

SIR MICHAEL FRANCIS ADDISON WOODRUFF

3 April 1911 — 10 March 2001



W. Woodruff

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Elected FRS 1968

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Michael Woodruff, one of the pioneers in transplantation, performed the first successful kidney transplant in the UK in 1960. But in addition he was a true surgeon scientist, who made many major contributions to transplantation biology. These included studies of the immunosuppressive activities and mechanisms of action of antilymphocyte sera, tolerance induction and mechanisms of tissue allograft rejection. He was a lateral thinker, a trait he displayed from his earliest days, and not least during his three and a half years as a prisoner of war in the notorious Japanese prisoner-of-war camp at Changi.

EARLY YEARS

Michael Woodruff was born in Mill Hill in London but at the age of two years he was taken to Melbourne when his father, Harold, was appointed Professor of Veterinary Pathology and Director of the Veterinary Institute at the University of Melbourne. His father was Professor of Veterinary Medicine at the Royal Veterinary College in London at the time, and Michael Woodruff admits to have been continually amazed in later life that his father gave up a secure chair in London for a post in the antipodes, presumably because of a sense of adventure. Later his father was to become Professor of Bacteriology, also in the University of Melbourne. At the outbreak of World War I his father was commissioned in the Australian Army Veterinary Corps and sent to Egypt, and Michael and his younger brother were taken back to London by their mother and lived with her mother in Finchley.

In 1915 Michael had an otitis media as a complication of measles, and his mother, who was nursing him, developed a staphylococcal septicaemia and died, leaving the two little boys motherless. He and his brother returned to Melbourne on a troop ship, cared for by an aunt, Elsie Cooper, while their father returned at about the same time but separately in 1917. Michael had few memories of those early childhood years but did have clear memories of the

Zeppelin air raids on London! In 1919 his father married again and their stepmother was to become a much-loved mother to the two boys. Michael and his brother were sent to Trinity Grammar School for their early schooling. Then in 1924 he and his brother spent a year as boarders at Queen's College in Taunton, Somerset, while their father was on sabbatical leave at the Pasteur Institute in Paris. Michael does not recall his time at Taunton with any pleasure for the headmaster (as he told his father) believed that 'colonial boys were backward' and as a result Michael had been placed in a class far below what would have been appropriate. Despite the virtual loss of an educational year they did have a marvellous summer holiday in Paris with their father. On return to Melbourne Michael went to Wesley College, a Methodist Public School, for his secondary education. This he found to be a stimulating environment and his love of mathematics developed there and continued for the rest of his life. He also became a keen rower and would have stayed on for an extra year with the hope of getting into the first crew if he had not won a senior government scholarship to the University of Melbourne and a scholarship to Queen's College, a residential college of the university.

UNIVERSITY OF MELBOURNE

Because of his enjoyment of mathematics he enrolled not only for the four-year engineering course but also for an honours course in mathematics, beginning in 1929. His tutor at Queen's was Harrie (later Sir Harrie) Massey (FRS 1940), a young physicist who later became Professor of Physics at University College London and Physical Secretary of the Royal Society. Although he enjoyed his studies, by the end of the third year he was doubtful about the future for a young engineer in an Australia that was in the midst of a deep recession, and decided to switch to medicine. Although his parents were supportive they felt that he should finish his engineering degree before embarking on medicine. This he did and finished top of the year with first-class honours. Furthermore he completed two years of the mathematics course, also with first-class honours. While in Queen's he became interested in the organ in the chapel, to which he had easy access, and decided to learn the instrument properly. He became a pupil of Dr A. E. Floyd, the distinguished organist and chorister of St Paul's Cathedral, and later was to become the college organist at Queen's College.

In 1933 he embarked on his medical course; his teachers included the renowned Professor of Anatomy, Frederic Wood Jones FRS, the Professor of Pathology, Professor Peter MacCallum, Dr Rupert Willis, who later was to turn his lecture notes into the classical textbook of the time in pathology, and a surgeon and lecturer in pathology, Mr E. S. J. King, later to become Professor of Pathology in succession to Professor MacCallum. In 1934 the Royal College of Surgeons of England held the primary FRCS exam in Melbourne (it then being possible to do this as a student), and Woodruff was one of four who passed. He graduated in medicine in 1937 with honours and won both the Beaney and Ryan prizes in surgery.

After graduation he became house surgeon at the Royal Melbourne Hospital to Mr E. S. J. King, an honorary consultant surgeon who not only lectured in pathology but was also the only surgeon who engaged in serious research. This obviously influenced Woodruff's decision to pursue an academic career as well as a career in surgery. He did a further year of internal medicine on the advice of Sir Sidney Sewell, under whom he had served as a house physician, took his MD by exam and then embarked on his surgical training.

MILITARY SERVICE AND CHANGI PRISONER-OF-WAR CAMP

Just as Woodruff embarked on his surgical career, war had broken out in Europe and although he was a pacifist in his student days the evil of Hitler led him to enrol in the Australian Army Medical Corps. He was advised that he would be more useful in the army if he had a higher surgical degree and as he had passed the primary exam of Fellowship of the Royal College of Surgeons as a student, he was able to take the second part of the Master of Surgery degree of the University of Melbourne (the second part of the FRCS had to be taken in London, and at that time that was impossible). He was successful and was then posted to the 10th Australian Army General Hospital in Malaya as a Captain in the Australian Army Medical Corps.

Life in Malacca in the 10th Army General Hospital was, for a few months, allegedly that of a lotus land with a mixture of tennis, gin slings and just enough work to keep him interested. However, after the bombing of Pearl Harbor life changed rapidly. He was posted to a casualty clearing station in Malaya, where he was engaged in giving anaesthetics and assisting at major operations; it should be remembered that at this time he had little actual surgical experience. He was then moved across the causeway into the Singapore General Hospital under the command of Albert Coates, later to become a famous plastic surgeon in Melbourne. Shortly afterwards the allied troops had surrendered to the Japanese, and Woodruff and his medical colleagues with their patients were marched to the Changi prisoner-of-war camp to join some 55 000 other Australian and British troops as prisoners of war (POWs).

In Changi there was not enough work to occupy all the surgeons, particularly one as junior as Woodruff. However, he realized that malnutrition, and especially vitamin deficiency, was likely to be a major problem on the meagre rations they were allocated. Thus he successfully sought permission to be the person responsible not only for the care of prisoners with deficiency diseases but also for developing methods of avoiding the inevitable vitamin deficiencies. This involved using rice polishings, husks, dead weevils and extracts rich in riboflavin made from literally tons of grass that they would harvest each day (figure 1). A report on this outstanding work was published by the Medical Research Council (MRC) after the war (25)*. Later during his three and a half years as a POW he was sent as a surgeon to look after POWs in outlying camps and because these prisoners were not allowed to be sent back to Changi for treatment he had to do everything on the spot as best he could. This even included the successful use of hypnosis in the absence of chloroform (2).

Of particular note to his future career was that in the camp they had a copy of Maingot's textbook of surgery (Maingot 1936). As a young trainee surgeon no doubt he spent a lot of time devouring everything in the book, but he recalls in his memoirs that he read with interest that skin allografts were accepted initially but later rejected after a couple of weeks, and allegedly decided then to investigate this phenomenon if he ever left Changi.

Woodruff is extremely reticent about his time in Changi even in his autobiography, in contrast to the accounts of other POWs such as Sir Edward (Weary) Dunlop and Sir Albert Coates. His reminiscences are very matter-of-fact accounts of his activities, with barely a mention of any interaction with his captors. Nevertheless although he says little, it is of interest that years later when he was visiting William Longmire's department at University of California, Los Angeles, a young scientist working in the department, Paul Terasaki, was asked to take him to

* Numbers in this form refer to the bibliography at the end of the text.

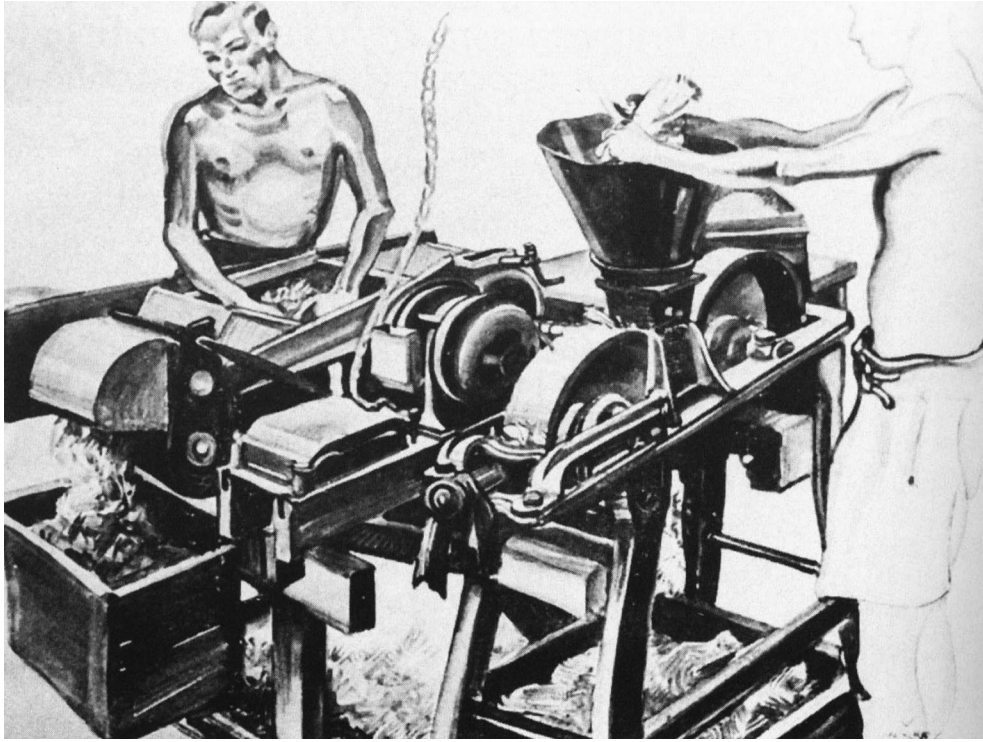


Figure 1. The machine for grass extract in the Changi POW camp. (Reproduced from *Nothing venture nothing win* (Scottish Academic Press Ltd, Edinburgh).)

dinner by his chief. Terasaki recalls how innocently he took him to a Japanese restaurant, not knowing of Woodruff's time as a Japanese POW. Woodruff politely suggested that he would prefer to eat elsewhere!

RETURN TO MELBOURNE

Woodruff returned to Melbourne in 1945, anxious to resume his surgical training. No doubt this was a very competitive arena, with many young budding surgeons returning from the war on top of the more recent graduates seeking a surgical post. However, he was fortunate to be appointed as a Surgical Associate to Albert Coates, who had just rejoined the staff of the Royal Melbourne Hospital. As this was an unpaid post he took a part-time lecturer post in the Department of Pathology, which provided a modest income.

In January 1946 he accepted an invitation to attend a meeting of the Australian Student Christian Movement, which he had been a member of and enjoyed as a student. The meeting was in Mittagong in New South Wales, where he met Hazel Ashby, a young science graduate from Adelaide. It was love at first sight and six months later they were married. She was to become a scientific colleague, the mother of their three children as well as a lifelong tennis and sailing partner.

SHEFFIELD

Michael was anxious to get to the UK as soon as possible to take the second part of his FRCS, and booked passages for himself and Hazel on a cargo passenger boat before he had any job to go to. Although he had been offered a travelling fellowship to Oxford for two years by the Australian Red Cross Society, he did not accept it because it was conditional on his returning to Australia at the end of the two years. Before he left he applied for the post of Tutor in Surgery at the University of Sheffield and while on the voyage received a cable to say that his application had been successful.

After his arrival in Sheffield he prepared for the FRCS exam, which he took in London in 1947 at the Royal College of Surgeons of England and was delighted to be informed that he had passed, in a strange ritual that continued for many years and will be familiar to all surgeons of that generation. By strange coincidence he had had tutorials from a surgeon, Colonel Julian Taylor, in the Changi POW camp, and in the clinical part of the exam Julian Taylor was his examiner, the only person he knew in the whole examination hall! Once he had his FRCS his clinical responsibilities back in Sheffield increased considerably and he received a much valued training in both emergency and elective general surgery.

Before Woodruff had left Australia he had decided to try to combine clinical practice and research, in other words to become what we call today an academic surgeon. There was no laboratory space in Professor Brockman's department of surgery in Sheffield but he was given space in Professor Green's laboratories in Pathology. Here he and Hazel began an extensive study of thyroid allografts in the anterior chamber of the eye with a particular interest in why allografts were not rejected in this immunologically privileged site. This work was communicated in due course to the Royal Society and published in the *Philosophical Transactions* (3). This has to be regarded as a promising start to his academic career in transplantation. Soon after arrival in Sheffield he arranged to visit Peter (later Sir Peter) Medawar (FRS 1949), who was then Professor of Zoology in Birmingham, to discuss aspects of tissue transplantation and rejection, because his research ambitions were now firmly directed down that road. As all who had met Medawar would affirm, this must have greatly reinforced his interest in his chosen field.

Of interest is that after 18 months in Sheffield he applied for a vacancy on the staff of the Royal Melbourne Hospital but was unsuccessful. One wonders what impact he would have had on surgery in Australia if he had been given the job.

ABERDEEN

However, soon after that a Senior Lecturer post and Honorary Consultant Surgical post at the University of Aberdeen and the Royal Infirmary was advertised, and as this department under Professor W. C. (Bill) Wilson provided laboratory space he decided to apply. It should be noted that neither he nor Hazel were quite sure where Aberdeen was and had to find it on a map before he went for interview. However, he was thrilled by what he saw before the interview and was delighted to be told that he was the successful appointee.

There were good laboratory facilities in Aberdeen and despite a heavy clinical load Professor Wilson gave him every encouragement to pursue his research work. Furthermore he was successful in obtaining support for his work from the MRC, which included the salary of

a research assistant, a post that Hazel occupied for the first year till their first child was imminent. They continued the study of grafts in the anterior chamber of the eye but during a visit by Sir Macfarlane Burnet FRS and his wife, who in fact stayed with them, they undoubtedly discussed at length the classical book by Fenner and Burnet in which the hypothesis that the recognition of self occurred in the foetus *in utero* was presented (Burnet & Fenner 1949). After this visit he attempted to induce tolerance in rats by placing tiny skin allografts on the foetus *in utero* and challenging them several weeks after birth with a skin graft from the same donor. Alas, the technical aspects of these experiments proved too difficult, and of course shortly afterwards Billingham, Brent and Medawar were to publish their seminal paper on the induction of neonatal tolerance (Billingham *et al.* 1953). In Aberdeen he also began his work on antilymphocyte serum for immunosuppression, but this too was largely unsuccessful, although it was later to succeed in Edinburgh. However, he was able to make several observations on the mechanisms of action of this agent (4, 5). This work was combined with studies on the effect of cortisone, which he had brought back from the USA, on allograft survival.

In 1950 he spent four months in the USA, supported by a World Health Organisation (WHO) Travelling Fellowship. During this visit he took the opportunity to visit some of the surgical giants of the day such as W. Blalock, W. Longmire, F. Moore, E. Churchill, L. Dragstedt, J. Gibbon, W. Walters, W. Cole and C. Huggins, as well as their institutions. He came away with the realization that surgical research was a highly respected and successful field of endeavour in the USA, and undoubtedly this provided further fuel to his own ambitions, a not uncommon occurrence among visiting surgeons in the years after World War II. He also met and signed a contract with the publisher Charles C. Thomas to write a book entitled *The transplantation of tissues and organs*. In fact the book was not published till 1960, but what an extraordinary scholarly work it proved to be; it still is the most complete bibliography of tissue and organ transplantation up to the time of publication (26).

While in Aberdeen it had become known that in mice the rejection of a skin allograft was determined by red cell antigens and indeed later it was recognized that in rodents histocompatibility antigens were expressed on red cells as well as on white cells. He therefore availed himself of an opportunity to investigate this in humans when a colleague in the blood bank (Dr T. Allen) identified two unrelated individuals who were identical for all the red cell antigens known at the time. The two volunteers agreed to an exchange of skin grafts; however, the grafts were rejected promptly, in contrast to control autografts (7). It is of note that Woodruff suggested at that time that it would be logical to look for transplantation antigens on nucleated white cells. It was not till 1958 that Dausset described 'Mac', the first histocompatibility leucocyte antigen in humans (Dausset 1958).

In 1951 he was awarded a Hunterian Professorship of the Royal College of Surgeons of England; the title of his lecture was 'The transplantation of homologous tissue and its surgical application' (6). During his time in Aberdeen, Professor Wilson was encouraging him to apply for chairs in surgery and although shortlisted for the chairs of surgery at St Mary's in London and at St Andrews University he was unsuccessful. However, his application for the Chair of Surgery at the University of Otago, the only Medical School in New Zealand, was successful and in 1953 he and his family returned to the antipodes to take up residence in Dunedin.

NEW ZEALAND

His four years in Dunedin were very active at a research level and included continuing studies of tolerance in the rat to skin allografts by injection of leucocytes at birth, which proved relatively unsuccessful (9). He also attempted to induce tolerance to paternal antigens in the human by injecting infants at birth with leucocytes from their fathers, which also proved unsuccessful but fortunately did not produce graft-versus-host disease (GVHD) (10). Peter Medawar came to Dunedin as a visiting professor for a month in 1956 and told him about the unpublished work of Billingham and Brent (1957) describing GVHD, which in retrospect Woodruff was relieved not to have produced in those infants. During Medawar's visit they set up some collaborative experiments on tolerance induction in rats, which were completed and published after Medawar had left (12). Woodruff had also coined the term 'adaptation' to describe the phenomenon in which allografts become less susceptible to rejection with time.

On the clinical side apart from his general surgical responsibilities, Woodruff found himself responsible for the treatment of burns, there being no plastic surgeon in Dunedin, and established a frozen skin bank for temporary cover of the burn injury, no mean feat in those days. Although his time in New Zealand has to be regarded as very successful, Dunedin, with a population of about 100 000, was really too small for a clinical medical school as well as being relatively isolated, and it was really for those reasons that when the two chairs of surgery in Edinburgh became vacant he decided to apply. He was appointed without interview to the Chair of Surgical Science (later changed at Woodruff's insistence to the University Chair of Surgery) at the University of Edinburgh in 1957. Undoubtedly his appointment to Edinburgh was a result of his very productive scientific time in Dunedin.

EDINBURGH

In Edinburgh Woodruff had excellent facilities and over the next almost 20 years till his retirement in 1976 his department was to be a major contributor to the science of transplantation. The university had allowed him to appoint two scientists in the department apart from clinical colleagues and this undoubtedly contributed to the scientific success of the research activities. The two scientists were Donald Michie and James Howard (FRS 1984), both to become distinguished scientists in their own right. As Professor of Surgery about 50% of his time was devoted to clinical work and teaching, which he felt was an important aspect of any academic surgeon's life if they were to maintain the respect of their clinical colleagues.

The MRC had agreed to establish a Research Group on Transplantation with Michael Woodruff as Honorary Director. The research activities of the group included the study of immunological tolerance, the immunosuppressive action of antilymphocyte serum and thoracic duct drainage, autoimmune haemolytic anaemia in mice and various aspects of the immune response to cancer in animals. The clinical research programme included the establishment of a renal transplant programme, and indeed the first successful kidney transplant in the UK between identical twins was performed by Woodruff in 1960 (15). Woodruff felt that if renal transplantation was to get off the ground in a conservative medical environment in Edinburgh the first transplant had to be successful, and he had waited till this opportunity arose. Between 1960 and 1976, 127 patients with end-stage renal failure were treated with a kidney transplant. Other interests included the establishment of vascular surgery in Edinburgh, the treatment of autoimmune haemolytic anaemia by immunosuppression and the role of

immunotherapy in the treatment of cancer. The clinical transplant programme was enhanced by a large grant from the Nuffield Foundation to build the Nuffield Transplant Surgery Unit at the Western General Hospital in Edinburgh, soon to become known as Fort Woodruff because of the strict isolation protocols necessary in those days of enhanced susceptibility to infection in immunosuppressed patients.

During 1970 there was an outbreak of hepatitis B, a viral infection transmitted by blood contamination, in the dialysis and transplant unit; several patients and four staff died of fulminant hepatic failure. This was a devastating episode in Woodruff's life, which affected him gravely. The unit was closed for a time while the whole episode was reviewed and plans were made to prevent the transmission of hepatitis B in the future, but the decision to start again was not an easy one for him, and involved considerable courage and determination.

When Woodruff retired from the chair of surgery in 1976 he moved to the MRC Clinical and Population Cytogenetics Unit at the invitation of the Director, Professor H. J. Evans; supported by grants from the Nuffield Foundation, the Wellcome Trust and the MRC, he was to spend a productive 10 years studying aspects of the biology of cancer. Indeed during this period of posthumous research—as many of his colleagues described it—he was to write 25 scientific papers and two books, namely *The interaction of cancer and host: its therapeutic significance* (27) and *Host and cellular variation and adaptation in cancer* (28). He commented later on being amazed to find how much work he could do in the laboratory with no clinical or administrative responsibilities.

Before and after his retirement he served as an adviser to the WHO and as a visiting professor in several universities, mostly in the USA and Australia. He also visited several research institutes, usually for a month or two, where inevitably he became involved in collaborative experiments. For example, in the South African Institute of Medical Research in Johannesburg he established the technique of renal transplantation in vervet monkeys and baboons, which was later put to very good effect by a young surgeon Bert (later Professor) Myburgh, and at the Walter and Elisa Hall Institute in Melbourne he began studies with Noel Warner of an immunopotentiating agent in transplanted tumours in athymic mice. He was elected President of the Transplantation Society in 1972 and presided over the international congress in Jerusalem in 1974 with great aplomb. As a member of the council of the Royal Society and its Vice-president in 1978–79 he visited China under the Scientific Exchange agreement between the Royal Society and the Chinese Academy. The trip started off disastrously because he was not expected till the following month and they wanted to send him home! However, he happened to mention that he was a Vice-president of the Royal Society and all doors were opened. Finally he and his wife joined Lord Todd, the President of the Royal Society, and his wife, who had just arrived on an official visit and graciously accepted the Woodruffs in their party.

SCIENTIFIC CONTRIBUTIONS

Woodruff's first publication appeared in the *Australian and New Zealand Journal of Surgery* in 1940, and was a scholarly report of a well-planned clinical experiment describing the diagnosis of vitamin A and D deficiency and its management in patients with obstructive jaundice (1). Certainly this work was of a standard that suggested that his future career might lie in academic surgery. Interestingly, his co-author was Douglas (Pansy) Wright, later to become a

distinguished Professor of Physiology and Chancellor of the University of Melbourne. As mentioned above, Woodruff had been responsible for nutrition, or perhaps better described as lack of nutrition, in Changi. After the war he submitted a report to the Director General of Medical Services on deficiency diseases in Australian POWs in Singapore. A copy was sent to Sir Edward Mellanby FRS, Secretary of the MRC, who suggested that it be combined with a report of deficiency diseases in civilian internees in Hong Kong by Dr Dean Smith. This combined report was published as an MRC Special Report in 1951, *Deficiency diseases in Japanese prison camps*, and was regarded as a major contribution in this area at the time (25).

By this time he was in Sheffield and had embarked on an academic surgical career with his major research activity directed at transplantation biology. His first major experiment in this area was begun in Sheffield and continued in Aberdeen with his wife, Hazel; it was reported to the *Philosophical Transactions of the Royal Society* in 1950 (3) and was an extensive study of the transplantation of thyroid and spleen autografts and homografts (now known as allografts) in the anterior chamber of the eye and subcutaneously in the guinea-pig. In this paper the privileged state of the anterior chamber of the eye was confirmed and the term 'adaptation' was first used to describe the resistance to rejection of an established allograft in certain situations, a phenomenon still of considerable interest today. It is interesting to note in this report that he saw transplantation of tissues to 'be of great clinical importance, especially in endocrinology', but no mention is made of organ transplantation even though pioneer attempts at kidney transplantation were taking place in Paris and Boston. Indeed, in his Hunterian lecture delivered at the Royal College of Surgeons of England in 1952 he stated that 'At present, therefore, homotransplantation of a kidney in humans would seem likely to prove futile and possibly disastrous', which at the time was a reasonable assessment of the situation (6). This probably explains why after moving to Edinburgh he did not perform a kidney transplant till an identical twin recipient with renal failure presented.

He continued his studies on the induction of lymphopenia in rats both by an antilymphocyte serum (ALS) and thoracic duct drainage, the latter being a technical *tour de force*. Both these agents proved to be powerful immunosuppressive modalities, and this work was of pioneering significance in the field of transplantation (20). In fact his contributions to the mechanisms of action of ALSs were enormous over many years. Medawar, who was to enter this field later, is said by Brent (1997) to have often been regarded as the 'high priest' of ALS, but Brent feels that this accolade rightly belonged to Woodruff. Since then the use of ALS and other antilymphocyte biological agents have become a part of routine clinical immunosuppression in organ transplantation. Some years later Woodruff persuaded the Wellcome Foundation to produce an ALS for clinical use, but in a multicentre study in the UK funded by the MRC of its immunosuppressive activity in renal transplantation it proved relatively ineffective, presumably because it had been raised using lymphoblasts as the source of antigen and had little activity against T cells.

Prompted by the prediction of Burnet and Fenner that exposure of a foetus *in utero* to a foreign antigen would result in the subsequent recognition of that antigen as self, and no doubt after discussions with Burnet on the occasion of his visit to Aberdeen, Woodruff attempted to produce tolerance in rats by placing skin grafts on foetuses *in utero*, but the procedure was not tolerated by the experimental animals. However, after the later seminal publication of Billingham *et al.* (1953) showing that the injection of a cell suspension *in utero* would produce tolerance to subsequent skin grafts from the donor of the cell suspension in a mouse model, Woodruff repeated his earlier experiments in the rat with splenic tissue and was able

to induce tolerance to later donor skin grafts (8, 9, 11). It is a pity that he chose such a technically demanding model in the first instance.

He remained forever fascinated with the concept of tolerance induction, and after his observation that in rats the injection of a cell suspension could produce tolerance for as long as two weeks after birth he injected two male infants with leucocytes from their father at birth and then challenged them with a skin graft from the fathers at six months of age. Both grafts took and remained perfectly healthy for four weeks before beginning to shrink in size, suggesting that a degree of tolerance might have been produced. He then became aware of the as yet unpublished work of Brent and Billingham describing the phenomenon of GVHD in mice, and no doubt recalled his earlier rat work in which substantial numbers of rats injected with donor splenic tissue lost weight and died before they could be challenged with a skin graft, and so did no further experiments of this nature. Fortunately neither infant showed any evidence of GVHD, presumably because the cells had been injected intramuscularly rather than intravenously. Later he was to define GVHD or runt disease in the rat by the injection of thoracic duct lymphocytes at birth (14). A little later he was to switch his efforts in tolerance induction to adult animals, using a combination of irradiation and cytotoxic drugs to achieve a degree of immunological immaturity before exposure to donor antigen, a strategy that was successful (16, 17).

Another experiment on humans allowed him to confirm the observations of Owen (1945) and Billingham *et al.* (1952) and later Medawar describing the chimaeric state of dizygotic cattle twins, which allowed skin allografts to be successfully exchanged between the twins, when he had the opportunity of exchanging skin grafts between dizygotic human twins who were chimaeric for red cell antigens (13). Both grafts took and certainly the female twin was tolerant of her brother's skin although the picture was not so clear in the reverse direction. Over many years he also studied the effect of steroids on tolerance induction and on graft survival in rats, this being the only drug then available with apparently modest immunosuppressive activities.

On the clinical side he established a major renal transplant unit at Edinburgh, and indeed the first successful renal transplant in the UK was performed between identical twins in 1960. The unit was one of the world's pioneering units in the field as the surgical techniques and immunosuppressive protocols evolved. Indeed, Tom Starzl points out that the technique of extravesical ureteroneocystostomy by which the transplanted ureter is implanted in the bladder, generally credited to Lich, was in fact devised by Woodruff. The first custom-designed transplant unit was built for his requirements in Edinburgh at the Western Infirmary (23). The basis of the design was to provide isolation of the transplant patients, including an enclosed communication with radiotherapy, with strict barrier nursing protocols for all staff, because infection was the major cause of death in these heavily immunosuppressed patients in the early days of transplantation. As time has moved on and less immunosuppression is used, these precautions are no longer necessary. The experience of the transplant unit was reported regularly in the clinical literature, culminating in a total review of the Edinburgh experience during his last year in office (24). Another clinical interest was peripheral vascular surgery, and he was instrumental in establishing this other relatively new specialty in Edinburgh.

After his retirement in 1976 he spent 10 years engaged in full-time research in cancer, because, in common with many transplant biologists, he had always had an interest in tumour immunology, and indeed some of his earlier publications dealt with approaches to the immunology of cancer and the immunotherapy of tumours with the use of *Corynebacterium*



Figure 2. Michael Woodruff with Rupert Billingham receiving the Transplantation Society Medal in Helsinki in 1986. From left: Peter Morris (President of the Transplantation Society), Michael Woodruff, Rupert Billingham and Pekka Hayry (Chairman of the Local Organizing Committee).

parvum (18, 19, 21, 22). During this time he published 25 papers, and also two books (27, 28) that summarized the work and concepts described in those papers. In the second book he describes the heterogeneity of the cell population making up a tumour, and proposes that this could explain the current difficulties in treating cancer, an important concept.

AWARDS

Woodruff received several awards during his career, including the Lister Medal and the Transplantation Society Medal (figure 2), and gave many named lectures around the world. In 1968 he was elected a Fellow of the Royal Society and in 1969 he was knighted by the Queen for services to medicine (figure 3). He was made an Honorary Fellow of the American College of Surgeons, the American Surgical Association and the Royal College of Physicians of Edinburgh. He also served on several editorial Boards and on a number of WHO committees over several years.

OTHER INTERESTS

He and his wife remained keen tennis players almost up till his death and no doubt the tennis court in their home 'Bield' in Edinburgh ensured regular tennis for one and all. But also in



Figure 3. Sir Michael and Hazel Woodruff outside Holyrood Palace on the occasion of his Knighthood in 1969.

Edinburgh he became a very keen sailor, joining the Royal Forth Yacht Club, and soon cruising and racing became a continuing passion. For several years the family would tow a 26 foot sloop (*Therapist I*) on an old army truck from Edinburgh to the Mediterranean each summer, but eventually he bought a larger boat (*Therapist II*) and over two summers sailed it from Edinburgh to Toulon, where it remained for regular holidays in the Mediterranean. As an undergraduate Michael had had a major interest in rowing, and to a lesser extent in hockey. Music was another pleasure and although he had been the college organist at Queen's College as an undergraduate he did not play the organ very much thereafter; he did learn to play the piano, but not as well as he played the organ. Mathematics, and especially number theory, continued to fascinate him throughout his life and he does mention that he tried intermittently to find a general proof of Fermat's last theorem but without success, although finding it great fun.

His family were always an important part of his life. His wife, Hazel, was an early colleague as mentioned above, and a lifelong tennis and sailing partner. Geoffrey, his eldest son, graduated in medicine from University College London and became a consultant ophthalmol-

ogist at Leicester. Keith, the second son, read civil engineering at Sheffield University and now lives and practises in Tasmania. Margaret, the third child, who was born in Dunedin, took an Honours BSc in botany at Sheffield University. Obviously Sheffield University had made a favourable impression on the Woodruffs during their time there!

WOODRUFF THE MAN

Michael Woodruff was a commanding presence in any gathering. It has to be said that he was not a particularly good lecturer because he had a rather ponderous delivery with a tendency to mumble, but he did have a great turn of phrase and a rather wicked sense of humour. Tom Starzl recalls that when Woodruff had just retired from clinical practice at the age of 65 years and at a meeting he (Starzl) was suggesting to Sir Roy Calne FRS and Michael Woodruff that they had arrived at just the right time in transplantation, Woodruff remarked that Roy and Tom 'might really have amounted to something if they had not been so preoccupied with surgery'! Starzl regarded this as a vintage Woodruff endearment.

He was a pioneer in transplantation both clinically and scientifically, and followed in the steps of Lister as a true surgeon scientist. What is surprising is that he was not successful in producing many surgeons in his own mould, despite the intellectual talent that was entering surgery and especially transplantation in the 1960s. However, his influence in transplantation at all levels was enormous.

Although he left Melbourne in 1946 never to return, except as a visitor, he never forgot his Australian roots, and Gus Nossal FRS recalls that his home in Edinburgh was a veritable Mecca for Australian visitors. However, many countries can claim a bit of this remarkable man, apart from Australia: namely, New Zealand, England and Scotland.

ACKNOWLEDGEMENTS

I obtained considerable information from Michael Woodruff's autobiography, *Nothing venture nothing win*, published in 1996 by the Scottish Academic Press (Edinburgh) as well as from his scientific publications. I was also glad to have known him quite well professionally and I am also most grateful to the following who wrote to me of their recollections of Woodruff: Tom Starzl, Sir Roy Calne FRS, Sir Gus Nossal FRS, David Hamilton, Paul Terasaki, Bernard Nolan, Leslie Brent and Gordon Clunie.

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