No. 3, Volume 13 of the Journal of General Microbiology was issued on 12 December 1955

Obituary Notice (1956). *J. gen. Microbiol.* **14**, 1–13

Obituary Notice

SIR ALEXANDER FLEMING, 1881–1955

By the sudden death of Sir Alexander Fleming at his home in London, on 11 March 1955, the world has lost one of the most outstanding and best-known figures of the present century. It is given to few during their lifetime to have a world-wide reputation and to command universal respect and admiration, but it was undoubtedly given to Fleming for his discovery of penicillin. The honours and rewards that began to be showered on him from all over the world, more than sixteen years after his original discovery, he accepted with the innate quiet modesty that was typical of the man.

The youngest of the eight children of an Ayrshire farmer, Fleming was born at Lochfield Farm, near Darvel, on 6 August 1881. His father died when he was only 7 years of age. Fleming received his first schooling at Loudoun Moor School; at the age of 10 he went to the village school at Darvel, and two years later he continued his education at Kilmarnock Academy. When he was 14 he joined an elder brother in London where he continued his education for two years at the Polytechnic, Regent Street; then in 1897 he took a junior post in the offices of a shipping company in the City, where he worked for four years. In 1901 his share of a small legacy enabled him to reconsider his future, and with encouragement from his brother he returned to his studies, passed the London Matriculation and decided on a medical career. He chose to enter St Mary's Hospital Medical School, simply because he had played water-polo against St Mary's. He easily won the Senior Entrance Scholarship in Natural Science and entered St Mary's in 1902. During his undergraduate career he won almost all the scholarships and class prizes: he obtained his medical qualification under the Conjoint Board in 1906, and in 1908 he graduated M.B., London University, with honours in five subjects, and won a University Gold Medal. A year later he took the F.R.C.S. His memory was described by his contemporaries as phenomenal, and learning came easily to him. In 1900 he had joined the London Scottish Volunteers and represented the London Scottish Shooting Team when they won the *Daily Telegraph* Cup at Bisley in 1908, two days before his M.B. examination. As a student he was a regular member of the hospital shooting team, the water-polo team, and took part in amateur theatricals.

In 1902, Sir Almroth Wright had been appointed to the Chair of Pathology at St Mary's Hospital Medical School, and Fleming first came into contact with him in 1906 as pupil and assistant in the Inoculation Department. Immunology was at this time in the forefront in bacteriological laboratories, and the controversy between two opposing schools of thought—'the cellular theory' of immunity with Metchnikoff and his disciples as the main protagonists, and the 'humoral theory' represented by Koch, von Behring, Pfeiffer

and others—was at its height. Wright and Douglas had already published several papers on the phagocytic power and opsonic power of the blood in skin infections with staphylococci, and Fleming, influenced by Wright's personality, energy and fertility of ideas, and by the attraction of research work, entered Wright's laboratory immediately after he qualified in 1906. Here he worked in close association with Wright and his team of workers till the death of Wright in 1947, when Fleming succeeded him as Director of the Inoculation Department, which latterly became the Wright–Fleming Institute.

Wright and Douglas, ably assisted by other members of the team, including Colebrook and Parry Morgan, were developing new techniques for the measurement of the bactericidal power of the blood and of the number of viable organisms in cultures. In the development, elaboration and use of these new techniques, based on the microscope slide and Pasteur pipette, Fleming played a full part, and his invaluable help was recognized with the publication by Wright and Colebrook in 1912 of *The Technique of the Teat and Capillary Glass Tube.*

In April 1908, Fleming and another member of Wright's team, Dr Leonard Noon, published an article in the *Lancet* on 'The Accuracy of Opsonic Estimations', and the first paper under his name alone appeared in *The Practitioner* in May of the same year—this dealt with the accuracy of methods used for estimation of the opsonic index and sources of error to be avoided.

During the next few years Fleming developed a modified method for carrying out the Wassermann test, which eliminated the use of haemolytic amboceptor prepared by immunizing rabbits with sheep red cells, and substituted the haemolysin for sheep red cells normally found in fresh human serum (1909*a*). This technique was widely used for many years and was later combined with the Harrison technique. In the same year (1909*b*) he described a simple medium for the growth and isolation of the acne bacillus, consisting of ordinary nutrient agar with the addition of 1–5% of oleic acid. Subsequently, the successful treatment of cases of acne with autogenous vaccines was reported. Fleming & Colebrook were the first (1911) in Great Britain to test and report on the use of Ehrlich's newly discovered Salvarsan (606) for the treatment of syphilis, following the gift of a supply for trial from Ehrlich to Wright; the results were described as remarkable and no toxic or other effects were noted following intravenous use. This was the beginning of chemotherapy, and the beginning of Fleming's interest in the investigation of chemical antiseptics in the treatment of infection, an interest which became the mainspring of his future work.

During the first World War, Fleming served in the R.A.M.C. and worked with Wright and his team in a laboratory set up in Boulogne. Here they investigated the infections of war wounds and new methods of treatment, and many of the techniques evolved for the study of the physiology and immunology of infected wounds were devised by Fleming. The lack of value, and even the harmful and sometimes toxic effects of antiseptic packs for treatment of war wounds was soon realized, and the destructive effect of phenol and other antiseptics on the bactericidal power of the blood was

clearly demonstrated (1919) by Fleming in his classical experiment with *Bacillus perfringens* (*Clostridium welchii*). Similarly, he showed that a solution of sodium hypochlorite (Dakin's fluid) used to dress or irrigate war wounds was only transiently of value as an antiseptic, and that its main good effect was to increase the amount of exudate from the walls of the wound, an effect which could equally well be produced by the application of hypertonic saline solutions. Later he showed that flavine and acriflavine, widely used dyestuff antiseptics, had a highly destructive effect on leucocytes in the strengths recommended for use in wounds, that they delayed wound repair, and failed to sterilize infected wounds. In further experiments made some years later (1924, 1940*b*), using the slide-cell technique, he noted that the antileucocytic effect of acriflavine in blood was not so great as his original observations had led him to believe, and that, for short periods at least, leucocytes could retain motility and phagocytic power in the presence of concentrations of acriflavine regarded as being antiseptically effective in the treatment of infected wounds. Another ingenious experiment devised by Fleming, the so-called 'artificial wound', illustrated the difficulty of ridding an infected wound of its organisms by means of antiseptics; this consisted of a test-tube with several conical spikes drawn out in its lower half, filled with serum and infected with faecal matter; the serum heavily infected after incubation was replaced by antiseptic solution which was in turn after some hours replaced by fresh sterile serum. This procedure, repeated for several days, failed to sterilize the contents, due to failure of the antiseptic to penetrate to the tips of the glass spikes, called by Wright 'ecphylactic foci' and corresponding to crevices and pockets in a wound, inaccessible to antiseptics. During the course of investigations of gas-gangrene due to *C. welchii* in war wounds, Fleming found that the organism, although an obligate anaerobe, would grow under aerobic conditions if a piece of asbestos, fabric or potato were added to the fluid medium—an *in vitro* reproduction of the conditions pertaining in many wounds in which fragments of clothing had become embedded. With Douglas & Colebrook (1917) he also showed the important role played by bacterial symbiosis in wound infections, especially in the occurrence of gas-gangrene. It is of interest that in 1915 Fleming, in a paper on the bacteriology of septic wounds, recommended *débridement* for the treatment of severe wounds as a means of reducing infection, a method which became a standard surgical procedure in the second World War, over 30 years later. He must also have been one of the first to suggest, in 1919, in a joint paper with Porteous, that infection of war wounds with *Streptococcus pyogenes* was in the great majority of cases due to cross-infection in hospital, a deduction that was amply to be confirmed some 15 years later, when serological typing of *S. pyogenes* enabled the sources and paths of spread of infection with this organism to be traced with considerable precision.

After the war in 1918, Fleming returned to St Mary's as assistant to Sir Almroth Wright and was also appointed Lecturer in Bacteriology in St Mary's Hospital Medical School. In 1920 he became director of the Department of Systematic Bacteriology and assistant director of the Inoculation Department.

For some years he also acted as pathologist to the London Lock Hospital and to the venereal diseases department at St Mary's. He continued his investigations on the action of antiseptics in septic wounds, and in a series of experiments produced evidence in support of the 'physiological' school of Wright, the aim of which was to aid the natural protective agencies of the body against infection, and showed that the treatment of septic wounds with chemical agents, practised by the 'antiseptic' school, was not only ineffective in sterilizing wounds but inhibited or killed the leucocytes, and under certain conditions stimulated the growth of the infecting organisms. The evidence showed that all antiseptics in use at that time damaged the body cells, when used at a concentration necessary to kill the infecting organisms.

Towards the end of 1921, shortly after the writer began to work with Fleming, the latter made a discovery to which he later ascribed more importance than his discovery of penicillin. This was lysozyme, 'a substance present in the tissues and secretions of the body, which is rapidly capable of dissolving certain bacteria'. The circumstances leading to this discovery were in many respects similar to those which led to his discovery of penicillin, seven years later. His investigations of the nature and properties of lysozyme formed the subject of his first contribution to the Royal Society in February 1922. Subsequent investigations (1922*a*, *b*) convinced him of the enzyme-like nature of lysozyme and its importance as a factor contributing to natural immunity, acting as one of the body's natural defences against infection. Two techniques in particular which he adapted to his investigations on lysozyme were the slide-cell devised by Wright for investigating the bactericidal power of whole blood, and the agar plate with a gutter or a cup punched out with a cork-borer, later used with modifications in the assay of penicillin and other antibiotics.

Coincidental with his investigations on lysozyme, Fleming continued his experiments on the activities of antiseptics on bacteria and leucocytes, experiments in which the slide-cell played a large part, and he showed that the antiseptics then in common use, iodine, phenol, picric acid, mercuric chloride, eusol, alcohol, ether, and flavine, could never be successfully introduced into the blood stream for the treatment of septicaemia, nor indeed were they effective in the treatment of septic wounds—time and experience have fully confirmed his views.

In 1928 Fleming was appointed Professor of Bacteriology in the University of London, the post being tenable at St Mary's, and in September of the same year he made the discovery of penicillin, which was not to see full fruition till 1941, during the second World War. The circumstances of the discovery have been repeated so often that it suffices to say that it occurred as an observation made while he was working with colony variants of staphylococci with a view to writing an article for the Medical Research Council's 'System of Bacteriology' (1929*a*)—'it was noticed that around a large colony of contaminating mould the staphylococcus colonies became transparent and were obviously undergoing lysis'. This simple observation, and the subsequent investigations undertaken to study the nature and properties of the anti-

bacterial substance produced by the mould, later identified as *Penicillium notatum*, were the genesis of a revolution in the therapy of bacterial infections, and the introduction into medical parlance of a new word—antibiotics. Fleming's first paper on the subject was published in the *British Journal of Experimental Pathology* (1929*b*). In this he recorded the results of his investigations on the antibacterial substance, to which he gave the name 'penicillin'; the temperature range of production of penicillin, its solubility, resistance to heat, filterability, rate of production and stability were accurately described, and a measurement was made of the degree of susceptibility of almost all the known bacteria pathogenic to man, and commensal organisms found in man. Penicillin was shown to possess bacteriostatic, bactericidal and bacteriolytic powers, and the lack of toxicity of the crude penicillin-containing filtrate for animals by intravenous injection, for man by irrigation of infected surfaces and for leucocytes by *in vitro* experiments, was demonstrated. Another fundamental property of even crude penicillin, pointed out by Fleming, was that in contradistinction to all antiseptics its action on bacteria was not neutralized, inhibited or weakened in the presence of blood serum, pus or other exudate. In the original paper (1929) he stated: 'It may be an efficient antiseptic for application to, or injection into, areas infected with penicillin-sensitive microbes', and again in 1931 in an article on some problems in the use of antiseptics: 'It is quite likely that it (penicillin) or a chemical of a similar nature will be used in the treatment of septic wounds.' Unfortunately the instability of the crude penicillin and the small number of septic cases in hospital in peace time, led to its clinical use not being seriously pursued.

Although the use of penicillin for practical therapeutic purposes remained in abeyance till the Oxford workers, Florey and Chain and their colleagues, started their investigations, Fleming used penicillin constantly in the laboratory for selective culture. One of the practical laboratory uses recommended for penicillin was as an aid to the isolation of *Haemophilus influenzae*, which was 'penicillin-insensitive', from nasal and throat swabs and sputum where its presence was often masked or its growth was inhibited by other organisms. In a later communication (1930), it was shown that by the use of penicillin on blood agar plates, *H. influenzae* could be isolated regularly from the gums, tonsils and post-nasal spaces of healthy subjects. The separate and combined uses of penicillin and potassium tellurite for the selective isolation on solid media of organisms from mixed cultures, covering some twenty-six species, and for the demonstration of some bacterial antagonisms, were the subject of a paper in 1932. Subsequently (1942*a*) he demonstrated the value of combinations of penicillin, potassium tellurite and gentian violet in media for differential culture, following Garrod's description (1942) of the selective value of gentian violet for the isolation of *Streptococcus pyogenes*. Maclean (1937), a colleague of Fleming, also used penicillin in a similar manner with great success for the isolation of *Haemophilus pertussis* on cough plates and from swabs. Incorporated in glucose broth penicillin proved invaluable for the isolation of the acne bacillus from pus which contained both the acne bacillus and staphylococcus (Craddock, 1942).

In the meantime, Prontosil, a new chemotherapeutic agent in the treatment of infection, and the first of the sulphonamide drugs, had proved successful in the treatment of infections due to *Streptococcus pyogenes*, meningococcus and gonococcus. Fleming turned his attention to the study by *in vitro* methods of the mode of action of sulphanilamide and the later derivatives, sulphapyridine and sulphathiazole. Although the mode of action remained unsettled, he showed that the action of the sulphonamide drugs was bacteriostatic rather than bactericidal, and that the numbers of infecting organisms, sensitive to the drug, had an important bearing on the ability of the drug to act on them, thus confirming the work of Colebrook and others. He stressed the importance of the bacteriostatic action of the drugs, which allowed the natural defences of the body to deal with the most virulent infections (1940*a*). He also advocated vaccine therapy as an adjuvant to sulphonamide therapy, with a view to increasing the specific immunity (1939).

With the outbreak of the second World War in 1939, interest was again focused on the antiseptic treatment of wounds, and several workers, including Fleming, Dorothy Russell and Garrod, investigated the newer methods of treatment. The older methods of treatment used in the first World War were quickly discarded and investigations centred on the use of sulphonamides and acridine compounds. Fleming, a confirmed antagonist of the use of the older antiseptics, began to find virtue in the use of the sulphonamides and acridines, and although he was not hopeful about the application of sulphonamides as a dressing in septic wounds, with the advent of sulphathiazole he admitted that 'because of its potency and its wide range of activity it would seem that sulphathiazole should be the most effective of the sulphonamide drugs for application to an infected wound with the object of inhibiting the infection until the wound can be surgically cleansed' (1940*b*). He also agreed that the acridine compounds might have equal value, although he had reservations about their possible damage to tissues, a view which was not universally accepted.

In 1941, the Oxford workers, led by Florey and Chain, published a full account of their first investigations on penicillin, and Fleming (1942*b*), using some of the impure solid penicillin powder, supplied by Chain, described *in vitro* methods of testing its potency against *Staphylococcus aureus* and *Streptococcus pyogenes*, using the slide-cell technique for assaying the bacteriostatic power of penicillin in blood. By a comparison of the action of sulphathiazole and sulphapyridine with that of penicillin, which even then had a purity of only 5%, he showed that the latter was eight times more potent against *Staphylococcus aureus* in blood than sulphathiazole and thirty-two times more potent than sulphapyridine. In 1943 he had his first experience of treating a patient with penicillin; the case was one of streptococcal meningitis, and was the first case in which penicillin was administered intrathecally. The rapid and unexpected cure of an almost moribund patient stimulated Fleming to bring penicillin to the notice of the then Minister of Supply, Sir Andrew Duncan; this led to the setting up of the Penicillin Committee, which became instrumental in stimulating the British production of penicillin on

a commercial scale, and encouraging the investigation of methods for its purification, standardization and assay.

Interest in penicillin now became almost world-wide, and the success of trials in treating war wounds during the North African campaign opened up a new vista for research workers in the field and in the laboratory. Fleming, although he was inevitably drawn more and more from the laboratory to deliver lectures and to receive honours which began to be showered on him, yet found time to investigate micromethods of estimating penicillin in blood serum (1944), the penicillin content of blood serum after various doses of penicillin administered by different routes (1947), and the influence of penicillin on blood coagulation (Fleming & Fish, 1947). With May & Voureka (1947) he described a method of titration of streptomycin in patients' serum, and showed that the determination of the end-point depends on the culture medium used, the nature of the test organism, the size of inoculum of the test organism and the presence or absence of oxygen. He also made use of the development of phase-contrast microscopy to demonstrate the extraordinary variations in morphology developed by *Proteus vulgaris* when grown on penicillin agar on microscope slides; by applying intermittent radiant heat to the cultures and studying its effect on motility in the penicillin-induced forms he produced evidence to support the traditional theory of flagella being regarded as the organs of motility in bacteria, contrary to Pijper's claim that bacterial motility was due to gyratory undulating movements of the bacillary body, and that flagella were 'protoplasmic twirls' thrown off from the surface of the organism (1950*a*, *b*).

Fleming's last published work appeared in 1951, when he advocated with experimental evidence the efficacy of liquid paraffin at a temperature of 130° C. for the sterilization of syringe needles after immersion for 10 sec., a method which had been used effectively by Wright, Fleming and their colleagues for nearly fifty years.

During his medical career of 49 years, Fleming devoted himself to laboratory research on bacteriology and immunology, to teaching and to the application of new knowledge to the prophylaxis and therapy of infective disease. At the time of his death he had more than ninety scientific publications to his name, all based on original work and many of them being descriptions of new methods and techniques which he had evolved. He was also the instigator of many research problems investigated and published by junior members of the staff of the Institute.

There is no doubt that Fleming's choice of career in medicine and his development in the chosen specialty of immunology were largely due to his teacher and friend, Sir Almroth Wright. Wright, like Fleming in later life, did not suffer fools gladly, and no one, as the writer knows, was immune from his incisive and penetrating criticism, but he was a stimulating and inspiring teacher, and Fleming, like many others, owed much to him. Fleming proved an apt pupil at mastering the techniques of the teat, capillary glass tube and slide cell, and soon became a master technician of the art, an art which he retained to the end, because he remained his own technican. He showed great

ingenuity in devising apparatus from the simplest materials, often for the purpose of carrying out an experiment to prove or disprove some immunological idea. His technique was a joy to watch and many of the methods used by Wright and his team owed their origin or perfection to his deft hands. Along with the intellectual ability and phenomenal memory he had shown during his undergraduate career, he developed an originality of thought; this was outstandingly shown round the tea table in the Inoculation Department library, when Wright would raise some immunological problem or propound a theory, and a discussion would follow. Time and again the discussion would finally resolve itself into an argument in which Fleming, the 'little man' as Wright affectionately called him, pitted his mind against the logical and keen insight of 'the old man'. Then, the issue undecided, each would go off to devise an experiment to see which was right. He was possessed of an insatiable curiosity to find out the why and the wherefore of anything that was unusual or new, not only in his work at the bench but also in everyday life; for example, the observation of the stereotropism of leucocytes in fresh blood led him to try the effect of passing blood under the pressure of a rubber teat through the cotton-wool plug of a sterile Pasteur pipette, and he found that this simple procedure removed the leucocytes and platelets from the blood. This in turn led to experiments on the bactericidal power of deleucocyted blood and further study of the functions of phagocytes *vis-à-vis* staphylococci. The main theme which runs through all Fleming's work is the study of the natural defences of the body against infection, in particular the antibacterial powers of the phagocyte and the blood serum and their interrelated functions. During the first World War and after, he became one of the antagonists in chief against the use of antiseptics for the treatment of wounds or systemic infections, and much of his research was devoted to proving the adverse effect of antiseptics on the natural defences of the body, a subject which he pursued with a missionary zeal and on which he was at times outspoken.

His discoveries of lysozyme and penicillin are two outstanding examples of his perceptive powers and curiosity to investigate the unusual. He made no secret of the fact that the discovery of lysozyme gave him more pleasure than any of his other work, not excluding the discovery of penicillin which was to make his name a household word. Lysozyme, later shown to be an acetylamino polysaccharidase, is the only one of the 'cytases' postulated by Metchnikoff, so far shown to be able to cause lysis of living bacteria, and subsequent studies have confirmed Fleming's views of its importance as a factor in natural immunity.

Surprise has been expressed in some scientific circles that Fleming did not pursue further his investigations on lysozyme and penicillin, especially the latter, but it must be remembered that Fleming was a bacteriologist and immunologist, not a chemist, and there was no chemist available to co-operate with him. As he himself pointed out, even skilled chemists had failed in their attempts to concentrate, stabilize and purify penicillin, before success was eventually achieved through the joint efforts of a team of workers, each a specialist in his own field. Although, working unaided, he was not able to

pursue his investigations of penicillin to their ultimate fulfilment, tribute must be paid to his views expressed in 1929 and again in 1931 that penicillin had a future for the treatment of infection, and to his initiative in persuading the Ministry of Supply and Ministry of Health of the importance of penicillin in the war effort. Great technical advances in scientific knowledge and its application occur in the stress of war, and penicillin was discovered at a time unpropitious from this point of view. Again, team work in medical science is a comparatively recent development, especially in the field of the chemistry of bacterial metabolism, and without such team work, both in England and U.S.A., the pursuit of penicillin to its full fruition might still be 'a consummation devoutly to be wish'd'. Although his main interest was immunity and infection, a list of his published work shows that Fleming carried out a considerable amount of research on current problems, in particular the development of selective media for differential culture of the common pathogenic bacteria, the uses of nigrosin, alone or combined with stains, as an excellent method of demonstrating bacterial morphology and spores, and a simple and rapid technique for staining bacterial flagella, used with success in the teaching of students.

In 1948 Fleming retired as Professor of Bacteriology with the title Emeritus but continued as Director of the Wright–Fleming Institute of Microbiology until his death, although he had decided shortly before to hand over the reins to his successor, Professor R. Cruickshank. After the establishment of penicillin as a therapeutic agent of the highest potency against infection, it was inevitable that Fleming should be drawn from his laboratory to deliver lectures and receive the honours accorded him by universities, societies, cities and nations throughout the civilized world, as a tribute to his work. He received the Fellowship of the Royal Society in 1943, of the Royal College of Physicians of London in 1944, and of the Royal College of Physicians of Edinburgh in 1946. In 1945 the Nobel Prize for Medicine was awarded jointly to the three men most concerned in the discovery, purification and application of penicillin for therapeutic use—Fleming, Florey and Chain. Fleming was knighted in 1944, and was the first foreign citizen to receive the United States Medal of Merit. In the years that followed, the honorary degree of Doctor of Science was conferred on him by six European and three American Universities; the honorary degree of Doctor of Medicine by seven European Universities, and the honorary degree of Doctor of Laws by two Scottish Universities. Medals and prizes awarded to him included the Gold Medal Royal Society of Medicine, Hon. Gold Medal Royal College of Surgeons of England, the Moxon Medal Royal College of Physicians, the Harben Gold Medal Royal Institute of Public Health and Hygiene, the Albert Gold Medal Royal Society of Arts, the Medal for Therapeutics of the Society of Apothecaries, the John Scott Medal City Guild of Philadelphia, the Actonian Prize Royal Institution, and the Cameron Prize University of Edinburgh. He was William Julius Mickle Fellow of London University in 1942, and Charles Mickle Fellow of Toronto University in 1944. He was Linacre Lecturer to the University of Cambridge, Harben Lecturer to the Royal Institute of Public

Health and Hygiene, Cutter Lecturer to Harvard University, Mayo Foundation Lecturer to the University of Minnesota, Lister Memorial Lecturer Society of Chemical Industry, Robert Campbell Lecturer Ulster Medical Society, and Shattuck Lecturer Massachusetts Medical Society, among others. He was made a Fellow or Honorary Member of many Academies of Medicine and Science, including the French Academy of Science, the Pontifical Academy of Sciences, and the Royal Society of Copenhagen. He had been President of the Society for General Microbiology, and of the Sections of Pathology and Comparative Medicine, Royal Society of Medicine. From 1945 to 1949 he was a member of the Medical Research Council and in 1946 he became chairman of a committee set up to organize clinical trials of streptomycin and other antibiotics in non-tuberculous conditions. In 1951 he was elected Rector of Edinburgh University. He was Honorary Freeman of Darvel, Chelsea and Paddington, the Boroughs where he was born, lived and worked; in 1949 he was made an Honorary Freeman of the City of Athens, and of the City of Verona in Italy on the occasion of the International Medical Congress. He was made Commander of the Legion of Honour in France, Honorary Chief of the Kiowa Tribe, and received the Grand Cross of Alphonse X The Wise, in Spain. Shortly before his death he had completed plans for a lecture tour in the Middle East on behalf of the British Council.

Fleming, the man, was short, broad-shouldered and deep chested, and his eyes were keen and expressive. During 34 years as pupil and friend, the writer never saw him lose his temper or speak ill of anyone, although on the rare occasions when he was annoyed his eyes could flash fire, and a look was more expressive than the spoken word. Although he was not a great lecturer, he had the gift of lucid exposition, and made up in sincerity what he lacked in eloquence. He has been described as taciturn and laconic, but he was a good listener, quick to grasp the essentials of an argument or discussion and give the *coup de grâce* to any ill-conceived theory. In informal discussions he delighted to take views opposite to those expressed, although he may have secretly agreed with them, and in this way he often extracted valuable ideas for experimental work; he used this technique to enable him to assess the originality and agility of mind of young workers, and to encourage in them clear thinking and reasoned argument. His phenomenal memory and quick mind served him well in reading the journals; his reading was done in short spells, as he could not remain inactive for more than half an hour or so, whether in the laboratory, at home, or in the country. He was a strong and loyal supporter of St Mary's Hospital Medical School, and was always ready to undertake any work to advance its interests and help the students in all their activities, in the class, in the ward and in the field of sport. Although he was fond of people and company and made many friends in different walks of life, he was not easy to know, due perhaps to his modesty and diffidence. To his close friends and intimates he was 'Flem', and only to the few was he 'Alec'. He was an excellent host and entertained much, both at his flat in Chelsea and his country home at Barton Mills in Suffolk. He had a keen artistic sense and was no mean performer with water colours. His handwriting was small

and copperplate, and the beautiful neat draughtsmanship of his lantern slides and innumerable diagrams in black and white and in colour, prepared both for teaching purposes and for illustrations in scientific papers, will be treasured in the Wright–Fleming Institute. He was for many years an honorary member of the Chelsea Arts Club, and numbered many artists among his friends—he was indeed the unofficial medical consultant to the club. He was a keen and expert photographer and applied his skill in this art both in the laboratory and as a leisure occupation, with excellent results. In his younger days he was a fine rifle-shot and a good swimmer, but in middle life he played a vigorous game of billiards, and could defeat younger and more experienced players at tennis, golf and croquet. Of all his leisure activities there is no doubt that gardening gave him the greatest pleasure—fruit, flowers and vegetables grew in profusion at his country residence at Barton Mills; he had 'green fingers' and was forever experimenting with cuttings, cross-pollination, new plants or seeds and grafting—much of the produce of his garden went to the wards of St Mary's Hospital. He loved to browse in second-hand bookshops and was specially interested in history and colour drawings of birds and insects. He was a collector of old silver and glass and had some fine examples of Georgian silver and old English cut glass.

In 1921, the year in which he discovered lysozyme, he married Sarah Marion McElroy of County Mayo, who shared many of his interests, especially love of gardening and the collection of antiques. She died in 1949, leaving one son Dr Robert Fleming. In 1953 he married Dr Amalia Coutsouris from Greece, who had come to work on the staff of the Wright–Fleming Institute in 1947, and had returned to Greece in 1952 to become head of the bacteriological department of a hospital in Athens. During the war she commanded respect by helping British soldiers during the Greek campaign, for which she was imprisoned by the Germans.

Fleming remained active and interested in his work to the last, and he had planned in retirement to set up a laboratory, where he could continue his work, in a studio in the grounds of his country home. It was fitting that at the end his ashes were interred in St Paul's. He had served his day and generation well and had been instrumental in saving more human lives and suffering than anyone in the history of medicine. His name will surely be remembered for evermore.

V. D. Allison

BIBLIOGRAPHY

Of papers mentioned in this Obituary Notice

Abraham, E. P., Chain, E., Fletcher, C. M., Florey, H. W., Gardner, A. D., Heatley, N. G. & Jennings, M. A. (1941). Further observations on penicillin. *Lancet*, ii, 177.

Craddock, S. (1942). Use of penicillin in cultivation of the acne bacillus. *Lancet*, i, 558.

Douglas, S. R., Fleming, A. & Colebrook, L. (1917). On the growth of anaerobic bacilli in fluid media under apparently aerobic conditions. *Lancet*, ii, 530.

FLEMING, A. (1908). Some observations on the opsonic index, with special reference to the accuracy of the method and to some of the sources of error. *Practitioner*, i, 607.

FLEMING, A. (1909*a*). Serum diagnosis of syphilis by a simple modification of Wassermann's method. *Trans. med. Soc. Lond.* **33**, 91.

FLEMING, A. (1909*b*). On the etiology of acne vulgaris and its treatment by vaccines. *Lancet*, i, 1035.

FLEMING, A. (1915). On the bacteriology of septic wounds. *Lancet*, ii, 638.

FLEMING, A. (1919). The action of chemical and physiological antiseptics in a septic wound. *Brit. J. Surg.* **7**, 99.

FLEMING, A. (1922). On a remarkable bacteriolytic element found in tissues and secretions. *Proc. Roy. Soc.* B, **93**, 306.

FLEMING, A. (1924). A comparison of the activities of antiseptics on bacteria and on leucocytes. *Proc. Roy. Soc.* B, **96**, 171.

FLEMING, A. (1929*a*). The staphylococci. In *A System of Bacteriology in relation to Medicine. Spec. Rep. Ser. med. Res. Coun., Lond*, **2**, 11.

FLEMING, A. (1929*b*). On the antibacterial action of cultures of a penicillium, with special reference to their use in the isolation of *B. influenzae*. *Brit. J. exp. Path.* **10**, 226.

FLEMING, A. (1931). Some problems in the use of antiseptics. *Brit. dent. J.* **52**, 105.

FLEMING, A. (1932). On the specific antibacterial properties of penicillin and potassium tellurite. *J. Path. Bact.* **35**, 831.

FLEMING, A. (1939). Serum and vaccine therapy in combination with sulphanilamide or M. & B. 693. *Proc. R. Soc. Med.* **32**, 911.

FLEMING, A. (1940*a*). Antiseptics and chemotherapy. *Proc. R. Soc. Med.* **33**, 127.

FLEMING, A. (1940*b*). The effect of antiseptics on wounds. *Proc. R. Soc. Med.* **33**, 487.

FLEMING, A. (1942*a*). A simple method of using penicillin, tellurite and gentian violet for differential culture. *Brit. med. J.* i, 547.

FLEMING, A. (1942*b*). *In vitro* tests of penicillin potency. *Lancet*, i, 732.

FLEMING, A. (1943). Streptococcal meningitis treated with penicillin. *Lancet*, ii, 434.

FLEMING, A. (1944). Micro-methods of estimating penicillin in blood serum and other body fluids. *Lancet*, ii, 620.

FLEMING, A. (1947). Estimation of penicillin in serum. *Lancet*, i, 401.

FLEMING, A. (1950). Further observations on the motility of *Proteus vulgaris* grown on penicillin agar. *J. gen. Microbiol.* **4**, 457.

FLEMING, A. & ALLISON, V. D. (1922*a*). Further observations on a bacteriolytic element found in tissues and secretions. *Proc. Roy. Soc.* B, **94**, 142.

FLEMING, A. & ALLISON, V. D. (1922*b*). Observations on a bacteriolytic substance ('lysozyme') found in secretions and tissues. *Brit. J. exp. Path.* **3**, 252.

FLEMING, A. & COLEBROOK, L. (1911). On the use of Salvarsan in the treatment of syphilis. *Lancet*, i, 1631.

FLEMING, A. & FISH, E. W. (1947). Influence of penicillin on the coagulation of blood. *Brit. med. J.* ii, 242.

FLEMING, A. & MACLEAN, I. H. (1930). On the occurrence of influenza bacilli in the mouths of normal people. *Brit. J. exp. Path.* **11**, 127.

FLEMING, A. & OGILVIE, A. C. (1951). Syringe needles and mass inoculation technique. *Brit. med. J.* i, 543.

FLEMING, A. & PORTEOUS, A. B. (1919). On streptococcal infections of septic wounds at a base hospital. *Lancet*, ii, 49.

FLEMING, A., VOUREKA, A. E., KRAMER, I. R. H. & HUGHES, W. R. (1950). The morphology and motility of *Proteus vulgaris* and other organisms cultured in the presence of penicillin. *J. gen. Microbiol.* **4**, 257.

GARROD, L. P. (1942). The selective bacteriostatic action of gentian violet. *Brit. med. J.* i, 290.

MACLEAN, I. H. (1937). A modification of the cough plate method of diagnosis in whooping cough. *J. Path. Bact.* **45**, 472.

MAY, J. R., VOUREKA, A. E. & FLEMING, A. (1947). Some problems in the titration of streptomycin. *Brit. med. J.* i, 627.

NOON, L. & FLEMING, A. (1908). The accuracy of opsonic estimations. *Lancet*, i, 1203.