BIOGRAPHICAL MEMOIRS

David Willis Wilson Henderson, 1903-1968

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DAVID WILLIS WILSON HENDERSON

1903-1968

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DAVID WILLIS WILSON HENDERSON was born in Glasgow on 23 July 1903, the only child of the late John Henderson, a chartered accountant, and his wife, Mary. He attended the Hamilton Academy where he perfected several ingenious methods of avoiding work in subjects he disliked, but acquired a genuine interest in science, though at this stage it was of a practical rather than academic nature. His initial leaning was to agriculture and he insisted on leaving school at the earliest possible moment to become articled to a farmer. He soon found that the application of science on this particular farm was scant and the same streak of impatience with arbitrarily imposed authority, so apparent in Henderson's later life, resulted in a sudden and dramatic termination of the apprenticeship. Though somewhat sceptical, his parents agreed to his proposal to read for a degree at Glasgow University. He chose agricultural bacteriology as his major subject, enrolled under Professor J. F. Malcolm, D.Sc., at the West of Scotland Agricultural College, and graduated in 1926.

His first post was as lecturer in bacteriology at King’s College, University of Durham, where he started to lay the foundations of his research career, and was subsequently awarded an M.Sc. degree in 1930 for work on anaerobic infection in lambs. In this same year he married his first wife, Beatrice Mary Davenport, daughter of Sir Westcott Abell, K.B.E., at that time Professor of Naval Architecture at the affiliated Armstrong College. Prospects of advancement in Durham University looked poor and with this added need to provide for the future, Henderson sought a move to London. Despite severe competition for research funds Henderson was successful in being elected to a Carnegie Research Fellowship and, in 1931, he came to work at the Lister Institute of Preventive Medicine. Here he immediately came under the influence of Arthur Felix and Muriel Robertson, both experienced workers, the latter on anaerobes, more particularly on the antigenic structure of these organisms. Up to this time work on the pathogenic spore-bearing anaerobes had received no adequate consideration, and a review of the literature on the immunity reactions to infection with these organisms indicated, with a few exceptions, that the work had been on the soluble toxins (exotoxins) they produce, and on the associated antitoxic mechanism developed in the host. Henderson’s new investigations at the
Lister Institute were designed to demonstrate the role of antibacterial mechanisms in limiting infection and were to involve a group of pathogenic spore-bearing anaerobes associated with the disease condition in man and animals known as 'gas-gangrene'. It is not surprising to find that Henderson's first investigation was on the application of 'qualitative receptor analysis', a method of antigenic analysis first introduced by Weil and Felix in 1917. The pathogen studied was *Clostridium chauvoei* and strains of bovine and ovine origin were collected from various parts of the world in an attempt to establish the relationship of their O and H antigens. He found the O antigen was common to all strains, a rather unexpected result in view of the diversity of antigenic constituents previously established in other species of anaerobes, particularly in *C. septicum* and *C. welchii*. Henderson then demonstrated that suspensions of *C. chauvoei* after heating at 100 °C for 2 hours, conferred a very high degree of protection against infection with the homologous organism using calcium chloride as activator. Passive protection experiments made in mice indicated that goat anti-O sera gave protection and that the O agglutinin titre of the goat serum used reflected the relative value of the protecting immune body. In 1932 Henderson was elected to a Beit Memorial Research Fellowship. He stayed on at the Lister Institute and extended his investigations to include the immunization of guinea-pigs against *C. oedematiens*, using a bacillary suspension (O antigen) freed from toxin and rendered sterile by heat. The animals were protected against many hundreds of certain infecting doses of an activated suspension of the homologous organism. The results of this work indicated a new development for the active immunization of rabbits against the intramuscular injection of activated suspensions of *C. oedematiens*. The investigations had shown that rabbits were more readily immunized than guinea-pigs and that quantities of O antigen insufficient to protect guinea-pigs afforded complete protection in rabbits. It was also demonstrated that formolized whole culture, or the bacterial substance it contained, gave protection against multiple infective doses of spores, whereas formolized, filtered toxin gave no protection. In the light of his experience, Henderson believed that no claim could be made as to the impracticable nature of pure antibacterial prophylaxis until field experiments had been conducted with the animal species (sheep) involved in the naturally-occurring disease. Antibacterial methods similar to those used in gas-gangrene infection were not successful and no protection was obtained against *C. tetani* infection.

The work he had undertaken since he joined the Lister Institute in 1931 was presented under the title of 'Studies on the spore bearing anaerobes with experiments on active and passive immunity' for the Ph.D. degree of London University; this he received in 1934.

At this juncture Henderson started a series of experiments with the Institute's Director, Professor J. C. G. Ledingham, F.R.S., on the cultivation *in vitro* of louping-ill virus, an entirely new field of enquiry for Henderson. The virus was passed through a series of twelve sub-cultures in a medium of
whole mouse-embryo pulp, sheep serum and Tyrode solution and it was estimated that the increase in virus over the series was of the order $10^{16}$. The medium was then greatly simplified and after centrifugation of the cell debris it was found that 'free' virus remained in the supernatant. During this period Henderson developed an interest in the medical aspects of immunology, a field which was to be a major concern for the rest of his research life.

In October 1935 David Henderson was appointed to the bacteriological staff of the Institute’s Serum Department at Elstree where, in addition to helping with the routine examination of therapeutic sera and the production of antigens for the immunization of horses, he started to investigate the properties of anti-sera produced against three serological types of *Streptococcus* isolated from human infections. High titre agglutinating sera were obtained, but on testing in mice the sera were shown to possess no protective value. At about this time David Henderson and one of the authors (W.T.J.M.) started to examine the antigenic substances present in different strains of *Salmonella typhi* by extracting the acetone-dried bacilli with diethylene glycol and other similar organic solvents. Substances corresponding to the Vi and O antigens were obtained and used to immunize rabbits and to produce Vi and O antibodies. The results indicated that the Vi and O antigens existed in the intact bacterial cell as distinct and separate chemical entities with strictly specific immunological properties. Some evidence was obtained for believing that the Vi antigen was modified during treatment with diethylene glycol, and later Henderson’s experimental results indicated that the structure concerned with the production of complement-fixing antibodies was altered but, nevertheless, still induced the formation of protective antibody. It was at this time that Henderson showed his remarkable technical skill in being able to grow pathogenic micro-organisms on a very large scale, equivalent to several hundred grams of dry bacterial bodies, and with remarkable freedom from contaminating micro-organisms. These were important days for both of us and we not infrequently worked in the laboratory well into the night in order to obtain sufficient culture and extracted antigen to make our own small contribution to the clarification of the chemical nature of bacterial antigens, at that time a rapidly developing facet of immunochemistry.

While working at the Lister Institute at Elstree, Henderson also collaborated with Douglas McClean in an investigation on the influence of tissue permeability on bacterial invasion. Gas-gangrene organisms elaborate a factor that increases the permeability of tissues and by using the factor obtained from the two anaerobes *C. welchii* and *C. septicum* he and McClean demonstrated that anti-sera obtained by immunizing rabbits with these organisms inhibited the activity of this diffusing factor. The inhibition brought about was strictly specific: a serum prepared against *C. welchii* diffusing factor neutralized that factor but not a similar factor elaborated by *C. septicum* or vice versa.
With his colleague, Peter Gorer, Henderson investigated the complementary or synergic action of combined treatment with drug and immune serum, of infections caused by certain spore-bearing anaerobes. In an intradermal infection in animals with C. septicum the combined action of sulphapyridine and antitoxin, or of sulphapyridine and antibacterial serum, effects a saving in life much greater than would be expected if a simple summation effect was in operation. The result was much less definite with a C. welchii infection. These results were of some considerable importance because the drugs alone could not be relied upon to control gas-gangrene infection and therefore Henderson and Gorer's observations indicated that an attempt should be made in man to develop the synergic effect produced by the combined action of drug and serum. This paper shows Henderson's introduction to more sophisticated quantitative methods of handling biological data which he was later to exploit.

Henderson's last contribution from the Elstree laboratories at this time of national crises dealt with the differentiation into four groups of a complex group of anaerobes closely related to the classical C. welchii. The antigenic analysis of the Wilsdon types B, C and D and the recognition of a heat-labile antigen designated 'L' antigen within this group of organisms brought to an end his main contribution in this field, which embraced the influence of bacterial variation on the serological behaviour of particular strains of anaerobes.

During their stay at Elstree David Henderson and his wife lived in a beautiful early-Georgian house, 'Robin Hill', now demolished, situated about half-way up the hill at Stanmore, Middlesex. Here the Hendersons had a most attractive home and many of his colleagues at that time remember with delight the pleasant evenings spent there, the warmth of their hospitality and the vigorous discussions that went on into the early hours of the morning.

In September 1939 Henderson was transferred from Elstree to Chelsea where he became a member of the staff of the Bacteriology Department of the Lister Institute. However, at this moment of great national upheaval the move to Chelsea never took place and Henderson remained for a short time at Elstree. It was at about this time that he reported to Sir John Ledingham the outcome of some preliminary experiments that demonstrated the very high toxicity in mice of toxins administered by the respiratory route. These observations were of sufficient importance for official action to be taken by Sir John Ledingham and, as a result, Henderson was seconded for special duties to the Ministry of Supply and found himself, until the end of the summer of 1940, working either at the Chemical Defence Experimental Establishment, Porton, where he found considerable experience in handling toxic aerosols already existed, or at the Lister Institute at Elstree. Before he finally left Elstree he was awarded the D.Sc. degree of the University of London.

In October 1940, as a result of instructions from the War Council, a 'Biology Section' was founded at Porton with a mandate to assess the
feasibility of the use of biological agents against man and to devise protection against such attacks. Henderson joined this research group, extended his work on the toxicity of bacterial toxins and initiated work on the infections of experimental animals with aerosols of pathogenic organisms, including both *Bacillus anthracis* and *Pasteurella pestis*. The ‘Henderson’ apparatus, known familiarly as ‘the piccolo’, in which mice could safely be exposed to such aerosols was evolved in the course of this work. In 1942 the results of these laboratory investigations were confirmed in the open air, using *B. anthracis* dispensed from ‘impromptu’ weapons, against sheep on Gruinard Island. By the time these trials were completed, the United States had entered the war and was starting to evaluate the potential of biological agents. Henderson crossed the Atlantic in 1943 to assist the Americans with the culture of virulent organisms and their aerosol testing. Thereafter, till the end of the war, he shuttled across the Atlantic carrying out experiments and trials wherever the better facilities were to be found. In the course of his studies during 1939 and 1940, Henderson (with P. A. Gorer) had refined and improved the quantitative evaluation of the results of experimental infection to yield more accurate estimates of infective dosages. These concepts he introduced to his fellow workers in the U.S.A. Apart from short-term visits by experts, Henderson carried the main burden of the British end of this liaison himself, becoming a valuable and fruitful collaborator with a number of American microbiologists and making friendships there which survived to the end of his life. In 1946 Henderson was awarded the U.S. Medal of Freedom, Bronze Palm.

By the end of hostilities, both the American and British teams were convinced that attack on man by biological agents was possible, and that provision of protection against it was at that time rudimentary. Henderson considered that the magnitude of the threat was unestablished and that *ad hoc* experiments such as had been done during a war for survival, though justified at that time, were not likely to give a realistic assessment. A long-term programme was required to identify the physical, chemical and biological factors which determined the survival of micro-organisms in aerosols. The influence of the physiological conditions of culture and the genetic factors which determined their virulence and pathogenicity needed to be established. But during late 1945 the war-time scientific staff drifted back to civilian employment until only Henderson with the late G. M. Hills and the late J. F. S. Stone (a pre-war member of the Chemical Defence Experimental Establishment) remained. Fortunately a number of excellent, well-trained and indoctrinated technicians also decided to see if the Unit had any future. Henderson was determined to participate only on his own terms of a long-term basic study in microbiology broadly based on the programme sketched above, coupled with the provision of new custom-designed laboratories and with the highest priority to recruit the requisite staff to man the new establishment.

After a good deal of discussion, ultimately at Chief of Staff and Cabinet level, the Minister of Supply was instructed to implement a programme
much on the lines that Henderson had recommended, with the priority necessary to get the project moving. In January 1946, Henderson was offered the post of 'Chief Superintendent of the Biological Research Establishment' (a title rather grudgingly conceded) and, characteristically, accepted as 'Director, Microbiological Research Department'. A powerful advisory board was enlisted under the chairmanship of Lord Hankey, Minister without Portfolio in the War Cabinet, and thus Henderson's course was set for nearly 20 years. On several occasions the Advisory Board helped him to bring his many and frequently strong views on matters of policy to a succession of superiors, who operated at Ministerial level.

The new Department continued to occupy part of the animal house of the Physiology Section of the Chemical Defence Experimental Establishment which had been supplemented by prefabricated huddled accommodation built during the war. Additional laboratories of standardized unit construction were added to house the staff that Henderson was attempting to recruit. This was not easy, partly owing to a reaction against all activities associated with war and the opprobrium associated with biological work in this field, with an active but often ill-informed lobby against it, and partly to Henderson's belief that continuing top-quality research work could arise only from dedication, so that his standards of acceptance were very high. In consequence, he tended to recruit individuals rather than to man a formal programme, and to rely on his infectious enthusiasm and his powers of persuasion to weld the sometimes ill-matched group of individuals into co-operative effort.

Meanwhile, plans for the new laboratories went ahead, the design being based on the new laboratory for the National Institute for Medical Research at Mill Hill, the construction of which had been interrupted by the War. He wished to cover the spread of scientific disciplines from the physical sciences to the biological sciences and to make special provision for the growth and handling of micro-organisms, including pathogens, on a considerable scale and for their study as infectious agents rather than for their specific medical interest. Though he left detailed planning to his staff and to the professional architects and engineers of the Ministry of Works, Henderson often set them specifications so stringent as to be unrealistic. These he would only relax when convinced that they were unattainable and would then thrash out some compromise which got as near to the ideal as possible; and thereafter, he would not 'cry for the moon' that he had had to abandon. Building started in June 1948 and Henderson drove it forward every inch of the way using every weapon that he could muster to maintain the pace. In consequence, and despite a long electricians' strike early in 1951, the building was completed just 3 years after initiation against an estimate of 2 years 9 months to which Henderson had forced a sceptical Ministry of Works. He entered into possession of a laboratory, unique of its kind in the United Kingdom, which served for many years as a model for microbiological planning in many parts of the world.
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This activity and the effort to staff the laboratory, combined with the task of directing the growing group of research workers, left Henderson little time for personal research. The succession of papers, one or two a year in the ’30s, had been interrupted by the War and was scarcely restarted until 1952 when ‘the piccolo’ was described in full detail for the first time. Simultaneously, stimulated by his imagination and enthusiasm, the work of other groups within the establishment began to reach the reporting stage and the research effort started to generate its own momentum. By 1955 he had sufficient confidence in his programme and his staff to take a ‘Sabbatical year’. But no other laboratory could offer better facilities for studies of experimental infection than his own, so he spent the period at Porton. Any consultation on the affairs of the Establishment had to be accommodated in a couple of hours on Friday afternoon. For the rest, he spent his time filling in the experimental lacunae in previous work to make it suitable for publication and to extending the work started with the late Dr J. M. Ross on the pathogenesis of respiratory anthrax to other pathogens. In 1954 a ‘Virology Section’ had been formed under Dr (now Professor) J. C. N. Westwood, and, as a result of viral material and assay techniques made available to him, Henderson was able to evaluate the effect of a bacterial infection on an established viral infection and vice versa. Whether the effects were antagonistic or synergistic depended on the modes of action of the two agents.

In 1957 came Defence cuts, involving both finance and staff, but fortunately the Establishment was able to avoid their full force, largely as a result of a sustained offensive by Henderson, backed by members of his Advisory Board; losses in a staff which was still below its original planned strength were small. It was in this year that public recognition of Henderson’s contribution to the defence effort was signalled by the award of Companion of the most Honourable Order of the Bath. After a short while, however, recruiting was resumed and the output of research from the laboratory continued to grow, so that by 1959 the Establishment had acquired a national reputation and, in some specializations, an international one. These included microbial infections by the respiratory route, biological and chemical factors involved in virulence and the continuous culture of micro-organisms. It was a particularly proud moment for him when in 1955 he gave, at the invitation of the Council of the Royal Society, a lecture describing the development and research activities of the Microbiological Research Department. Henderson’s own scientific contributions to microbiology were acknowledged by his election to the Fellowship of the Royal Society in 1959.

The accumulating weight of experimental evidence convinced Henderson that an accurate estimate of the threat from biological agents was beginning to emerge, that it was substantial and that the United Kingdom was particularly vulnerable to such an attack. Despite this, when the dissolution of the Ministry of Supply was announced (October 1959) Henderson, with
substantial support from the Advisory Board, fought to have the Establishment transferred to civilian control, but in vain—it passed to the War Office. The increasing complexities of administration, the proliferation of returns and the multiplication of ‘authorities’ depressed him; the need to justify changes in programme and emphasis often to non-scientists frustrated him, but he continued to foster active research throughout the Establishment. The strain, however, was beginning to tell. Hypertension, established in the early 1950s, was becoming troublesome and Henderson, who had always been a heavy smoker, was increasingly subject to attacks of respiratory infection. By the time he reached the age of 60 these were beginning to make the winters miserable for him unless he could escape into sunshine for several weeks after Christmas. Within a year he who had ‘never been able to understand why people retire early’ was seeking hard for a successor. No one was more pleased than he when Dr C. E. G. Smith was appointed to the Directorship in August 1964. By the end of the year he had completed the hand-over and scrupulously avoiding any involvement in ‘management’ he ‘retired to his laboratory’.

Here, Henderson attempted to apply to viral aerosols the methods he had used 15 years earlier for the quantitation of infective doses of bacteria. He became increasingly interested in the pathological sequelae and showed the astonishing rapidity with which a respiratory infection with Semliki Forest virus in the hamster reached the brain. He was happy to be back once again at the bench, but several minor cerebral thrombotic events, from which he slowly and partially recovered, left him with an impaired capacity to walk. Another seizure in July 1967 brought his active work to an end. He was in and out of hospital several times during the following year but his condition slowly deteriorated and after a long and trying illness he died quietly in his sleep on 16 August 1968.

Henderson's research output was not large, but through the work of the Establishment his influence on contemporary microbiology was considerable. He maintained vigorously that the mandate of the Establishment forced him and his colleagues to view the process of infection from an angle somewhat different from the traditional—to understand enough about the infection process to be able to thwart the pathological sequel, emphasis on prevention and prophylaxis rather than on therapy and treatment.

He hated publicity and took little part in public life. Nevertheless he served in 1963 and 1964, his term as President of the Society of General Microbiology, of which he was a founder-member, and reviewed his work on mixed infections at the 14th Symposium of the Society. At the personal level few could remain indifferent to him. He was always forthright, sometimes rude, occasionally downright offensive and often a thorn in the flesh of his superiors, but his technical opinions were well considered in 'high places'. He suffered fools, particularly senior ones, with the illest grace but he had much personal charm. One suspected that his broad Glasgow accent which got more pronounced if he became excited, was sometimes 'turned up' to enhance the
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effect! He evoked friendship, admiration, in some cases almost devotion, from his staff and he fought valiantly for them ‘across the board’. Only rarely did his partisanship outrun his discretion. Until well into his fifties he worked long hours both in the laboratory and at home, and several research workers, now with international reputations, have good cause to thank him for the hours he spent in clarifying their papers for publication. As the reputation of the Establishment as a ‘centre of excellence’ grew, a number of overseas visitors asked for the use of its specialized facilities, and Henderson would go to much trouble to ensure not only that the attachment was agreed but that everything was prepared for the visitor to start work immediately he arrived. Dr Sanford S. Elberg, Dean of the Graduate School at Berkeley, U.S.A., in a letter to the London Times mentions what he regards as the outstanding features of the Microbiological Establishment: ‘... the novel design of the laboratories, their extreme flexibility and the remarkable degree of voluntary team work among the scientific staff.’ He goes on to record his own verdict: ‘... In many respects the laboratories of Porton are the models after which scientists all over the world would pattern their own personal arrangements. The Porton establishment is a great credit to the United Kingdom’s medical and biological research community for which Henderson spent himself with the greatest distinction on behalf of his scientists and those who were privileged to spend time there as overseas visitors for varying periods of very productive work.’

His first wife died in 1952 and in 1953 he married Emily Helen, daughter of the late D. Theodore Kelly of New York, who was also trained as a bacteriologist and who had worked as his assistant in the U.S.A. during the War. They made their home in Great Durnford on the banks of the Avon between Amesbury and Salisbury. Here they entertained both their local friends and the stream of scientists from all over the world who visited the Laboratories. Sometimes this hospitality took the form of a small dinner party, at others, when there might be quite a number of visitors from N. America, a large cocktail party might be arranged. Their fifteenth-century cottage with its large garden formed a perfect setting for both. From a small group of friends of long standing Henderson would usually invite to his home one or two elderly colleagues to spend what might otherwise well have been for them a lonely Christmas. Henderson was very proud of his garden in which he expended much time and labour. And on the rare occasions when he had leisure and the weather was right, he would fish in the small stream which separated his property from the main course of the Avon. His second wife survives him and now lives in the United States. There were no children by either marriage.

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