Samuel Phillips Bedson, 1886-1969

A. W. Downie


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SAMUEL PHILLIPS BEDSON

1886-1969

Elected F.R.S. 1935

SAMUEL PHILLIPS Bedson was born on 1 December 1886 in Newcastle upon Tyne. His father, Peter Phillips Bedson, was born in Manchester, educated at Manchester Grammar School and studied chemistry under Sir Henry Roscoe at Owens College, later Manchester University. After a period of postgraduate study at the University of Bonn, Peter Bedson returned to this country and was appointed to the Chair of Chemistry in the University of Durham (Durham College of Science, Newcastle upon Tyne). He held this Chair for 37 years until his retirement in 1921. His wife was the daughter of Samuel Hodgkinson, cotton spinner (Hollins Mill Co.) of Marple, Cheshire.

There were three children of this marriage, Sam being the second. Along with his elder brother and four other boys he was educated privately until the age of ten. Then after one year at Newcastle Preparatory School he went to Abbotsholme School in Derbyshire where he spent the next six years. This school had been founded by Cecil Reddie as an experiment in secondary education because of his dissatisfaction with the narrowness of the curriculum in most Public Schools. Reddie planned 'a programme of general education catering for physical and manual skills, for artistic and imaginative development, for literary and intellectual growth and for moral and religious training'. English, not classics, was to be the foundation of the curriculum and French or German was to be first foreign language. In addition he was most anxious to prepare the boys for their place in society and arranged numerous expeditions and excursions to familiarize pupils with their own neighbourhood. Reddie was a man of great personality and a most stimulating teacher. His experiment found favour on the continent, several schools being started in Germany on similar lines. These were closed by Hitler. Abbotsholme still flourishes. Sam Bedson always felt that he owed much to the stimulating influence of Reddie and the six years he spent at Abbotsholme.

He had by this time decided on medicine as a career, but his father insisted that he take a degree in science first. Consequently in 1904 he entered Armstrong College (now part of King’s College), Newcastle upon Tyne. Three years later he graduated B.Sc. (with distinction), his chief subject being zoology with botany and chemistry as subsidiaries. From 1907 to 1912 he studied medicine at Durham University College of Medicine,
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Newcastle upon Tyne, and graduated M.B., B.S. with Honours, in March 1912. One of the most stimulating teachers at the medical college was H. J. Hutchens, Professor of Bacteriology. It was largely his professor’s influence and his own previous laboratory experience in zoology which determined Bedson’s specialization in this branch of pathology. To further his aim, Bedson went to Paris to attend the course in microbiology given annually at the Institut Pasteur. Among the lecturers were a number of distinguished French microbiologists, including Mechnikoff, Roux, Borrel, Laveran, Besredka and Mesnil. During this year, however, Bedson also worked in Weinberg’s laboratory investigating the effect on animals of toxic substances obtained from parasitic worms (Ascaris and Taenia). This work, published in the Annales de l’Institut Pasteur (1) was presented for the degrees of M.Sc. and M.D.(Dunelm). The thesis for the latter degree was awarded a gold medal. This valuable period of postgraduate training was an experience made more interesting for Bedson by the personalities and rivalries which existed among the heads of certain departments in the Institut Pasteur at that period. In 1913 Bedson started work, as British Medical Scholar, in the Lister Institute in London in the Bacteriology Department then under the direction of John Ledingham. This was another valuable formative period in his research training. After a short period of study of the effect of nucleic acid on antibody (2) he joined Ledingham in the work he was doing on antisera to blood platelets—‘indeed a happy and stimulating experience’. This work was interrupted by the outbreak of war in 1914. Bedson applied for a commission in the R.A.M.C. but was told that there were no vacancies for doctors trained in research. Consequently he joined the Northumberland Fusiliers as a combatant officer and went with the 8th Battalion to Gallipoli in 1915. His men were said to be devoted to him. He suffered a severe chest wound in August and was evacuated to England. He was gazetted Captain in that year and while in France in 1916, he was transferred to the R.A.M.C., largely through the influence of Lord Dawson, then a colonel in the Medical Corps. From then until his demobilization in June 1919 he served as pathologist in various laboratories in France and became Adviser in Pathology to the 5th Army (France).

After demobilization he returned to the Durham University College of Medicine, Newcastle upon Tyne, as lecturer in comparative pathology under his old teacher, Professor Hutchens. Dr S. C. Dyke, a junior colleague at this time, remembers particularly the beautiful calligraphy in which he wrote out all his own slides. As Bedson rightly maintained, a slide with material written by hand in this way could never be overcrowded and when projected would be easily legible to those at the back of the lecture room.

In 1921 he was appointed assistant in the Department of Bacteriology of the Lister Institute and returned to his work on blood platelets and their role

* The numbers in parentheses refer to the numbered items in the Bibliography at the end of this Memoir.
in the production of purpura and other haemorrhagic states. In this he was supported by the interest and guidance of the Director of the Institute, Sir Charles Martin, for whom he had the greatest admiration (67). 'I had returned to the Lister Institute in 1921 as a junior member of staff and, living nearby and being unmarried then, I often returned to work in my laboratory after the evening meal. And often Martin would look in and take me off to his flat where, over cups of tea, which in the absence of Lady Martin, he invariably made Australian fashion in a billycan, we would discuss my research projects. These were indeed good days.'

In 1924 a research committee was formed by the Ministry of Agriculture and Fisheries to advise on research on foot and mouth disease which was becoming a serious economic threat to farm animals in this country. There were at that time no adequate facilities for conducting research on farm animals, although this difficulty was later met by the acquisition of the Cattle Testing Station at Pirbright, later to become the Ministry of Agriculture Foot and Mouth Disease Research Institute and still more recently the Animal Virus Research Institute. In 1924, however, research was confined to small laboratory animals and this was started at the Ministry of Agriculture Laboratory at Weybridge and at the Lister Institute. Bedson was seconded to the work at the Lister in August 1924 and was later joined by Mrs Burbury and H. B. Maitland. Arkwright who was on the committee and a senior member of the Lister Institute staff supervised the work. In this way, Bedson (and Maitland also) began his investigations into virus infections which were to remain his main scientific interest for the rest of his working life.

In January 1926 Bedson married Dorothea Annie Hoffert, the elder daughter of Henry Herman Hoffert and Annie Hoffert (née Ward). Henry Hoffert was a senior inspector of schools for the Board of Education. One son, Dorothea's twin, studied chemistry at Oxford and became chief chemist to National Benzole Ltd. Dorothea herself also specialized in chemistry at Cambridge and at the time of her marriage to Bedson was research assistant to Dr Smedly MacLean at the Lister Institute. Bedson's marriage was a happy one and visits to their charming home with its beautifully kept garden were memorable occasions. The eldest of their three boys, Peter George, took a B.Sc. with first-class honours in engineering at London University; the second, Henry Samuel, studied medicine at the London Hospital Medical College and is now Reader in Virology in the Medical School, Birmingham University, and the third, Ivan Francis, obtained his degree in veterinary medicine at London University and is now in practice in Devonshire. Bedson derived great pleasure from the company and accomplishments of his three sons. He took pains to teach them batsmanship and instructed them in the art of fly fishing, in which he was expert. Later on, when one or all the boys accompanied him on fishing holidays, his skill on North Country streams evoked their envy and admiration. He took especial pleasure in the knowledge that Henry had developed a keen interest in viruses and the infections caused by them, as this field of study had provided him
with satisfying and often exciting occupation during his professional life. 

In 1926 Bedson left the Lister Institute on appointment to a Freedom Research Fellowship at the London Hospital. Philip Panton was at that time Director of the Clinical Laboratory and in relation to the Freedom Fellowships Bedson has written (59): ‘Realizing that the work of the laboratory was constantly throwing up research problems which he (Panton) and his staff had not time to investigate, he sought the means to establish full-time research posts in his department. In this he was successful, thanks to the generosity of his friend the Rev. M. S. Courtauld who provided a capital sum, some of the interest from which sufficed to establish in 1926 two Freedom Research Fellowships and a Freedom Research Studentship in the clinical laboratory. Sir Howard Florey and I were the first two Fellows appointed.’ Elsewhere he records: ‘Complete freedom was allowed us as to the choice of subject for research: we had no administrative, routine or teaching duties and the eight years during which I held a Freedom Fellowship were quite the most productive, satisfying and happy of my scientific career. I feel that I owe a great debt to Sir Philip Panton for this, since it was his vision which made possible these research posts in his department, and it was his qualities as a chief which made those eight years such a delightful episode in my life. Working in this hospital in close association with my clinical colleagues I enjoyed opportunities for medical research which could hardly have been better, and although I have enjoyed some of my duties as Professor of Bacteriology—the teaching of undergraduates, for instance—I cannot help regretting the increasing divorce from active participation in research which the occupancy of a chair has entailed.’ How often has one heard this last sentiment expressed in recent years when ever-increasing committee work has added to the administrative load of departmental heads!

While Freedom Research Fellow, Bedson continued with his work on platelets; he also, with the cooperation of junior colleagues J. O. W. Bland and R. T. Brain, continued the study of viruses and the nature of immunity in virus infections. These studies were made on the viruses of herpes simplex, vaccinia and varicella. Then, in 1929, there occurred in Europe and America outbreaks of psittacosis due to the widespread importation of infected parrots and parrakeets from South America and Australia. A few of the patients suffering from this primarily avian disease were admitted to the London Hospital and it was the investigation of these persons that started Bedson’s studies on psittacosis which were to remain his main scientific preoccupation for the rest of his working life and which assured his reputation in the field of microbiology throughout the world. As happened in most laboratories where work on psittacosis was being done, infection, either clinical or subclinical, was contracted by members of the laboratory staff. Bedson himself did not escape and suffered a severe attack which lasted for two weeks. Antibiotics which have since been shown to be effective in treatment were not then available and Bedson’s life was considered in danger.
Dr H. B. May recounts that while he was ill several physicians from the London Hospital were called in by Bedson’s family doctor. After the routine examinations the doctors retired to the drawing room to confer. On their return the Senior Consultant said: ‘Bedson, we have decided that you are not going to die.’ To this the patient replied: ‘If that’s all you can tell me after drinking all my sherry I have had poor value—I never thought I was going to die.’

In 1934 William Bulloch retired from the Goldsmiths Company’s Chair of Bacteriology at the London Hospital Medical College and Sam Bedson was chosen to succeed him. Whereas the Department of Bacteriology had until then occupied the top floor of the College building, Bedson and Panton decided that Bedson should remain in the hospital laboratories and that these should be expanded to house the whole department. It was not until 1947, however, when two wards next to his own room were evacuated so that a classroom and laboratories became available in the Hospital that these plans were completed. In the meantime classes were held in the top floor of the College and laboratories there occupied by research fellows. Bedson enjoyed teaching medical students and particularly the informal revision classes which he held every week. His knowledge of the students in the Medical School was unique and he had a remarkable memory for their names. His students responded to his personal concern for their welfare with affection and respect. Professor Clifford Wilson writes: ‘He was responsible for organizing the course in Pathology which embraced all departments, and I think this was one of the most successful courses of instruction which we have ever had at the London. I rank him with Turnbull as one of the two most important influences in laying a sound foundation in Pathology for the worldwide reputation in Medicine which the London Hospital has had over the last few decades.’

I had gone to the London as Freedom Fellow when Bedson was appointed to the Chair. In my first two years I worked in the College where Bedson visited regularly to discuss work with the Research Fellows. I was happy and gratified, however, when he suggested in 1937 that I should move over to the hospital to share his laboratory and return to virus research. For the next two years I greatly enjoyed our daily association. He was a tidy worker and I had perforce to mend my habits and keep my bench in reasonable order. I learned much from his exact serological techniques and the artistry he displayed in the beautiful staining methods he had developed. When he isolated, by pad inoculation of a guinea-pig, a virus from vesicles on the fingers of cowmen from a farm near Brighton, with typical generosity he passed the virus (cowpox) over to me for further investigation; for studies on the antigenic structure of psittacosis virus were then occupying most of the time he could devote to bench work. In his lectures to students, as in his writing, his style was clear and lucid. On one occasion he handed me the first draft of a paper written in his neat hand and asked for comment. I read it through carefully and could find nothing that I wished to alter as the
material was so clearly and precisely set out. When I asked him when he had written the script, he remarked that he had taken home his lab. book the day before and had written the paper in the evening. In those years we regularly attended meetings of the sections of Pathology and Comparative Medicine of the Royal Society of Medicine and of the Medical Research Club. He enjoyed the free discussions which followed the papers and readily contributed when the subject touched his own field of interests. His opinions of current research and research workers were often strongly held and his comments were always shrewd and frequently entertaining. Dr Myer Salaman, another colleague who worked in the department in the pre-war years, wrote in appreciation of him: ‘I have some vivid memories—his criticism of my first paper, which helped to form the pattern of everything I have written, or helped anyone else to write since; the simplicity and complete adequacy of his techniques; his notekeeping (largely tabular) which I have never managed to live up to; the times when he showed his constant sense of responsibility for his pupils. What one gets from a good teacher and friend is difficult to analyse and impossible to pin down. There are the obvious things—wise advice, faithful and unfailing support. But there are also many intangible ways in which a man of his quality can influence the work and outlook of his pupils.’ Dr H. B. May, also on the staff at this time, comments: ‘Meticulous accuracy of observation characterized all his bench work. His experiments were simple but beautifully designed to clear up a particular facet of a problem. He insisted on the same high standard in the work of all who studied under him. On one occasion he was examining a series of serological tests set up by an Australian postgraduate student who was learning his techniques. Bedson carefully measured the total volume of fluid in each tube and wrote down the quantities in tabular form. The results of the tests were clear cut but the volumes of fluid in the tubes somewhat variable. After a pause he remarked: “It isn’t enough to get the right answer; if your technique is slovenly you will miss the unexpected anomaly”.’

On the outbreak of war in 1939 Bedson was seconded to the Emergency Medical Service and was Pathologist to sectors I and II of region V. His sector laboratory was in a hastily erected hut in the grounds of the emergency hospital in Billericay in Essex. He visited most of his outlying laboratories in North Essex on his bicycle, for he enjoyed cycling and came to know most of the byways and country roads in the county. He returned to the London Hospital in 1944 and in 1946 succeeded Panton as Director of the Division of Pathology, thus adding to his responsibilities in the medical college. In 1949 he again followed Panton as Consultant Adviser in Pathology to the Ministry of Health and held this office until 1962. But the arduous task of building up the hospital pathological services for the country had been done by Panton during and immediately after the war so that visits to hospitals in various parts of England were no longer necessary. Moreover, he found the slightly rigid thinking of civil servants somewhat irritating—as when
regulations were made about the importation of parrots, without consulting
him. His minute on this indicated his irritation only too clearly.

When he retired from the chair at the London Hospital in 1952 Bedson
was invited to take charge of the British Empire Cancer Campaign Virus
Unit at the Bland Sutton Institute of Pathology in the Middlesex Hospital.
He continued research work on viruses until 1962 when he gave up this post
and the work for the Ministry. Dr J. V. T. Gostling, who assisted him during
most of his period at the Middlesex, has written of him:

‘My most lasting impression of him was his orderliness. This quality was
apparent in his work, his room and his person. His experiments were planned
to define the effect of one variable, with all others controlled, by the
simplest available method. His technician would bring him what he needed
and he would then do (‘carrying out’ and ‘undertaking’ were expressions
which led him to ask if one had used a stretcher or a hearse) the bench work
himself, whether it was just a passage, a series of titrations or the collection
of samples during a ‘growth-curve’ experiment. His bench and desk were
tidy. The results published by other workers were abstracted in his neat hand
in a small notebook where they were readily available for use in discussion.
When not at the bench he would be writing his lectures and reports or
annotating the drafts of the many papers which others submitted to him for
his opinion.

‘For most of his years at the Bland Sutton he had much to do outside the
Institute, being Adviser in Pathology to the Ministry of Health, serving on
various outside committees and being much in demand as a lecturer. But he
would be in the laboratory almost every day arriving and leaving always at
the same predictable times.

‘His biological opinions were tenaciously held and those who differed
would be questioned very searchingly upon the evidence for their beliefs.
The flaws in any published work and the deductions from it were always
sought and often found. But he would abandon, although very sadly, most
cherished beliefs when new evidence made their truth less probable. Apart
from his work he was very entertaining company, with a fund of anecdotes
gathered in the course of his busy days in committee rooms at the Ministry
and elsewhere. His social opinions were far from liberal; he regarded his
prejudices as something to be deplored but as not alterable. He was a
powerful friend, untiring and effective in promoting the interests of his
juniors; and his industrious example and the certainty that he would notice
each achievement and each omission extracted the best from them in return.’

Dr H. B. May, who had been a junior colleague at the London Hospital,
was later Dean of the Medical School and has this to say of their contacts at
that time: ‘I never had any hesitation about consulting him on any problem.
He always listened very carefully and then gave a wise opinion. I used to go
to the Middlesex when he was there and ask him about difficulties which
inevitably arose when I was Dean. His advice was always balanced,
meticulous in its detail and completely sound. I valued it enormously.’
In addition to his duties at the London and Middlesex Hospital Medical Schools, Bedson undertook a good deal of outside work. He was President of the Section of Comparative Medicine of the Royal Society of Medicine in 1937, a member of the 3rd Foot and Mouth Research Committee of the Ministry of Agriculture from 1938 to 1946, a member of the 4th Committee from 1947 to 1950 and was appointed by the Minister of Agriculture as a member of the first Governing Body of the Foot and Mouth Disease Research Institute at Pirbright in 1950; from this he retired in 1955. He was a member of the Army Pathology Advisory Committee from 1937 to 1962, a member of Council of the Imperial Cancer Research Fund from 1942 to 1955 and was made a Life Governor in 1955. He served on the Governing Body of the Lister Institute from 1944 to 1954, and on the Public Health Laboratory Service Board from 1950 to 1957. He was a member of the Medical Research Council from 1941 to 1945, served on various committees and was Chairman of the Whooping Cough Immunization Committee, of the Advisory Committee on Safety Tests for Poliomyelitis Vaccine and of the U.K. National Committee of the British Commonwealth Collection of Micro-organisms (1948 to 1962). He was an excellent Chairman whose summaries of discussion in Committee usually gave a clear indication of policy to be pursued or recommendations to be made. He was a member of Council of the Royal Society in 1937 to 1938 and again in 1941 to 1942. He served also on the committee of the Pathological Society of Gt Britain and Ireland 1946 to 1949 and on the Council of the Association of Clinical Pathologists 1948 to 1950. Among his published papers are several lectures he was invited to give by Societies and Colleges (39, 40, 49, 57, 60, 63, 66 and 71).

As in his work, Bedson was physically neat and tidy. He was under average height, slim and almost invariably wore a bow tie. He was a person of strong loyalties particularly to his departmental colleagues both senior and junior. The obituary articles he wrote of his older friends bear eloquent testimony to this (52, 53, 59, 67 and 69). He was keen on ball games; he had been a good cricketer at school and played scrum half for his college when at the University. When he worked at the Lister Institute and lived in Sanderstead he became a proficient golfer, although in his years at the London his golf was restricted to the annual staff match in which for some years he partnered the late Dr George Riddoch. Latterly he was an enthusiastic supporter of Sussex on the cricket field and a keen follower of Rugby football. On occasions I enjoyed his informed and uninhibited comments on international matches at Twickenham where he was strongly partisan in his support of the home team. His comments sometimes led to spirited arguments with opposition supporters in his immediate neighbourhood; at Calcutta Cup matches we contrived to occupy seats which were not in close proximity. On a personal note his junior colleague and successor to the chair at the London Hospital, C. F. Barwell, has written: 'I enjoyed many visits to his home where he was an excellent host, ready to share his various interests in gardening, sketching, cricket, bird life, fishing and good wine. His strong personality...
Samuel Phillips Bedson had an element of austerity but this was never evident then. Every year for sixteen years Sam and I went trout fishing together usually with one or more of his three boys. Almost all of these holidays were on the river Eden in Westmorland. His companionship, good humour and obvious enjoyment of the countryside and the fascination of fly fishing make these the happiest of all my memories of him.

Bedson was forced to give up work in 1962 because of failing memory and ‘blackouts’. Increasing cerebral vascular insufficiency prevented any real active enjoyment of his retirement. In the last year or two he became largely bedridden and he died quietly on 11 May 1969.

Honours

The Honorary degree of Doctor of Science was conferred upon him by Queen’s University, Belfast, in 1937, and by the University of Durham in 1946. He was elected a Fellow of the Royal College of Physicians (under Bye-Law xxxixb) in 1945 and was created a Knight in 1956. He was awarded the Conway Evans prize of the Royal Society and the Royal College of Physicians ‘given only for a valuable addition or contribution to Science’ in 1952 and was elected an Honorary Member of the Society for General Microbiology in 1963.

Scientific work

Although there was some overlapping in time in relation to his different fields of work, this can be most conveniently discussed under four headings: (1) the work on blood platelets done at the Lister Institute, (2) studies on foot and mouth disease again at the Lister—his introduction to the virus field, (3) the work on the characteristics of viruses and immunity to them done at the London Hospital, (4) the work on psittacosis done at the London and continued at the Middlesex Hospital.

Platelets and purpura

Prior to 1913 little was known about blood platelets, many observers believing that they had no existence in circulating blood and were formed only when blood was shed and coagulation began. Work by Le Sourd and Pagnier in 1906 had suggested, however, that this view was incorrect. They had devised a method of obtaining platelets in a state of relative purity and with them had prepared an antiserum which lysed platelets in vitro and caused their disappearance in vivo without appreciably affecting other formed elements of the blood. This work passed almost unnoticed until six years later when it was confirmed by Aynaud, and Duke published his clinical observations suggesting the importance of blood platelets in haemorrhagic diatheses. The French workers, on testing the effects of their antiplatelet sera in vivo, had not observed that a haemorrhagic state accompanied the thrombopenia produced. Ledingham considered that proof of Duke’s
hypothesis might be obtained by experiments similar to those of the French workers and that they had failed to produce purpura in their animals because their sera were not of sufficient potency. Ledingham in 1914 succeeded in producing experimental purpura in animals with injections of antisera to the platelets of guinea-pigs and rabbits, and invited Bedson to collaborate in the work. Bedson later continued the analysis of the mechanism of the experimental production of purpura, and extended the investigation to the genesis of platelets.

Sera were prepared in rabbits against guinea-pig whole blood, against blood platelets, red blood cells and white blood cells. The various antisera thus prepared would produce death in guinea-pigs several days to several weeks after subcutaneous injection, but only the antisera against platelets and whole blood would produce typical purpuric haemorrhages in the skin and internal organs (3). In the purpuric guinea-pigs there was great diminution in circulating platelets and marked changes in the peripheral red blood cells.

The effect of anti-platelet serum in the production of purpura was host specific in that antiserum to rabbit platelets prepared in the goat and antiserum to rat platelets prepared in rabbits would produce purpura only in rabbits and rats respectively but not in guinea-pigs. The antiserum to guinea-pig platelets had agglutinins to guinea-pig red cells but no antibodies to guinea-pig leucocytes or to guinea-pig serum. The agglutinins for red blood cells could be removed by absorption of the serum with red blood cells without affecting the titre of the serum for platelets (6). Such absorbed serum still produced fatal purpura in guinea-pigs (7). On the other hand guinea-pigs could be protected against the fatal effects of anti-platelet serum by injecting them with normal rabbit serum two weeks before. Such protection could not be achieved by previous injection of normal rat or horse serum (10).

Antiserum against red blood cells was found to produce damage to capillary endothelium but in the dosage used failed to produce purpura. On the other hand it was known that serum treated in various ways on injection into animals would reduce the number of circulating platelets without producing purpura. In rabbits an injection of anti-red cell serum followed a few hours later by serum treated with agar would produce fatal purpura. Bedson came to the conclusion that two factors were necessary for the production of experimental purpura, one the factor that damaged vascular endothelium and the other which markedly reduced circulating blood platelets (7). It had been suggested that the tendency to haemorrhage in scurvy was associated with a marked diminution in the number of blood platelets. Bedson failed to confirm this in a study of one scorbutic child and of guinea-pigs and monkeys fed on a scorbutic diet (5); nor did he succeed in producing a significant thrombocytopenia in rats fed on a vitamin A deficient diet, as Kramer, Drew and Mottram claimed to have done (8, 11). In his experiments on the fate of platelets in the body Bedson found that
Splenectomy or blockade of the reticulo-endothelial (RE) system of guinea-pigs with Indian ink was followed by a rise in the count of circulating platelets indicating that platelets were normally destroyed in the spleen and RE system (13 and 16). Splenectomized guinea-pigs did not suffer from purpura on injection of anti-platelet serum because of the increase in platelet count which followed splenectomy. If, however, the injection of antiplatelet serum was delayed until the platelet count had fallen to normal in splenectomized animals then purpura resulted. In blockaded animals splenectomy caused no further rise in platelet count presumably because the blockade had already put RE cells of the spleen out of action. Bedson concluded from his studies that splenectomy cannot be relied on to give anything but temporary relief in the treatment of purpura haemorrhagica in man—a conclusion borne out by clinical experience.

In his observations on platelet genesis made in collaboration with Mary Johnston (14) Bedson prepared antisera in rabbits against guinea-pig lymph gland, reticulo-endothelial cells, bone marrow and spleen. These antisera were tested by injection into guinea-pigs to find out if they would produce a reduction in circulating platelets or purpura. Neither of the first two sera produced these effects. Anti-bone marrow serum caused a great reduction in platelets but no purpura while anti-spleen serum produced both reduction in platelets and purpura. The effect of the anti-spleen serum, which was still active after absorption with guinea-pig red cells, was judged to be due to the high content of platelets in the spleen where they are normally destroyed. The conclusion was reached that the bone marrow was the parent tissue in which platelets originated and that the megakaryocyte was the cell concerned; these greatly increased in number in bone marrow during the period of regeneration following depletion by anti-platelet serum.

This work on blood platelets has been dealt with at some length for Bedson’s scientific reputation has been built on his contributions to virology and the earlier studies on blood platelets rather overlooked. The work on platelets, done so many years ago, was confirmed some fifteen years later and its importance in relation to purpura has been recognized and is quoted in Wintrobe’s comprehensive textbook on Clinical haematology (5th edition, 1961, p. 840).

Foot and mouth disease

The work done at the Lister Institute from 1924-1926 by Bedson, Maitland and Burbury under the general supervision of Arkwright was the first attempt to proceed with an organized study of a virus infection in this country. The workers had no previous experience in virus research. Arkwright and Burbury had confirmed the observation of continental workers that the guinea-pig could be readily infected with foot and mouth virus and that intradermal inoculation of the hind pad was the most sensitive route of infection. Vesicles appeared at the site of inoculation within 24 hours,
generalized lesions appeared in the mouth and feet in 48 hours when virus was present in the blood. A small proportion of the animals died of generalized disease and those that recovered were refractory to further inoculation. Guinea-pig vesicle fluid was infective for normal guinea-pigs in dilutions up to 1 in a million. In their studies on the resistance of the virus to various agents, Bedson and Maitland (15) measured the amount of virus in their material by titration in the foot pads or shaved skin of guinea-pigs. The virus in diluted vesicle fluid was found to survive best at pH 7.6 in phosphate and in glycerine 50% in phosphate at pH 6.2. The virus was relatively resistant to 0.5% phenol, 60% alcohol and chloroform but was inactivated by 0.1% formalin in 48 hours at room temperature. The virus would pass Chamberland L2 and L3 filters and was not sedimented by centrifugation at 5500 rev/min. In discussion they suggest that the infective agent was a minute organized living thing. Attempts to cultivate the virus on serum agar and other more complicated mixtures of body fluids and bacteriological culture media failed. Bedson, Maitland and Burbury (17) also investigated the production of immunity by the virus. They found that animals could be rendered immune by injecting 500 to 5000 skin infecting doses of diluted vesicle fluid intramuscularly, although no generalized disease followed the intramuscular injection. Living virus mixed with immune serum could also immunize without producing manifest disease but heat inactivated virus failed to do so. On the other hand filtered vesicle fluid inactivated with 0.1% formalin for 44 hours at 26 °C was an effective vaccine, thus confirming the observations of Vallée, Carré and Rinjard. Treatment with formalin for 5 days at 37 °C destroyed the immunogenicity of the vaccine. Animals which had received one or two injections of formalized vaccine were immune to generalized disease when challenged by intradermal injection of virulent virus, although a local lesion appeared at the injection site. After six intramuscular injections of formalized vaccine the animals became completely immune to intradermal challenge unless the dose employed was very large.

Further attempts to cultivate the virus in a serum medium to which guinea-pig embryo tissue had been added failed, although the addition of the tissue prolonged survival time (18). In a series of active immunization experiments with three strains of virus of different origins it was found by Maitland, Burbury and Bedson (19) that there was some cross immunity between the first two but none between these two and the third. These results were supported by serum neutralization tests. Subsequent work has confirmed the immunological diversity among strains of foot and mouth disease virus.

Viruses and immunity to virus infections

The years between 1925 and 1935 marked the beginning of an era of intense virus research which continues up to the present time. New methods were introduced for the cultivation of viruses, for their purification and for the study of their physical and chemical properties. Between 1927 and 1931
Ledingham showed that relatively pure suspensions of vaccinia and fowlpox viruses could be prepared from experimentally infected animals by fractional centrifugation, a method which he had used earlier to prepare suspensions of the rickettsia of trench fever. He believed that the elementary bodies visible under the oil immersion lens in stained preparations of his suspensions were the virus, as they were shown to be agglutinable by immune sera and were related quantitatively to infectivity. This view was at first not generally accepted. Research work in the virus field was at this time confined to a few laboratories, but Bedson, because of his earlier researches on foot and mouth disease and his close association with Ledingham, was well equipped to participate in virus research and played a prominent part in this rapidly expanding field.

The new knowledge acquired during the first ten years of active work on virus infections was reviewed by Bedson in the George Halliburton Hume lectures (39 and 40) and virus immunity was the subject of his presidential address to the Section of Comparative Medicine of the Royal Society of Medicine (43). In 1927 Bedson’s experiments to determine the size of the virus particles of herpes simplex were made by filtration and centrifugation (21). Elford had not yet developed the method for preparing collodion filters of graded pore sizes and Bedson controlled the porosity of his collodion membranes by the passage of serum protein and a tiny bacterium.

From the results of his experiments with collodion filters, conventional Chamberland L3 candles and centrifugation he came to the conclusion that herpes simplex virus was considerably larger than the virus of foot and mouth disease and was nearly within the limits of microscopic visibility. With Bland he demonstrated by a simple filter-paper technique that the electric charge carried by the viruses of vaccinia and herpes simplex varied within a relatively narrow range of pH and that this knowledge was important in relation to filtration and concentration of these viruses (24). Gildermeister and Herzberg in Germany believed that they had demonstrated by active immunity and neutralization tests in animals that the viruses of herpes simplex and vaccinia were immunologically related. Bedson and Bland could find no such relationship, although they used highly potent antisera in their neutralization tests (22).

Up to 1929 no reliable in vitro test was available for detecting virus antibody in human or animal sera or for the demonstration of virus antigen. In 1925 Mervyn Gordon had used the complement fixation technique in his study of variola and vaccinia viruses, and a few years later Tulloch and Craigie used a tube precipitation technique to detect virus antigen in extracts of crusts from cases of alastrim; but in general the in vitro serological techniques used in bacteriology had given variable and uncertain results in the study of virus infection. Failure was probably caused in many instances by the lack of sufficiently potent antigens. Bedson and Bland using herpes and vaccinial antigens with the corresponding antisera prepared in animals, and zoster vesicle fluid as antigen with convalescent zoster sera, showed that
specific interaction of virus antigen and antibody could be demonstrated readily and quantitatively by the complement fixation technique (26). This technique has had wide application in the diagnosis of virus diseases in man and animals.

In these early days there was some dispute as to the mode of action of antiviral sera. It had been shown by Andrewes that tissues from an immune animal would support the multiplication of a virus to which the animal was immune but the presence of the animal’s serum would prevent virus growth in normal tissues. There was, however, some disagreement as to how the serum exerted such protection, i.e. whether it acted on the tissues or on the virus. Bedson showed with herpes virus and antiserum about the same time as Todd working with the virus of fowl plague and Andrewes working with vaccinia that the antibody combined with the virus particle but that time was required for the union to become firm. Active virus could be recovered from a neutral mixture of virus and serum by simple dilution, but the period for which this occurred varied with the nature and concentration of the virus and antiserum and the temperature at which the mixture was held (23 and 25). In this respect viruses combined with their specific antibody in the same way as other antigens such as diphtheria toxin or snake venom did with their antibodies. Bedson returned to the study of immunity induced by inactivated virus, a subject then still controversial (32). Herpes virus suspensions prepared from infected guinea-pig footpads were used and heat and 0.1 per cent formalin served for inactivation, as in the earlier work on foot and mouth disease. The absence of active virus was carefully checked by passage through guinea-pig pads. The results were quite clear cut. Formalin inactivated virus induced good immunity, while heat inactivated virus induced none. Several injections of the formalized virus were necessary to induce a degree of immunity comparable to that resulting from infection with live virus—a finding in keeping with recent experience in the prophylactic use of Salk vaccine for poliomyelitis.

Psittacosis

Until the pandemic occurrence of psittacosis in man in 1929-1930 the cause of this human infection contracted from parrots was believed to be a Salmonella. The observations made on human cases, and on sick parrots from which the human cases derived their infection, quickly established that bacteria were not the aetiological agents of the disease in man or bird. In four papers published in 1930 by Bedson and his colleagues (27, 28, 29 and 30) it was established that the causal agent was filterable. From the majority of more than twenty human cases (blood, sputum, pleural fluid or organs obtained post mortem) an agent was isolated by inoculation into budgerigars and passed in series in this host. Many of the specimens which proved infective were bacteriologically sterile and passage to fresh budgerigars and later to mice was effected by bacteria-free filtrates of organ suspensions. A similar agent was isolated from sick parrots associated with human cases.
Because of its filterability through Chamberland L1, L2 and Seitz EK filters and failure to grow on bacteriological culture media the infective agent was believed to be a virus. The virus was also isolated from a canary, a budgerigar and a Java sparrow from the same aviary from which two human cases had been derived (30). Experimentally infected mice and budgerigars which recovered acquired a certain degree of immunity. Guinea-pigs were susceptible to intradermal infection but less so than mice injected by the intraperitoneal route (29). Tests on a few human convalescent sera suggested that the complement fixation test using as antigen a virus suspension prepared from infected mouse spleen would be useful in the diagnosis of human cases. Some strains of virus increased in virulence on mouse passage, others tended to die out. The virus in mouse spleen, unlike many other viruses, was not well preserved in 50 per cent glycerol. The presence of minute ‘elementary’ bodies, which had been described in 1930 by three other workers, seemed to be correlated with virulence of materials examined. Virus from tissue suspensions could be concentrated 10 times by centrifugation at 5000 rev/min for 2 hours, and this, together with the filtration studies, also suggested that the virus was relatively large. In a subsequent paper (33) Bedson provided evidence that the elementary bodies which could be seen under the oil immersion lens after staining with Giemsa or Castenada’s rickettsial stain were in fact the infectious agent. These elementary bodies obtained from mouse spleen and repeatedly washed by centrifugation until little protein was left in the fluid were highly infective and infectivity was correlated with the number of particles present. Moreover, the serum of a guinea-pig which had been immunized with virus propagated in the guinea-pig would agglutinate a suspension of the elementary bodies and would fix complement with a suspension of virulent mouse spleen, or washed elementary body suspension but not with a suspension of normal mouse spleen.

Various observers had remarked on the variation in size of virus particles (0.2 to 1.0 μm) seen in stained smears from infected tissue. In an elegant series of experiments, Bedson and Bland (34 and 38) and Bedson (36) showed that the virus underwent a regular cycle of development as infection progressed. Studies were made in mice and guinea-pigs after intraperitoneal injection of large amounts of virus and also in tissue culture of mouse spleen and fragments of chick embryo. Mice were killed at intervals after injection. Stained smears from liver and spleen were examined microscopically and suspensions from these organs titrated for infectivity in mice. Up to ten hours after injection spleen suspensions were of low infectivity and very little virus could be seen in smears. Thereafter infectivity increased and virus was seen in spleen cells and in tissue culture as large forms (1.0 μm) which stained pale blue purple with Giemsa. At 24 hours small and intermediate forms began to appear, derived apparently from the large forms by binary fission. After 48 hours practically all the virus was in the form of small elementary bodies (0.2 μm) which stained dark purple with Giemsa. With the appearance and increase in number of small forms infectivity increased greatly. In
the very early stages of infection large pale staining plaques were seen in some cells and these were at first interpreted as a plasmodial structure which later subdivided to give rise to a morula (34). However, it was later shown by supravital staining with cresyl blue, by improved methods of decolorizing stained preparations and by dark ground illumination of infected tissue culture on coverslips that the 'plasmodia' were in fact composed of large forms obscured by inclusion material. In living tissue cultures on coverslips examined continuously by dark ground illumination the development of large forms in early intracellular colonies could be followed through to the small forms in the large virus colony present after 48 hours (38).

In the discussion to this last paper the statements are made 'Psittacosis is a micro-organism with bacterial affinities which is essentially an intracellular parasite and which in the early stages produces forms much larger than normal' and 'Even at the present time it would seem to us premature to classify psittacosis as a bacterium, although we think that that is its probable nature.' Subsequent research was to prove the validity of these views, although for some time Bedson, like many other workers, came to accept the agent as a virus (see later).

Experiments on the antigenic structure of the psittacosis agent were made using immune sera from guinea-pigs and suspensions of infected mouse spleen as a source of virus (42). It was found that heating the spleen suspension at 60 °C for 30 min rendered it non-infective and greatly lessened its ability to fix complement with immune serum. When the suspension was boiled for 3 min, however, the complement fixing activity was restored. With relatively pure virus suspensions the same results were obtained. It was thought that boiling removed some inhibitory substance in the preparation and unmasked a heat stable antigen. Tests with sera absorbed with heated and unheated suspensions showed that there was a heat labile as well as a heat stable virus antigen. There was also a heat stable antigen in virus-free filtrates of infected spleen suspensions which would induce marked skin reactions in psittacosis infected guinea-pigs but this antigen may have been the same as that present in heated elementary bodies. Because of its safety in handling and its potency as an antigen in complement fixation tests, Bedson substituted boiled virus suspensions in place of living virus preparations for routine use in diagnostic serological tests for psittacosis (41 and 44). Virus suspensions inactivated with formalin would give good immunity in mice if several injections of vaccine were given. In mice which survived the challenge with virulent virus, living virus could be found in the spleen up to seven months later (45). Thus recovery in the mouse as in parrots (29) may be associated with the carrier state. With H. B. May he found that penicillin in large doses protected mice against 100 lethal doses of virus but virus could be recovered from the spleen of these animals for weeks afterwards (51).

In their study on laboratory methods of diagnosis of lymphogranuloma venereum (L.G.V.), Bedson and his colleagues found that the complement fixation test was reliable (56). The L.G.V. antigen used was usually heated
and heated psittacosis antigen would serve equally well, thus showing that these two agents shared a common heat stable antigen. However, when human sera from cases of psittacosis and lymphogranuloma were absorbed with heated antigens it was possible to show in the complement fixation tests that each virus had a specific heat labile antigen not shared by the other. However, the use of heat labile antigen in routine complement fixation tests to differentiate psittacosis and lymphogranuloma infections was not a practical proposition. The Frei skin test gave results which agreed well with the results of complement fixation tests, the heat stable antigens of either virus being suitable to test patients suffering from lymphogranuloma venereum.

For some years during which the agent of psittacosis and its relatives were regarded as true viruses its mode of multiplication by binary fission was not universally accepted. Much of the work that Bedson did with Gostling at the Bland Sutton Institute was related to this controversy. By the middle 1950s most virologists had accepted the view that infective virus particles lost their identity soon after entry into susceptible cells and that virus particles which appeared many hours later were derived by assembly of separately synthesized nucleic acid and protein components. Bedson believed that this conception had been too readily taken over from work done with bacteriophage and that adequate evidence of its validity was lacking for many viruses. At this time he accepted the agent of psittacosis as a virus; as he was convinced that it multiplied by binary fission he sought evidence that other viruses might behave in the same way. However, the growth curve experiments which he and Gostling made on herpes simplex virus growing in chick embryo tissue cultures supported the occurrence of an early eclipse phase and intracellular synthesis of infective virus from virus constituents separately manufactured in the infected cells under the influence of the viral genome (68 and 70). In contrast the results obtained with psittacosis virus growing in the spleen of infected mice gave no support to the occurrence of an eclipse phase for this agent but confirmed previous observations on the occurrence of multiplication by binary fission (64).

Studies by other workers with the electron microscope of cells infected with agents of the psittacosis-lymphogranuloma group seemed to show incomplete virus particles reminiscent of incomplete forms seen in cells infected with other viruses and indeed even variation in size of the agent was doubted. The latter doubt was in some cases caused by the use of procedures which selected one or other form in the preparation of purified suspensions examined. Moreover, Armstrong and Read (Nature, Lond. 1964, 201, 371-373) showed that the incomplete virus forms seen in electron micrographs were due to improper methods used in the fixation of the preparations to be examined. With improved preparative procedures they demonstrated the variation in size of the virus particles and the occurrence of binary fission. Thus the electron microscope finally confirmed the conclusions that Bedson, using conventional microscopic techniques had reached many years earlier.
In the Harben lectures delivered in 1958 (71) he reviewed much of his earlier work, and on the developmental cycle of the psittacosis agent he wrote: 'The sequence of these changes occurred with such regularity as to convince us that this virus passed through a cycle of developmental forms while multiplying by binary fission' and characteristically adds: 'nothing has occurred in the intervening 25 years to make me abandon this concept'. The importance of Bedson's great contributions to our knowledge of psittacosis and related agents has been widely recognized. K. F. Meyer, the American authority on the psittacosis-lymphogranuloma group, when discussing their classification, has written: 'The investigator, Bedson, responsible for the elucidation of the morphologic, physiologic and immunologic properties of this group should be recognized.' And: 'It was Bedson who furnished the first adequate proof that the elementary bodies cause psittacosis. It would therefore seem appropriate that Professor S. P. Bedson's name be associated with this group. The name Bedsonia is here proposed as a generic title for all the agents now grouped under the name psittacosis virus of avian, human and mammalian origin' (Annals of N.Y. Acad. Sci. 1953, 56, 381-622). Professor Meyer has not altered his views on this subject (personal communication). Moulder in his Ciba lectures on The psittacosis group as bacteria (John Wiley & Sons, New York, 1964) writes: 'Whatever the nature of the taxon under which these organisms are ultimately gathered, I enthusiastically endorse Meyer's suggestion that the name of Sir Samuel Bedson be reflected in its terminology.'

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The photograph is by Elliott and Fry, Baker Street, London W.1.

A. W. DOWNIE
BIBLIOGRAPHY


(12) 1924. (With E. Knight.) An anaemia in hens associated with an increase in the yellow pigment normally present in certain tissues of these birds. *J. Path. & Bact.* 27, 239.


(15) 1925. (With H. B. Maitland.) Observations on foot and mouth disease. II. The attempted cultivation of the virus and its reaction to various agents, chemical and physical. *J. comp. Path. Ther.* 38, 238-255.


(39) 1935. Some recent work on filterable viruses and its import, both practical and academic. Part I. (George Haliburton Hume lectures.) Newcastle med. J. 15, 55-70.

(40) 1935. Some recent work on filterable viruses and its import, both practical and academic, Part II. (George Haliburton Hume lectures.) Newcastle med. J. 15, 105-123.


(48) 1940. Virus diseases acquired from animals. Lancet, 2, 577-579.

(49) 1943. Some recent virus work and its practical import. (1st George Frederick Still Memorial Lecture.) Arch. Dis. Child. 18, 113-123.


Samuel Phillips Bedson


(66) 1956. Mode of virus multiplication and susceptibility of these bodies to antibiotics. (Panton Memorial Lecture for 1955.) J. clin. Path. 9, 83-93.


Contributions to books

Chapters on Cytolysins (Vol. 6, 322-331), Herpes Zoster and Varicella (Vol. 7, 157-168) and Filtration (with J. McIntosh, vol. 9, 118-129). A system of bacteriology in relation to medicine, 1931, Medical Research Council, H.M. Stationery Office.

