BIOGRAPHICAL MEMOIRS

Robert Royston Amos (Robin) Coombs. 9 January 1921 — 25 January 2006

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Biogr. Mems Fell. R. Soc. 2009 **55**, 45-58, published 14 May 2009 originally published online May 14, 2009

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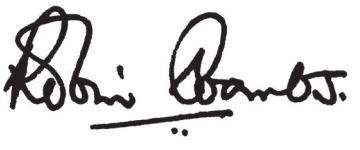

ROBERT ROYSTON AMOS (ROBIN) COOMBS

9 January 1921 — 25 January 2006

Elected FRS 1965

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Robin Coombs, one of the pioneers of British immunology, was responsible for the development of innovative approaches to identify the presence of diagnostic antibodies and antigens in body fluids, and for the use of red-cell-linked assays to identify important functional molecules on diverse cell types. He was responsible for the development of immunology as a discipline in its own right, and his mechanistic dissection of hypersensitivity reactions brought clarity to a hitherto confusing area of disease. Although best known for the development of the Coombs test for detection of Rhesus antibodies, the Cambridge 'school' that he established has spawned and disseminated a diverse array of talented immunologists worldwide, embracing virtually all areas of molecular and cellular immunology.

EARLY LIFE, 1921–43

Robin Coombs was born Robert Royston Amos on 9 January 1921 in Golders Green, the younger son of Charles Royston Amos and Edris Owen *née* Coombs.

Charles Amos served as an officer in the Royal Flying Corps during World War I and he is described as a company director in Robin's birth certificate. It was during the war that he met Edris. They were married in 1917 and had two sons, of whom the elder, Philip Royston (known as Peto), was born in 1918. The marriage, however, was short lived. Charles Amos had an affair with Peto's nursery maid and left the family shortly after Robin was born, taking no further part in the care of his children. Robin therefore never knew his father.

doi:10.1098/rsbm.2008.0021

Edris Owen Coombs was born in 1891, the youngest of four children of Robert Coombs (born in 1836) and his wife, Phillippa (born in 1851). Robert Coombs was a founder in 1872 of the firm of Clarke, Nickolls and Coombs, abbreviated as Clarnico, who were well-known manufacturers of sweets and jams and also owned property in London. Clarnico had their factory in Hackney Wick, where they were a leading employer and may have been, for a time, the country's largest confectioner. They were highly regarded as an excellent employer, being an early practitioner of profit sharing and having their own band and choir as well as a convalescent home and many social clubs. They eventually became part of Trebor Bassett but their name still survives as a particularly good peppermint cream! To his grandchildren Robert Coombs was known as Grandfather Clarnico Coombs.

After the break-up of the marriage, Grandfather Coombs took on the financial support of his grandsons, and when he died not long afterwards he left money in trust for their education. Edris resumed her maiden name and the two boys later adopted Coombs as their surname.

Edris was a talented singer and in 1924 joined a concert party going to South Africa, leaving the boys at a boarding school in Ascot. Here she met Mr Van der Linden, who came from Lourenço Marques in Mozambique and organized horse racing in South Africa. When Charles Amos died in 1929, Edris married Van der Linden and took her children out to South Africa. The Van der Linden family enjoyed a wealthy lifestyle there, but the older generation had no scientific or other wider intellectual interests, which Robin came to regret and to regard as a deprivation.

Both boys were sent to the Diocesan College in Rondebosch near Cape Town, and Robin, in later life, considered that he had not received the best possible education there. Nevertheless he was obviously academically very able. Reading *Microbe hunters* by Paul de Kruif turned his ambitions to becoming a bacteriologist. He was given a microscope and took to examining other people's tooth scrapings, among other objects, for their bacteria. He became friendly with a local veterinarian, who fired his interest in a career in veterinary medicine. After finishing his schooling in South Africa in 1938 by taking the London Matriculation examination when he was only 17 years old, he returned, on his own, to the UK to study veterinary medicine at the University of Edinburgh. He never returned to live in South Africa, and his brother subsequently settled in Canada. The family therefore became much dispersed.

In Edinburgh he lodged with the widow of a Moderator of the Church of Scotland, Jeanna Rudge Wilson, into whose slightly grand household (with two maids) Robin settled easily. He was a highly successful veterinary student and won all the available prizes. He qualified as a veterinarian in 1943.

The Central Veterinary Laboratory, Weybridge, 1943–44

The year 1943 was, of course, at the height of World War II, and Robin was directed to the Ministry of Agriculture's Veterinary Research Laboratory at Weybridge to work with Mr Norman Hole, the head of the diagnostic section, on the sero-diagnosis of glanders, a fatal disease of horses caused by *Burkholderia mallei*, which was considered as a possible biological warfare agent at that time and was so used by the Japanese. This was a seminal event in Robin's life and largely influenced the course of his subsequent scientific career. The sero-diagnostic test that was then used at Weybridge for glanders was complement fixation assessed

by the conglutination reaction, and this first introduction to research aroused Robin's interest in the techniques for measuring antibodies, in the complement system, and, indeed, in immunology in general. These interests he maintained throughout his life.

Norman Hole formed a high opinion of Robin's abilities and suggested that he study for a PhD in immunology in Cambridge where Henry Roy Dean—then the Professor of Pathology—was an immunologist. He duly came to Cambridge and was admitted to Trinity Hall as a graduate student in 1944. This too was to be a permanent move. He never lived anywhere other than in Cambridge again.

PhD studies in Cambridge, 1944–47: the discovery of the 'Coombs test'

The wartime Department of Pathology was not strong in immunology. Professor Dean was no longer actively engaged in research, and the supervisor to whom Robin was allocated, Dr Ronald Greaves, had his research interests in the freeze-drying of bacteria, at which he was very successful, but he was not interested in immunology. However, it was a matter of good fortune that during the war the Galton Laboratory serum unit was evacuated to the Pathology Department in Cambridge. This group, headed at the time by the eminent statistician R. A. (later Sir Ronald) Fisher FRS, was interested in the recently described Rhesus blood groups. It was one of the curiosities of this system that antibodies against Rhesus blood group antigens do not in normal circumstances agglutinate cells bearing these antigens, and this made their measurement extremely difficult. This problem was a concern of two of the distinguished members of the Galton Laboratory—Robert Race FRS and Arthur Mourant FRS, both great blood group experts, and they excited Robin's interest in how this might be overcome. The story goes that he was contemplating this problem one night returning from London on a dark wartime train when he realized that these non-agglutinating or incomplete antibodies, when they reacted with red cells, would coat these red cells with immunoglobulin and that a further antibody against the immunoglobulin fraction of serum, which contained the antibodies, could probably then agglutinate them. He pictured the red cell membrane as having humps and valleys in it with the Rhesus antigen low in the valleys so that when the antibody reacted with them it was still not clear of the red cell surface and out of reach, so that it was not able to react with the Rhesus antigen on another red cell. He was very rapidly able to test this hypothesis and showed that this second, antiglobulin, antibody would indeed agglutinate Rhesus-positive cells previously treated with sera containing anti-Rhesus antibodies, a procedure that became known as the 'indirect Coombs test'. Antiglobulin sera would also agglutinate cells, taken from children with haemolytic disease of the newborn, that had been coated with maternal anti-Rhesus antibodies *in utero* (the 'direct Coombs test'). The first results were published in 1945 (1)*. This paper made Robin Coombs's name internationally well known even before he finished his PhD in 1947. He always called the technique the 'antiglobulin reaction', but in the wider immunological and haematological world it became known as the 'Coombs test'. When entered as a search term on Google in 2007 the Coombs test still gave about one million hits, and to be quite so successful quite so early in one's research career does raise expectations among some colleagues that such a blockbuster success will be achieved every year, and hopes

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

among some others that it will never be repeated at all. Robin put up with both with equal and admirable detachment, but he did from time to time in later years express the wish that people were aware of some of his other work and did not remember him only and exclusively for the Coombs test.

In 1946 he was elected John Lucas Walker student in the Department of Pathology and he obtained his PhD in 1947. His thesis was entitled 'The conglutination and sensitization reactions', the first half being devoted to the work on the conglutinating complement fixation reaction and only the second to the antiglobulin reaction.

Further career in Cambridge

In 1947 Robin was elected the Stringer Fellow of King's College, Cambridge, and moved into college residence. It was his first experience at a Cambridge college as a fellow, and he found King's a little intimidating. In 1962 he was elected a fellow of Corpus Christi College and remained a fellow there happily for the rest of his life. From 1966 to 1969 he was the second warden of Leckhampton House, Corpus Christi's graduate student hostel, a post he filled with great distinction.

In 1950 he obtained his first university appointment when he became Assistant Director of Research (ADR) in Animal Pathology. In 1953 this appointment was transferred to the Department of Pathology, and he remained ADR there until 1963 when he was promoted to Reader. Promotion to Reader at Cambridge at that time was a personal promotion and was recognition of considerable distinction in research and scholarship. In 1968 he was elected to the Quick Chair of Biology, which he held until his retirement in 1988.

Although he spent his whole career in the Department of Pathology, he was not always in the same laboratory. Originally Robin and his students occupied space on the second floor of the department intermingled with everyone else. In the early 1960s Robin obtained a grant from the Wellcome Trust to create laboratory space in a new build on the roof of the Department of Pathology, accessible only via a cast-iron spiral staircase. These were the first dedicated immunology laboratories in Cambridge and gave Robin's Division of Immunology a distinct physical presence for the first time. In the early 1970s, when the first phase of the new Addenbrooke's Hospital in the south of the city opened, the Immunology Division was given a whole floor in the new laboratory wing and was able to expand its numbers and its scope; it was in these laboratories at the new Addenbrooke's Hospital that Robin spent the last 17 years or so of his working career.

The antiglobulin test and its development

The detailed chemical structure of antibodies was not known in the late 1940s. Indeed, the identification of antibodies as immunoglobulins, their structure, their formation and their genetics all lay in the future. However, the nature and detection of antibodies were from early on among Robin's major interests. He had a clear individual view of what antibodies were like, which was readily expressed in cartoon form. This picture of antibodies was very prescient and allowed him to develop a whole variety of detection techniques for those antibodies that would not themselves agglutinate or precipitate. Most of these techniques were based on

the antiglobulin reaction. He produced an extensive stable of variants of this test that could be used for detecting not only antibodies but also antigens. For example, he developed mixed agglutination reactions for detecting blood group antigens in blood smears, which proved to be of some forensic value. He also developed tests employing antibodies bound to red cells, which could be agglutinated by infectious agents. These tests are still potentially of great interest for 'near patient' detection of the nature of an infectious organism using very simple apparatus—basically a microscope slide and a preparation of stable antibody-coated erythrocytes. These techniques were developed much further after the discovery of monoclonal antibodies, and this is discussed in more detail below.

Robin's preference for working with simple techniques and a minimum of expensive apparatus was very marked, especially in the 1950s and 1960s. He believed strongly that immunological reactions, particularly the serology in which he was then interested, could be done using very simple tools. Some he devised himself, and they became closely associated with the Coombs laboratory. Doing serial dilutions with an insulin syringe to which a blunt hypodermic needle had been attached by a small piece of rubber tubing—the result being known as a 'plonker'—was highly characteristic of the Coombs laboratory, until it eventually gave way to the universal Eppendorf pipette. Similarly, he very much liked to use small 2 ml lipped glass tubes that could be suspended in water baths from hanging racks and thus allowed temperature to be controlled quickly and accurately. These hanging racks were made for him in the pathology workshops by the workshop manager, Frank Mitchell, and they too became a trade mark of the Coombs laboratory and travelled to many parts of the world, as did the wooden blocks hollowed out to take various sizes of glass bottle. Robin also liked to examine reactions directly down a microscope, and techniques such as mixed agglutination and its many derivatives depended very largely on direct microscopic examination. This sort of technology, although it did not require expensive apparatus, did require skilled technical assistance, and Robin was fortunate that for most of his career he enjoyed the services of Bert Gurner, an extremely skilled and devoted personal technician. His laboratory manager, Ray Matthews, also ran the laboratory during Robin's entire career, having entered the department as a school leaver in the early 1950s and acquiring the necessary skills and qualifications on the job. For the last 20 years, Dr Anne Wilson worked with Robin as the Quick fellow. Anne was a meticulous experimentalist and contributed greatly to the development of all the variants that were developed from the original antiglobulin reaction.

A particularly difficult antibody to detect was the reaginic antibody, responsible for the Prausnitz–Küstner reaction and the transfer of immediate-type hypersensitivity. This was later discovered to be IgE, an immunoglobulin class present at such a low concentration that the unmodified antiglobulin reaction could not detect it. Once specific anti-IgE antibodies became available, an enhanced antiglobulin technique for identifying reaginic antibodies was developed.

Allergy

Robin fought a lifelong battle, courageous but eventually unsuccessful, for the correct use of the word 'allergy', which literally means 'altered reactivity'. Therefore, to Robin, an allergic state was any specifically altered reactivity to the second exposure to an antigen, whether this resulted in immunity or in hypersensitivity. In this usage he was, of course, completely correct.

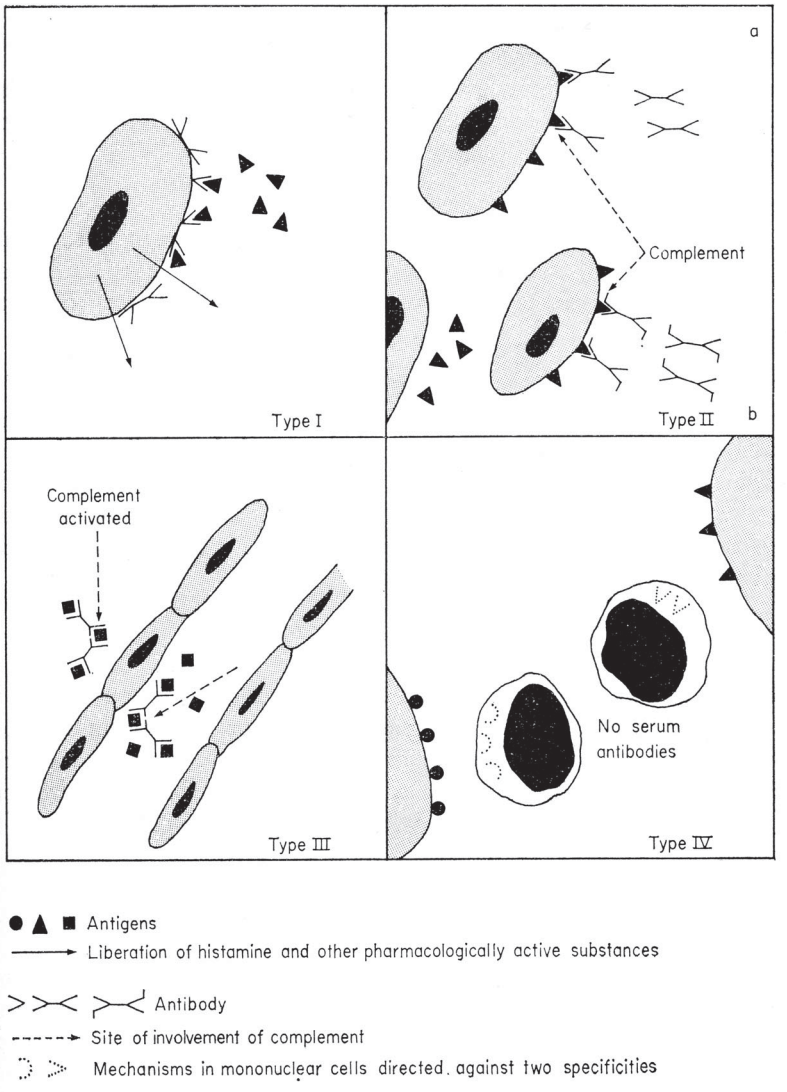

FIG. 20.1. Highly diagrammatic illustration of the four types of allergic reaction which may be deleterious to the tissues and harmful to the host.

Type I. Free antigen reacting with antibody passively sensitizing (allergizing) cell surface.

Type II. Antibody reacting with (a) cell surface or (b) with antigen or hapten which becomes attached to cell surface: complement plays a major destructive role.

Type III. Antigen and antibody reacting in antigen excess forming complexes which, possibly with the aid of complement, are toxic to cells.

Type IV. Specifically modified mononuclear cells (actively allergized cells) reacting with allergen or antigen deposited at a local site.

Figure 1. Highly diagrammatic illustration of the four types of allergic reaction that may be deleterious to the tissues and harmful to the host. From (4); figure reproduced with permission.

However, the use of the word allergy as a synonym for hypersensitivity, and indeed increasingly for immediate-type IgE-based hypersensitivity reactions, was widely adopted first in the USA and then also in the UK; and this particular battle was lost. Nevertheless, a major contribution that Robin, together with his close friend Philip Gell (FRS 1969), the Professor of Immunology at Birmingham, made in their textbook *Clinical aspects of immunology* (4) was to classify the allergic mechanisms of tissue damage; that is, the mechanisms by which the results of the immune response could give rise to tissue damage rather than to immunity. The four types then described are still best shown in the original cartoon form in which they were presented (figure 1), which differentiated between immediate-type hypersensitivity due to IgE antibodies (type 1), tissue damage caused by antibodies reacting with cell-bound antigens, with or without complement fixation (type 2), allergic damage due to immune complexes (type 3) and the delayed tissue damage that was caused entirely by T lymphocytes (type 4). This classification proved extremely durable and continues to be used, with only very minor modification, to this day.

The study of allergic mechanisms of tissue damage, which came to be called immunopathology, remained one of Robin's major interests throughout his career. He studied in some detail experimental models of arthritis induced by the injection of antigens into joints, and he also studied the effects of antibody and complement on organ culture of cartilage and bone, together with Dame Honor Fell FRS at the Strangeways Laboratory. These studies demonstrated the importance of type 2, 3 and 4 reactions in allergic damage in joints and cartilage, but none of the available models at that time could really explain the existence of polyarthritis because they generally involved the administration of antigens into the joints. It remains doubtful to this day whether there is truly a reliable animal model of rheumatoid arthritis.

However, the dominant focus of Robin's interests in immunopathology centred on the phenomenon of cot death.

Cot death

Robin's interests in cot deaths arose from the observations of Max Barrett (see chapter 6 in (5)), the histopathologist at Addenbrooke's who had a special interest in cot death and believed that the cause was due to asphyxia. He had found (as Bodian and Heslop had originally described in 1956) that the lungs of children who had died of cot death showed at post mortem a characteristic single-cell desquamation in the bronchi. Robin, together with a PhD student, Bill Parish, then experimentally produced anaphylactic reactions to milk introduced into the lungs of sensitized and anaesthetized guinea pigs and found that such animals died very quietly, their lungs showing the typical Bodian–Heslop desquamation. This suggested that cot death could be explained, at least in part, by an allergic reaction to cows' milk regurgitated and inhaled when children are asleep. He explored this hypothesis for many years and the idea is, indeed, very plausible. Robin and his colleagues were able to demonstrate that some milk preparations were much more antigenic than others and that there was an association between children being given cows' milk when very young and the incidence of cot death. He certainly persuaded many of the younger members of his laboratory not to give their children cows' milk in the first months of life. The findings were also compatible with the important clinical observation that laying children on their backs protected against cot death because the position of the epiglottis under those conditions is such that the aspiration of milk becomes less likely.

After his retirement, Robin wrote, with Bill Parish and Andrew Walls, a book summarizing all their work (5). The evidence assembled was persuasive, and he was disappointed that there was no major response from the clinical community concerned with cot death. It is almost certain that cot death is not a single phenomenon and that several causes may be involved, but the idea that anaphylaxis to inhaled cows' milk is one causative factor remains highly plausible and deserves greater attention than it has yet received.

Work on the complement system

To some extent, complement was Robin's first immunological love. With Norman Hole, he investigated the complement fixation test for glanders, comparing a haemolytic with a conglutinating reaction. Conglutinin was a substance present only in the serum of cows and other ruminants, which reacted with cells once they had been coated with antibody and complement and caused very powerful clumping of the cells. It was later recognized as the first mammalian lectin to have been described. Robin worked on this together with his first-ever graduate student, Anne Blomfield, who came into the laboratory very shortly after he had finished his PhD and who wrote her own PhD in 1951 on conglutination. Once she had achieved this end, Robin proposed to her. They were married in 1952 and enjoyed over half a century of very happy married life. Together with Anne and with a Canadian visitor, Don Ingram, they studied not only conglutinin in cows but also the related phenomenon of immunoconglutinin, a set of autoantibodies that are formed in response to bound complement in most species. They defined the differences between them and began to look at the levels of conglutinin and immunoconglutinin in various diseases, showing that immunoconglutinins are indeed a good marker of complement activation *in vivo*. They published a book, *The serology of conglutination in relation to disease*, on this topic in 1961. Robin did not, after this time, continue experimental work on the complement system, although he remained very interested in it. He turned this area over to Peter Lachmann (FRS 1982), who joined him as a PhD student in 1958 and worked in the Immunology Division as an ADR until 1971. During the 1960s, studies on complement became very much more immunochemical and this was not, at that time, Robin's particular interest.

The Coombs laboratory

In pursuing his chosen research projects, Robin liked to seek out collaborators with their own expertise rather than trying to learn all the expertise himself, and he liked to build a team of such workers. He attracted graduate students and postdoctoral workers from all over the world, and his laboratory was always an extremely interesting mix of immunologists from different countries and with different scientific backgrounds. He did not seek to build up a large separate department of his own, being perhaps happiest interacting with individual students and seeding the Coombs way of doing immunology around the world. However, he had a series of associates in the Immunology Division who stayed for longer periods, and some of them held university appointments. Bill Parish has already been mentioned. David Franks came to Cambridge in the mid 1950s and remained in the Division until 1983. He was an ADR in the department from 1966 to 1980 and was a University Lecturer from 1980 to 1983. Among other projects, he worked on the detection of the species of origin of cells

by using mixed agglutination reactions and was one of the first to demonstrate that, at that time, many tissue culture lines were not in fact what they were thought to be and were often HeLa cells that had contaminated other cultures with great efficiency. Alan Munro joined the Immunology Division as a lecturer in 1971, was promoted to a readership in 1980 and left to found Cantab Pharmaceuticals, an immunology-centred biotechnology company, in 1989. Alan had originally trained as a biochemist and he greatly strengthened this discipline in the Coombs laboratory. He also brought a focus on T-cell immunology. Herman Waldmann (FRS 1990) came as a PhD student in 1971 and stayed until 1994, finally as Professor of Therapeutic Immunology. He brought monoclonal antibody technology into the laboratory.

Coombs's laboratory in New Addenbrooke's Hospital

Robin was keen to connect immunology to the clinic, and in the mid 1970s he moved a section of the Immunology Division to laboratory space at the New Addenbrooke's site. In time he was joined there by Peter Lachmann, who had returned from the Royal Postgraduate Medical School in London, and by Herman Waldmann, just returned from a sabbatical with César Milstein FRS. Both colleagues were also keen to promote the clinical interface. With the recent discovery of monoclonal antibodies by Köhler and Milstein just across the road, Robin's interest in the red cell assays was reinvigorated. He saw enormous diagnostic potential for simple immunoassays based on red blood cells. He had hopes for rapid and large-throughput use, particularly in technology-limited environments. Uppermost in his mind were possible opportunities for such assays in developing countries, in patient-side and pen-side testing, in home use and in other non-laboratory settings. The monoclonal antibody technology opened up the prospect for one-step homogeneous assays. Unlike polyclonal antisera, in which the relevant antibody species were a tiny minority of the protein, the purified monoclonal antibodies could be directly coupled to red cells at high antibody density. Although concepts such as reverse passive haemagglutination were not new, monoclonal antibodies enabled an easier and more reproducible process.

For many of the improved assays, antiglobulin monoclonal antibody reagents were chromic chloride coupled to enzyme-treated red blood cells. These cells could be fixed with glutaraldehyde and freeze-dried for longer-term storage and use.

For the detection of antigens on cells, assays were performed in U-well microtitre plates by using monolayers of fixed cells bearing these antigens. Wells were incubated with monoclonal antibodies and washed, and then the detection red blood cells were added and allowed to settle. If there were antigen-specific antibodies in the wells, the red blood cells would adhere as a monolayer over the whole surface rather than rolling to the centre of the well. It was as simple as that.

Slight variations would enable the detection of antibodies in sera. For example, with Martin Cranage and Tony Minson, Robin developed assays for the rapid detection and typing of herpes simplex virus (HSV). Two monoclonal antibodies against a single glycoprotein of HSV, when chemically linked to red blood cells, failed to bring about agglutination in the presence of HSV antigen. However, the addition of anti-HSV antiserum resulted in a very sensitive agglutination reaction. The monospecificity of the monoclonal antibodies precluded cross-linking of the coated red blood cells by the antigen, but the addition of polyclonal antibody completed the bridging between the reactants. This simple and rapid assay for antibodies against HSV gave excellent correlation with neutralization of virus infectivity (a far more complex, technically

demanding and expensive plaque reduction assay). Robin demonstrated that such assays had great potential in many real-world situations with unmet needs. One such situation was the detection of pathogens, particularly viruses, directly in clinical samples. He collected from numerous collaborators a vast array of clinical samples, including a collection of 'nasal aspirates' from David Tyrrell FRS at the Medical Research Council's Common Cold Research Unit, and a set of rotavirus-containing stools from Tom Flewitt. The laboratory freezers were overflowing with almost every imaginable biological sample, including those donated by Robin himself to act as controls! He did not stop at clinical and veterinary samples but also moved into the area of phytopathology, analysing extracts of tobacco, potato, cucumber and strawberries!

There were two critical problems to be overcome: the first was the biophysical properties of the specimens such as dispersability, pH and tonicity; the second was the presence of 'natural agglutinins'. Robin and his colleagues were not deterred. They tapped into the expert network he had coordinated world-wide to advise on topics as diverse as cell-surface charge physics, sonic disruption, coordinate chemistry, lectin chemistry and cryobiology.

Although they were elegant and powerful, it was a disappointment to him that these types of assay were to find limited application, owing largely to the complexity of scale-up, the perception of the technology as 'old-fashioned', and an inadequate quantitative readout. Nevertheless, the principles of homogeneous assays based on monoclonal antibodies were established within the field, and they rapidly found wider application when associated with newer readout modalities such as enzyme-based amplification. Sadly, those newer modalities were not as suitable for application in the developing world. Martin Cranage, one of his close colleagues, has since pondered on what the outcome might have been if the Bill and Melinda Gates Foundation had existed back then.

His colleagues have recalled that Robin always insisted on personally scoring the results of haemagglutination assays. As reported by one of them,

> He would appear regularly in the laboratory, brandishing his magnifying glass and then holding the assay plates up to the light would reel off a series of scores: 2 plus, 2 plus, 2 plus, 1 plus, 1 plus one bracket, 1 plus bracket, negative, etc. This was delivered with the cadence of a mantra; indeed my colleague Jane Welsh, with whom I shared a laboratory, put the mantra to music as the Chattanooga two, two!

No doubt for him the red blood cell was an object of emotional beauty, especially when 'rosetted' around a white blood lymphocyte. This 'artistic' pleasure he obtained from the technology reveals something of the complexity of Robin's approach to his science. He wanted science to be fun, and undoubtedly in this very active era of the 1980s his mix of translational and mechanistic research left a strong influence on many of his colleagues, dictating the path of their future careers.

What will always remain in the memory of one of us (H.W.) was the use of Robin's technology to detect extremely rare class-switch variants of an antibody directed against CD52—an antigen on all lymphocytes. We had hoped that this antibody would be a powerful anti-lymphocyte-depleting agent *in vivo*, but initial clinical trials had proved disappointing. The subclass of the antibody was rat IgG2a, and we knew that its ability to harness lytic mechanisms was much lower than that of the rat IgG2b subclass. In those days antibody engineering was in its infancy, and the only way we had of deriving an IgG2b form of this antibody was to search for a very rare class-switch variant arising in prolonged tissue culture. Robin's red cell technology enabled us to do this—the rat IgG2b form proved very lytic *in vivo*, and so emerged Campath-1 or alemtuzumab.

Robin and the British Society for Immunology

During World War II, immunology in the UK went into some decline, and in the immediate aftermath of the war, the discovery of penicillin and the promise of antibiotics led to the (mistaken) view that the problems of infectious disease were likely to be fully conquered very quickly. The renaissance of immunology that happened after the war was led by a remarkable group of people who formed the core of what became the British Society of Immunology. They included, besides Robin, John Humphrey (FRS 1963), Head of Immunology at Mill Hill; Philip Gell, Professor of Immunology at Birmingham; John Marrack, who had been Professor of Chemical Pathology at the London Hospital but who joined Robin in Cambridge after his retirement; and Robert White, who was Professor of Microbiology and Immunology at Glasgow. Slightly apart was another group who were greatly involved in the birth of transplant immunology, and among whom Peter Gorer (FRS 1960) and Peter (later Sir Peter) Medawar FRS were the main figures. The British Society for Immunology was founded in 1955, and Robin became its first General Secretary. He devoted a great deal of energy and effort to establishing it; the society was, and has remained, remarkably successful. Its meetings, from that time to this, have never been short of exciting scientific controversy and have maintained a very high standard. Robin was devoted to the idea that immunology should stand as an independent discipline for university teaching and among the pathological disciplines. The fact that this largely became the case is due in no small part to his efforts. After he retired from office at the society in 1965, he never again involved himself in the public aspects of the subject; he decided that what he really liked was to be in his laboratory with his students and that the world of London committees was perhaps not one in which he would care to be too closely involved.

His other main endeavour in the early 1960s was to undertake the editing, with Philip Gell, of *Clinical aspects of immunology* (3), which became the leading textbook in its field. It was in this book that the classification of allergic reactions already mentioned was published. *Clinical aspects of immunology* went through three editions with Robin as one of its editors, and two more after he and Philip Gell gave it up. It grew remarkably in size, but it remained very much along the lines that the two original editors had laid out.

Home and family

Robin and Anne, after their marriage, bought a fine house at 6 Selwyn Gardens, which was their home throughout their married life. In the early days it was slightly spartan, but as Robin grew more successful and financially more secure they showed a great passion for modern furniture, modern decoration and modern craftsmanship, and the house became very splendid. Robin and Anne were always very hospitable to their colleagues, and we all have happy memories of time spent there discussing science with Robin, and God and the world with them both. Anne became a skilful carpenter and wood turner and had a workshop in the house.

They had two children, Robert and Rosalind, who gave them great satisfaction. Robert became a physician and works as a neonatologist at Sheffield. Rosalind is active in the book trade; she and her husband now live in a cottage in Butley in Suffolk, which Robin and Anne bought as a holiday home and where Robin greatly enjoyed spending his free time.

When he retired in 1988, Robin gave up all scientific work; however, this did not entirely suit him and he returned to writing up his theories on cot death. His last few years were blighted by progressive dementia and he died on 25 January 2006.

He was the last survivor of the great group of postwar British immunologists, and probably the last to aspire to keep up with the field of immunology as a whole. He holds an enduring place in the annals of British immunology.

Honours and distinctions

1961 Landsteiner Award of American Association of Blood Banks
1965 Elected Fellow of the Royal Society
Gairdner Foundation Award
1966 Henry Steele Gold Medal of the Royal College of Veterinary Surgeons
1967 James Calvert Spence Medal of British Paediatric Association
1969 Philip Levine Award of the American Society of Clinical Pathology
1973 Elected Honorary Member of the American Association of Immunologists
Honorary MD, University of Linköping, Sweden
Elected Honorary Fellow of Royal College of Physicians, London
1979 Honorary Fellowship of the American College of Allergists
Honorary Doctor of Veterinary Medicine, Royal Veterinary and Agricultural University of Copenhagen
Elected Foreign Correspondent of the Royal Belgium Academy of Medicine
1981 Honorary DSc, University of Guelph, Canada
1984 Honorary Member, British Blood Transfusion Society
Honorary DSc, University of Edinburgh

Acknowledgement

The frontispiece photograph was taken in 1965 by Walter Bird and is reproduced with permission from Godfrey Argent Studios.

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The following publications are those referred to directly in the text. A full bibliography is available as electronic supplementary material at http://dx.doi.org/10.1098/rsbm.2008.0021 or via http://rsbm.royalsocietypublishing.org.

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(2) 1961 (With A. M. Coombs & D. G. Ingram) *The serology of conglutination and its relation to disease*. Oxford: Blackwell.
(3) 1963 (Editor, with P. G. H. Gell) *Clinical aspects of immunology*. Oxford: Blackwell.
(4) 1968 (Editor, with P. G. H. Gell) *Clinical aspects of immunology*, 2nd edn. Oxford: Blackwell.
(5) 2000 (With W. E. Parish & A. F. Walls) *Sudden Infant Death Syndrome: could a healthy infant succumb to inhalation-anaphylaxis during sleep leading to cot death?* Cambridge: Cambridge Publications.