school for Australia. Dick and Dr H. C. Coombs, governor of the Reserve Bank of Australia, also participated in this endeavour.

In 1957, with a cohort of surgically prepared sheep with adrenal autotransplants, the team of Denton, McDonald, Goding and Wright went to work studying the response of these animals to sodium depletion and its correction. Over the next couple of years, they were able to show that blood flowing from the adrenal gland contained a hormone, probably aldosterone, which regulated the sodium and potassium concentrations of saliva and urine when bodily sodium balance was altered. 20 However, their most important finding resulted from a cross circulation experiment showing that an unidentified hormone in the blood of a sodium-depleted donor sheep could stimulate aldosterone from the transplanted adrenal of sheep in normal sodium balance.²¹ The search for this agent was on, and others later showed that angiotensin was a major hormonal stimulant of aldosterone secretion. These findings were consequential in the subsequent development of drugs for treatments of hypertension and heart failure.

Towards the end of 1959, Denton, Goding and Wright realised that they needed a chemical assay for measurement of blood aldosterone concentration if they were to maintain their international standing in the aldosterone field. In September that year, they sent a young laboratory worker in the Physiology Department, John Coghlan, to Cornell University's New York Hospital to learn from Professor Ralph Peterson a double isotope procedure for measurement of aldosterone. Having the knowledge to make the assay

work was only half the battle, however, because equipment (in the form of a liquid scintillation counter) was also needed and this was an expensive item.

Dick Denton approached the NHMRC to fund the equipment, but they were not forthcoming. Deciding to go to the top, he used his contacts to arrange a meeting with the Prime Minister, R. G. Menzies, to lobby for extra funds for this equipment. Funds were obtained and, together with those from Ken Myer, a liquid scintillation counter was on its way to Australia. ²²

The Physiology Department in which Dick Denton performed his experimental work was an old red brick building situated on Swanson Street, Carlton. By 1960, the staff that Wright had brought to the Department along with Dick included other outstanding scientists, such as Drs Ray Bradley, David Dewhurst, Doug Coates, John Coghlan, Mary Chennells, Ted Trethewie, Sam Rose, Edward Trautner and Paul Pincus. However, by this time, the state of the laboratory facilities in which they worked was an anachronism. They even prompted Dick Denton to keep a coil of rope by the window of his first floor office overlooking Swanson Street, so that he could escape if a fire broke out in a laboratory.

Initiation of the Howard Florey Laboratories of Experimental Physiology

Maggie and Dick Denton's wide circle of friends came from academia, medicine, the arts, politics and business. They included Dick's tennis partners Ken and Bails Myer of retailing fame, the eminent public servant Dr H. C. (Nugget) Coombs, Toorak neighbour Harold Holt (the federal treasurer and future Prime Minister), Pansy Wright, artist Russell Drysdale and stockbroker Ian Potter. At one of their gatherings, Ken Myer expressed his dismay at the primitive conditions in which Dick performed his experiments; Nugget Coombs responded with the suggestion that a modern laboratory building was needed. Within days, Ken Myer and Ian Potter had agreed to back an approach to the University of Melbourne to build a new laboratory building. Dick and Ken Myer drafted a letter to the Vice-Chancellor, Sir George Paton, signed by Myer and Potter who would underwrite the project to the tune of £150,000.²⁴ After the proposal was considered by the University Council, Sir George announced on 2 May 1960 that a four-story research block would be built on the University's Sydney Road frontage. When asked by Melbourne's Age how urgent was the need for the new laboratory, Prof. Wright replied, 'In our present quarters, we have to employ a watchman on at night to stop rats getting at experimental sheep'.25

¹⁹McPhee (1999).

²⁰Goding and Denton (1956).

²¹Denton and others (1959).

²²Hewat (1990).

²³McPhee (1999).

²⁴Denton (2013).

²⁵Anonymous (1960).

Denton and Wright were now galvanised into action to make sure that the new laboratory happened. They became a formidable team. Dick's part was to take care of the 'top end of town' and the politicians, while Pansy Wright concentrated on dealing with the University's power brokers and bureaucracy. Dick (with help from his friend, Treasurer Harold Holt), again approached the Prime Minister. The federal government agreed to provide £100,000 towards the project. In addition Dick travelled to the United States of America (USA) in 1961 and gained support (US\$50,000) for the building project from the Rockefeller Foundation in New York, and a grant of US\$690,000 over five years from the National Institutes of Health in Washington, DC, to fund scientific programs in the new laboratory. Dick was also heavily involved in its design, which ended up as an eight-story building, called the Howard Florey Laboratories of Experimental Physiology. Dick and Pansy relied on their colleagues in the Physiology Department, such as Jim Goding, John Blair-West, John Coghlan, Marelyn Wintour, Ben Dyzenhaus, Rod Patterson and Conrad Rabl to keep the scientific programs running while they sorted out the many aspects of the building project.

The Howard Florey Laboratories were ready for occupation by autumn 1963, with Derek Denton appointed as its Chief Scientist. Wright remained Professor and Head of the Physiology Department. On 30 August 1963, the Prime Minister, Sir Robert Menzies officially opened the building accompanied by Sir Howard Florey. It was a triumphant day for Dick Denton and Professor Wright to see the fulfilment of their efforts.

Derek Denton's interest in sodium balance and aldosterone continued during the 1960s, and extended to studies of the renin-angiotensin system and renovascular and steroidinduced hypertension. He also began to focus heavily on the physiology of salt cravings of his sodium-depleted sheep, a drive that he demonstrated to be an innate response to sodium depletion. Several PhD students, Elspeth Bott, John Funder, Graeme Boyd, Bruce Scoggins and Sigrid Weller, played key roles with Dick and his team in those investigations. Dick Denton gave great encouragement to his junior scientists, trusting them with the freedom to test their own ideas. He also brought a stream of outstanding visiting scientists to the Florey from all over the world. They came for either short or more extended stays, and provided great encouragement and 'contacts' for the young graduate students and scientific staff of the Florey. Dick also recognised unconventional but talented individuals, who may not have gained straight-A grades in their degree courses, but who were able to develop into excellent scientists. This skill was a manifestation of his tolerance for the unusual, his sense of humour, and respect for diverse opinions.

The large increase of sodium intake of lactating animals led Dick to consider how much sodium was being ingested by their offspring. This spurred him on to measure the salt content of commercially-available baby food given to infants in Australia. The results showed the sodium levels of baby food to be far in excess of the needs of the infant; presumably, it was to appeal to the taste of the mother, rather than the infant's need. This work led the commercial manufacturers of infant foods to reduce the salt content of their products to levels more appropriate to the nutritional needs of infants, and hopefully reduced the likelihood of them becoming habituated to a high salt intake.²⁷

In 1970, Dick Denton met the owner of the King Ranch in Texas (USA), Bob Kleberg, who mentioned that a significant proportion of his cattle were dying from an unknown cause at another of his ranches (Big B) in Florida. Denton suggested that a rigorous scientific investigation of the problem be made, and undertook to lead the effort. The upshot of this work was that the pastures that the cattle grazed on were found to be deficient in the trace element, cobalt. Provision of cobalt to the animals corrected the problem, resulting in considerable financial benefit to the Kleberg family. As a consequence, the Klebergs became strong philanthropic supporters of Dick's scientific work at the Florey Institute in Melbourne. This financial support continued for more than thirty years, contributing many millions of dollars over that period. 28 To facilitate the transfer of these funds from the USA, Dick organised the establishment of the Howard Florey Biomedical Foundation of the USA.

The support Denton gained from the Kleberg Foundation was just one of many examples of his unique ability to draw financial support for the work of the Florey Institute, and biomedical science in general. In this regard, he teamed with another scientific leader, Sir Gustav Nossal, Director of the Walter and Eliza Hall Institute, to successfully lobby Prime Minister Gough Whitlam for increased biomedical research funding in 1974.²⁹ Dick's connection with Nugget Coombs was crucial for the success of this initiative. One of

In addition to his laboratory studies, Dick carried out field observations in collaboration with Dr Ken Myers of the CSIRO Division of Wildlife, Canberra, on sodium-deficient wild animals in regions where the sodium concentrations of soil and vegetation were low, particularly in the Snowy Mountains of south-eastern Australia. There he showed that herbivorous and ruminant animals were species most affected by lack of sodium, especially during reproduction. Later, he and Jack Nelson brought wild rabbits from salt-depleted areas back to the laboratory, and demonstrated that they exhibited large increases of salt intake during pregnancy and lactation that were driven by the reproductive hormones oestrogen, progesterone and prolactin. ²⁶

²⁶Denton and Nelson (1971).

²⁷Blair-West and others (1970).

²⁸Hewat (1990).

²⁹Nossal (2007).

the keys to Dick's success in garnering funds for science was his ability to form long-standing personal friendships with those in control of large sources of philanthropic funds.

Foundation Director, Howard Florey Institute of Experimental Physiology and Medicine

In 1971, a bill was passed by the Victorian Parliament converting the Howard Florey Laboratories into the Howard Florey Institute of Experimental Physiology and Medicine. While affiliated with the University of Melbourne, it would be independent of the Department of Physiology and have its own board of directors. The impetus to this move was the impending retirement of Professor R. D. Wright as Head of the Department of Physiology. Derek Denton was appointed as the Director (Fig. 2) and an originating member of the Institute's Board, chaired by Kenneth Myer, and Sir Ian Potter as vice-president. In 1977, Denton was appointed Research Professor of Experimental Physiology and Medicine in the University of Melbourne.

During the 1970s, several post-doctoral fellows came from the USA to work with Denton at the Florey Institute on the regulation of sodium and water balance. They included David Mouw from the University of Michigan, Ed Blaine from Missouri, and Richard Weisinger from University of Washington, Seattle. Much of the work focused on the brain mechanisms regulating renin, aldosterone and vasopressin secretion, renal sodium excretion, 30 salt appetite 31 and thirst. They were joined in these endeavours by local PhD students Arthur Shulkes, Gary Whipp, Suzanne Abraham and Michael McKinley, under Dick Denton's supervision. In 1973 he became a member of the Jury of the Albert and Mary Lasker Foundation Basic and Medical Research Awards in New York, and continued in this role until 1991. In 1974, Dick hosted, and was chairman of, the Fifth International Symposium on Olfaction and Taste at the Florey Institute in Melbourne.

As Director, Dick Denton, together with the Board, worked to expand the Institute's areas of investigation by recruiting new scientific groups and expertise. Bryan Hudson, Monash University's Foundation Professor of Medicine, joined the Florey as an Assistant Director in 1971 and set up a research unit devoted to studying reproductive endocrinology and infertility in males. A major coup for Dick was bringing Hugh Niall and Geoffrey Tregear, two expatriate Australians who had worked at Harvard University, to the Florey to sequence and synthesise peptide hormones, such as the hormone relaxin. Dick considered that bringing expertise in molecular biology to the Florey was crucial if the Institute were to remain relevant into the future, and actively recruited molecular biologists.



Fig. 2. Derek Denton, Director of the Howard Florey Institute, 1971–89. Photograph courtesy of the Florey Institute of Neuroscience and Mental Health.

As well as directing an Institute of scientific renown, the ambience that Derek Denton created at the Institute was one of grace and style. His unparalleled network of friends and colleagues in the arts, ballet, politics, academia, science, business, and the media throughout the world ensured this. He provided works of art to enhance the intellectual environment and entertained visitors and members of staff at monthly Friday afternoon wine tasting sessions. Denton was keen to expand his scientific horizons into consideration of the evolutionary aspects of his investigations. As Director, he reached out to the general community not only to convey his scientific message, but also to discuss ethical aspects and the future direction of science (Fig. 2).

In 1979–80 Dick took time away from the Florey to work on a book. He spent many hours in the British Library in London researching this volume, and his friend Evelyn de Rothschild provided him with a residence at Lodsborough Mill in Kent to work on it. *The Hunger for Salt* was published by Springer Verlag in 1982 and soon became the 'bible' for those wanting to understand anthropological, physiological and medical aspects of salt ingestion.³²

³⁰Blaine and others (1975).

³¹Weisinger and others (1979).

³²Denton (1982).



Fig. 3. Derek Denton and his wife Dame Margaret Scott chatting with the Swedish King Carl XVI Gustav and Queen Silvia in Stockholm at a banquet of the Royal Swedish Academy of Engineering following the OECD review of Swedish science policy in October 1986. Derek Denton was one of the reviewers. Photograph courtesy of the Denton family.

In addition to his scientific endeavours at the Florey Institute, Derek Denton had many other roles to play in the 1980s. He was elected to the Board of the Australian Ballet Foundation and the Australian Ballet in 1982. He also served from 1984 to 1994 on the Board of Directors of David Syme and Co, publishers of the Melbourne Age. In 1985-6, he was invited by the OECD to be Examiner of Science and Technology Policy of the Government of Sweden (Fig. 3). From 1977, Derek Denton served as a member of the Council of the International Union of Physiological Sciences (IUPS), then was elected its First Vice-President (1983-9). From 1987 until 1989, he was Chairman of the IUPS Commission on the Impact of Molecular Science on Physiology. In 1989, Maggie Denton was awarded the title Dame of the British Empire for services to the performing arts, she could now be called Dame Margaret Scott (Fig. 3).

Retirement

Derek Denton stepped down as Director of the Florey Institute in 1990, because a condition of the NHMRC block funding of the Institute required the director be no more than sixty-five years of age. He was succeeded by Professor John Coghlan, his deputy, who was also the Deputy Vice-Chancellor (Research) at Melbourne University. While both Denton and Coghlan were powerful intellects, their styles were different (the good cop/bad cop analogy is fitting). Dick, being the urbane, cultured, diplomatic intellectual who never raised his voice, while John Coghlan was the hard man, more

prone to profanities and with a short fuse, someone who struck fear into his adversaries. Although Dick had supported Coghlan's bid for the Directorship, for reasons that are not clear, Coghlan's relationship with Denton soured. The strained relationship between these two men, who had once been friends and partners in many scientific projects, never healed.

On relinquishing the Florey Directorship, Dick had more time to pursue science and other interests. While his focus on salt and water homeostasis was undiminished, an interest in the question of consciousness and awareness of self had developed. Dick was keen to use state-of-the-art brain imaging techniques to attack this question. Together with Peter Fox in San Antonio, Texas, and Gary Egan and Michael Farrell at the Florey, he investigated the brain regions involved in generating the conscious sensation of thirst as well as those regions that generated subjective states of feeling hot, cold or breathless in human subjects.³³ Dick Denton noted that such mental states are only possible if the subject is conscious, and proposed that consciousness may have initially evolved in animals from drives and rewards associated with needs for nutrients such as water, food and oxygen.³⁴ These ideas were encapsulated in Dick's next book, the Pinnacle of Life (1993) followed by another book, Primordial Emotions: The Dawning of Consciousness in 2005.

The relationship of sodium intake to high blood pressure has long been a matter of controversy. In 1991, Dick and his wife Maggie, who assisted in the experiment, journeyed to Franceville, Gabon in West Africa to study a colony of chimpanzees who ate a natural diet in which the sodium content could be manipulated. Dick, together with colleagues in Gabon and San Antonio, Texas, showed unequivocally that increased dietary salt intake for twenty months increased blood pressure in the species most closely related genetically to humans. After he suffered a dangerous bout of cerebral malaria resulting from a trip to Gabon, Maggie demanded that he refrain from further visits there.

Dick took an active role in advocating for dissident scientists persecuted for their political views during the early 2000s, as an Australian representative on the International Commission of Academies and Learned Societies on Human Rights. His interests in the performing arts were another activity that he pursued keenly. In 1994 he was appointed to be one of the Directors of the Sydney Dance Company.

Dick Denton was always keen to embrace newly evolving techniques as they came into vogue. After he turned eighty in 2004, he set out to examine changes in gene expression in the brain of sodium-depleted mice that exhibited a salt appetite. He was aided in this investigation by collaborations with Wolfgang Liedtke at Duke University North Carolina and Andrew Lawrence, Lesley Walker and John

³³Denton and others (1999).

³⁴Denton and others (2009).

³⁵Denton and others (1995).

Drago at the Florey. These experiments yielded data that showed an involvement of brain dopaminergic mechanisms in the generation and satiation of sodium appetite.

As Dick and Maggie Denton approached their nineties, they spent their summers at their sea-side holiday home on the Central Coast of New South Wales overlooking the Pacific Ocean. There, they were often hosts to family and friends in a relaxed atmosphere and cherished the time they could spend there with grandchildren, Josh (son of Matthew and Annie Denton) and Olympia (daughter of Angus and Paolina Denton), and their families. Despite their maintaining exercise regimes involving daily swimming and walking, advancing age was affecting their health. Nevertheless, Dick still grappled with scientific questions and continued to drive to his office, where he was aided by Lesley Walker and his long-time secretary Eira Parry in preparing letters, emails and scientific manuscripts. A portrait of Derek Denton was painted by the artist Evert Ploeg in 2016 to hang in the National Portrait Gallery, Canberra (Fig. 4).

At the start of 2019, Dick and Maggie were enjoying their summer retreat to Pitaedie when Maggie's health began to decline. She passed away there on 24 February 2019 with Dick and other family members at her side. Maggie and Dick were together for more than seventy years, and the State of Victoria accorded her a State Memorial Service held at the Arts Centre in Melbourne.

Dick Denton also suffered health setbacks late in life; he underwent back surgery in 2014, then in 2018 he was diagnosed with bladder cancer that also required surgery.

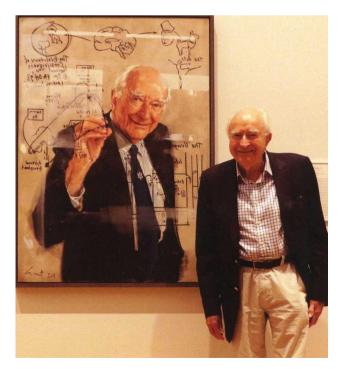


Fig. 4. Derek Denton stands beside his portrait painted by Evert Ploeg in 2016. Photograph courtesy of Denton family.

He recovered well. Like most people, he was grounded by the COVID-19 lockdowns, but still maintained contact with his colleagues by phone. He could be found at home in the last years of his life in front of a log fire and surrounded by piles of scientific journals, experimental results and correspondence spread around the room; a Bach sonata would provide background music as he planned experiments, usually with a glass of French wine at hand.

By November 2022, Derek Denton realised that his long life was drawing to its conclusion and he was able to phone colleagues and friends to say that he wished to say goodbye. Several were able to visit him, and his family was with him in his last days. Befitting a man that loved science and scientists, when he died on 18 November 2022, one of his scientific colleagues at the Florey, Andy Lawrence who had come to visit, was at his side. The State of Victoria accorded Derek Denton a state memorial service.

Derek Denton was remembered as a person of high integrity who fought for the principles that he believed in. He combined a sharp analytical mind with a strong competitive instinct. He had an enormous enthusiasm for scientific enquiry, a disciplined and logical approach to solving problems, both scientific and organisational, and the sheer willpower to 'have a go' at any endeavour no matter how seemingly difficult. He had enormous self-confidence as well as a 'hide as thick as a rhinoceros'. Like all of us, he had his foibles; riding in the passenger seat of a car that he was driving required considerable courage, for he was not a good driver. Dick did not seem to observe normal hours and would telephone colleagues at all hours of the day or night if he had a new idea for an experiment. Gregarious by nature, he loved a good story and good debate over a glass of wine. He was a legendary name-dropper. As well as a tolerance for different opinions, and the ability to see the 'big picture', Dick's personality was marked by another characteristic, which at times some would find infuriating, but none-theless was admirable. This was his tenacity and sheer will to win. Dick never gave up any pursuit without a hard fight regardless of the odds. He was tenacious in pursuit of his goals; he never gave in. Finally, Derek Denton cared deeply for his family, friends and staff of the Florey Institute. If staff had a medical problem, he would use his contacts in the medical world to ensure that they were receiving the best treatment possible.

Major honours and awards

In 1974, Derek Denton was elected a Foreign Medical Member of the Royal Swedish Academy of Sciences. Then followed election as a Fellow of other learned societies; the Australian Academy of Science in 1979, American Academy of Arts and Sciences in 1986, Foreign Associate of the National Academy of Sciences USA in 1995, Fellow of the Royal Society (London) in 1999, and the Academie des Sciences, Institut de France in 2003. Dick was elected as

an Honorary Fellow of the Royal Australian College of Physicians in 1979 and Honorary Fellow of the Royal College of Physicians (London) in 1999. He received the Pavlovian Award of the Pavlovian Society of North America in 1975, and the First Moscow Medical Institute awarded Dick the P. K. Anokhin Medal in 1982 for 'contributions to world physiology'. Dick probably enjoyed being awarded the Burnet Medal by the Australian Academy of Science in 1987, considering his enigmatic relationship with Sir Macfarlane Burnet early in his career. In 2005, Derek Denton was made a Companion of the Order of Australia, the nation's highest civilian honour, as was his wife Maggie later that year, a rare double for a married couple. In 2006 he was made Doctor of Laws (Honoris Causa) by the University of Melbourne.

Supplementary material

Supplementary material is available online.

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Conflicts of interest. The author is a trustee of Derek Denton's Estate. There are no other conflicts of interest.

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