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Derrick Graham ff. Edward: A Pioneer in Mycoplasmology

Dr. Derrick Graham ffarington Edward, one of the founders of modern mycoplasmology and a man whose impact over a wide front within that field cannot be overestimated, died on September 11, 1978, at the age of 67.

Edward was born on October 14, 1910, in Esher, Surrey. He was only three years old when his father died, and he spent his childhood with his mother and a maiden aunt. He received his early education at Bromsgrove School near Birmingham and studied medicine at St. Bartholomew's Hospital in the city of London. Although his mother made great sacrifices to allow him to obtain medical training, Edward's poor financial situation as a student enforced hard work and a quiet and rather lonely life. He was awarded a Junior Scholarship in premedical subjects and Kirkes Scholarship and Gold Medal in Medicine, and he was *proxime accessit* in the Brackenbury Scholarship in Medicine. He qualified in 1934.

After qualification, Edward served as House Physician for one year at St. Bartholomew's Hospital and hoped to continue with a career in clinical medicine. However, salaries of junior staff were very low at that time, and because he believed that private means would be required for a career as consultant physician, he turned to clinical pathology. He held appointments as Junior Demonstrator of Pathology from 1935 to 1937 and Cancer Registrar from 1937 to 1938, both at St. Bartholomew's Hospital, and became Assistant Pathologist at the Hospital for Sick Children in London in 1938. A two-year tenure of the Lawrence Research Scholarship in Pathology during this period enabled him to obtain his first training in research. He was granted the M.B. and B.S. in 1935 and the M.D. in Pathology by examination in 1937.

The turning point in Edward's career occurred in 1939 when, just before the outbreak of the Second World War, he obtained a position at the National Institute for Medical Research in London, where he was introduced to virology by Sir Patrick Laidlaw. As a declared pacifist, Edward was drafted in 1941 to serve at the Emergency Public Health Laboratory in Cardiff. In 1945, he was invited to join the scientific staff of "Operation Tyborn," the secret code name of a project sponsored by the British Government and the War Office and run by the Wellcome Foundation at laboratories in Frant, Sussex, for the large-scale production of a scrub-typhus vaccine in cotton rats. Soon after the end of the war, Edward received an appointment as virologist by the Wellcome Foundation and worked for a few years at the Veterinary Research Station at Frant on the improvement of a vaccine against louping-ill. In 1948 he was transferred to the Wellcome Research Laboratories at Beckenham, Kent, to take charge of the production of yellow fever vaccine and to develop a vaccine against dog distemper (Epivax) using the egg-adapted Haig strain. Then in 1953, Edward became head of the Department of Virology, a new department created at Beckenham. At that time only Edward and one technical assistant formed the nucleus of the department, without a personal laboratory. Thus, fully committed to administration, Edward at first designed temporary laboratories and eventually three new buildings to house the growth of the virology department. Because the new department was created primarily for the production of vaccine, a number of viral vaccines were developed and manufactured under Edward's responsibility and enthusiastic leadership: a Salk-type inactivated polio vaccine, a Sabin attenuated polio vaccine, and an attenuated vaccine against measles, as well as various veterinary vaccines. It is an astonishing fact that those years of heavy administrative burdens and preoccupation with purely practical matters were at the same time the most creative period of Edward's scientific accomplishments in quite another field.

These years of intense professional happiness and gratification ended with the first appearance, in 1964, of a serious illness. As a result Edward was asked to resign his position as head of the Department of Virology. However, after an operation for what turned out to be a meningeoma, he made an unexpected and apparently full recovery. Since his former job had already been taken over by a colleague, he was, as a sort of compensation, eventually appointed Research Officer and was

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responsible for all research and development under the head of the Biological Division. In 1967 Edward was himself appointed head of that division and in 1968 was appointed to membership of the Wellcome Group Research and Development Committee. Much to his regret, the pressure of work in the new job was not challenging, and he found himself even further removed from laboratory facilities. But another and even more distressing surprise still awaited him. In 1969, under a new directorship of the Wellcome Research Laboratories, he was most unexpectedly asked to retire early at the age of 59. Since there appeared to be no alternative, he reluctantly accepted an offer to join the Public Health Service, whereby he was provided with a small laboratory and very limited facilities for research. Edward finally retired in 1975. By that time he had suffered a relapse of the symptoms of the disease he had battled and apparently conquered years earlier.

Edward's scientific accomplishments lend themselves to division into two major groups. Although, of course, his achievements as a mycoplasmologist won him international renown and will preserve his name in the history of microbiology, the research he performed in other areas certainly deserves to be remembered. In addition to some early studies in clinical pathology, he was the author or coauthor of a number of bacteriological papers dealing with, for example, the possible pathogenicity of nontoxigenic strains of *Corynebacterium diphtheriae* and the epidemiology of nosocomial infections caused by hemolytic streptococci. The main concern of the Institute for Medical Research at the time of his employment was the investigation of the cause and control of airborne infections. Edward became particularly interested in dust-borne infections; he used an experimental setup to study the inactivation of aerosols of influenza and ectromelia viruses by exposure to ultraviolet radiation and to certain chemicals, as well as the resistance of these viruses to drying. In a later study, he described simple measures for treating floors and bedclothes to reduce the dissemination of dust-borne bacteria as a source of cross infections in hospital wards. When associated with the Wellcome Veterinary Research Station, Edward was the first to carry out a thorough study of the growth of louping-ill virus in embryonated eggs, a study aimed at developing an improved virus vaccine. He was also the first to demonstrate the close serological relationship between louping-ill virus and the viruses of Central European and Russian spring-summer encephalitis.

Edward's first experience with mycoplasmas (organisms of the class Mollicutes, named by Edward and Freundt), or as they were known at that time, "the pleuropneumonia-like organisms," occurred in 1939, soon after his arrival at the National Institute for Medical Research. At the suggestion of Sir Patrick Laidlaw, who a few years earlier had isolated from sewage the mycoplasmal organism later named after him (*Acholeplasma laidlawii*), he investigated a transmissible pneumonia of mice induced by intranasal instillation of varicella material. Although the pneumonia-producing agent was exceptionally difficult to grow, especially on solid media, Edward successfully identified it as a member of the pleuropneumonia group and provided a description of the organism that was much above contemporary standards. His interest in the mycoplasmas was further stimulated by their isolation from humans by Dr. Louis Dienes, and Edward himself made a few early isolations from the human urogenital tract. However, he did not resume the serious study of mycoplasmas until about 1945, when he became involved in the scrub-typhus vaccine project. Here again, an organism picked up during intranasal passage of another organism (rickettsia) in mice, which produced in its own right upper respiratory tract catarrh, was identified by Edward as a mycoplasma. From that time his investigations in the field of mycoplasmology were continuous and intense throughout the rest of his active life, although they were, as indicated already, carried out to a great extent as a left-hand effort.

In the late 1940s the mycoplasmas were regarded —with a few notable exceptions—as bacteriologic curiosities. Whereas considerable attention had been paid to their peculiar morphology, the physiology and general biological characteristics of the group had been the subjects of rather limited interest. Also, very few attempts had been made to examine the potential suitability of such properties for differentiation between strains of mycoplasmas. One of Edward's early accomplishments was the demonstration that mycoplasmas could be characterized by a variety of the cultural and biochemical methods commonly used in bacteriology and that such methods could be utilized, together with serology, for classification of the mycoplas-

mas at the species level. The results of extensive comparative studies based on these principles were presented in general surveys published in the *Journal of General Microbiology*. They are among the classics of the literature on mycoplasmas. Also, his description and proposed classification in subsequent papers of a number of mycoplasmas from bovine, canine, avian, and human sources served as a model for other authors in this field, as did his acutely critical evaluation of the possible pathogenicity of some of these organisms.

The difficulties encountered in the early attempts to grow mycoplasmas on artificial media prompted a series of studies on their nutritional requirements. Thus, Edward's observation of satellitism around contaminating colonies of staphylococci on media yielding poor growth of mycoplasmas provided a clue to the missing factor(s): the addition of yeast extract produced a similar enhancement of growth. As a result of this observation, yeast extract was universally adopted as a component of most mycoplasma growth media. Edward also was the first to demonstrate the requirement shown by some mycoplasmas for an extraneous source of DNA. Since bacterial contamination remained a constant problem in any attempts at isolating mycoplasmas from clinical materials, Edward performed a systematic study of the effect of various bacteriostatic agents on the growth of mycoplasmas. Taking advantage of the combined action of penicillin and thallium acetate on a broad range of bacteria, he developed a selective medium that became of considerable practical importance as a standard medium in every mycoplasma laboratory. However, Edward's most significant contribution to our knowledge of the nutritional requirements of mycoplasmas was his demonstration with W. A. Fitzgerald in 1951 that cholesterol is needed for the growth of serum-dependent species. From a theoretical and taxonomic point of view, the fundamental importance of this discovery is that sterol, although required by some protozoa, is not known to be an essential nutrient for any species of bacteria, even in the L-phase.[1] The nutritional dependence of members of the Mycoplasmataceae on cholesterol or certain other sterols became a major criterion, moreover, for differentiation among species of this family and members of the family Acholeplasmataceae. Several years later, Edward devised a very convenient method for the determination of sterol requirement.

As a chance finding in connection with his studies of the growth-promoting effect of animal serum, Edward discovered the specific inhibition of the growth of mycoplasmas by antibody. He thereby revealed another important difference between mycoplasmas and other prokaryotes, a difference that could later be ascribed to the absence of a cell wall in the mycoplasmas. Although the method originally used by Edward has been modified considerably for contemporary use, the antibody-dependent growth inhibition test has proved of inestimable value in the identification and classification of mycoplasmas at the species level.

Edward made a significant contribution to the foundation and further development of a rational taxonomy for the mycoplasmas. When he started as a mycoplasmologist, he was confronted with confusion and inconsistency in the nomenclature and classification of the organisms of the "pleuropneumonia group." As the need for improvement in the taxonomy of this group became more urgent with the discovery of increasing numbers of new organisms, proposals for a new taxonomic approach were, by mere coincidence, published separately by Edward and myself in 1955. The contact subsequently made between us with the purpose of coordinating our efforts became the beginning of a close, lifelong collaboration and friendship. As a result, we created, step by step, an elaborate system of nomenclature and classification for the mycoplasmas, covering the taxonomic categories of order, families, genera, species, and subspecies. In recognition, furthermore, of the unique properties denoting the group as a whole, in 1967 we formally proposed the establishment of a separate class under the name of Mollicutes. This step implied that mycoplasmas were regarded as essentially different from L-phase variants of bacteria, a view that both of us had strongly expressed for years. Another constructive contribution to taxonomy, a review of the type strains of species of the order Mycoplasmatales, was published in 1973. The fact that neotypes had to be proposed for only a very few species or subspecies was very much due to the foresight of Edward, when, in 1953, he established at the Wellcome Research Laboratories the first collection of lyophilized mycoplasma cultures (the

[1] Very recently, sterol requirement for the growth of *Treponema hyodysenteriae* was demonstrated by R. M. Lemke and M. R. Burrows (J. Gen. Microbiol. 116:539-543, 1980).

"PG" strains), including strains isolated by Edward as well as by earlier investigators. This collection became the nucleus of the collections of type strains of mycoplasma species subsequently established by the American Type Culture Collection, the National Collection of Type Cultures in London, and the Food and Agricultural Organization (FAO)/World Health Organization (WHO) Collaborating Centre for Animal Mycoplasmas in Aarhus.

Finally, Edward's repeated, strong emphasis on the importance of a precise characterization of mycoplasma species led directly to the preparation of a "Recommendation on Nomenclature of the Order Mycoplasmatales," with the object of improving the standard of published descriptions of new species. In publishing these recommendations in 1967, the Subcommittee on the Taxonomy of Mycoplasmatales in fact anticipated a request made some years later by the International Committee on Systematic Bacteriology (ICSB). As a further result of the pattern laid down by its publication in 1967, the Subcommittee on the Taxonomy of Mycoplasmatales was among the very first ICSB subcommittees to present, in 1972, a more comprehensive "Proposal for Minimal Standards for Descriptions of New Species of the Order Mycoplasmatales." The amount of effort devoted by Edward to tackling taxonomic problems depended primarily, of course, on his genuine interest in this subject and on his awareness of the need for developing a mycoplasma taxonomy. On the other hand, he regarded the time he spent at the desk writing about taxonomy as compensation for the lack of sufficient opportunities he had to work in the laboratory, which more than anything else had his heart.

Considering Edward's substantial accomplishments, many are surprised to learn that he regarded himself as an amateur in taxonomy. He received some satisfaction, therefore, when during his association with the Public Health Service, he was able to devote himself full-time to laboratory work, although at his age (over 60), he found it difficult to undertake original research. As a final effort, he studied the mycoplasmal viruses, thereby, in his own words, "providing a synthesis between [his] interests in virology and mycoplasmology."

The influence Edward exerted on more than a generation of mycoplasmologists in fostering and stimulating international cooperation was in no way less significant than his scientific accomplishments, outstanding and extraordinary though these were. Because of his initiative, in particular, the New York Academy of Sciences Second Conference on Biology of the Mycoplasma in 1966 established a provisional Subcommittee for Classification and Nomenclature of Mycoplasmas, which soon obtained formal recognition by the International Committee on Bacteriology. Edward was the obvious first chairman of the Subcommittee, a position he held for 10 years until forced by his illness to withdraw. Under his eminent and enthusiastic leadership, the Subcommittee made a great many important decisions and recommendations, thereby solving taxonomic problems that had often been at issue for years. In recognition, moreover, of the vital importance of international reference centers for the functioning of the Taxonomy Subcommittee, Edward advised WHO and FAO that two such centers be established, one for human mycoplasmas at the National Institutes of Health, Bethesda, Maryland, United States and one for animal mycoplasmas at the University of Aarhus, Denmark. With the formation in 1969 of the FAO/WHO International Program on Animal Mycoplasma Characterization (later known as the Program on Comparative Mycoplasmology), he became a member of the board established to implement the aims of the program and remained one until his death. Also, Edward was the first Chairman of the Working Team for Avian Mycoplasmas under the board. The importance of his efforts to the widespread activities of the program and the impact of his personality on the policy made by the board during the early days of its existence are obvious. Finally, he was one of the founder members of the International Organization for Mycoplasmology (IOM).

Edward's original contributions to mycoplasmology, all of which have withstood the test of time, were recognized by his fellow mycoplasmologists, who awarded him Honorary Membership of the IOM at its first meeting, held in Glasgow, September, 1976. In 1979, the IOM established a Derrick Edward Award and Lecture in his memory, given in recognition of outstanding research contributions in the field of mycoplasmology.

In addition to membership in organizations and committees concerned with mycoplasmology, Edward was Fellow of the Royal Society of Medicine,

Member of the Pathological Society of Great Britain and Ireland, Original Member of the Society of General Microbiology, and Member of the Research and Development Society.

In his private life Edward took great interest in politics, though, as he said himself, his views were very independent. For several years he was Chairman of the local Liberal Constituency Association, but gave this interest up when he was pressed with adminstrative work at the Wellcome Laboratories. In his brief leisure moments and after retirement, Edward sought relaxation by gardening and by walking in the countryside with his family. Also, although he did not claim to be musical, classical music was one of the joys of his life.

Edward's intellectual capabilities, intelligence, clarity of thought, and firm decisiveness in pursuing his aims are clear from his accomplishments. However, some personal remarks may finally be appropriate in an endeavor to complete the portrait of a remarkable personality. Although always very kind and cooperative in his relations with colleagues and associates and extremely helpful to those who sought his advice on professional matters, Edward usually maintained an external facade and a certain distance from his surroundings. He was certainly not a man to establish easy relationships on a personal level. It was felt much as a privilege, therefore, to be reckoned among his very few close friends. Founded on mutual scientific interests as our friendship originally was, it gradually developed into a consensus of thoughts on many of the basic aspects of life and human nature. The ties of friendship became further strengthened during years of adversity and misfortune experienced by both of us, each in his way. Most of our discussions and the exchange of thoughts and ideas that led to a considerable number of joint publications naturally had to be carried out through correspondence, which over a period of more than 25 years became a very extensive record of a most ideal and fruitful collaboration. Many of the letters reflect, also, Edward's basic attitude toward the science he was serving. Exacting as he was in the demands he made of his own scientific work, he could give way, for example, to scornful expressions for those who tended to seek easy solutions and who did not, in his opinion, live up to the standards of quality required in science. On the other hand, he might often reveal a deep sense of humor, a humor that calls forth, moreover, the remembrance of his very characteristic laughter, a laughter that might be provoked even in sad moments. The sufferings that he had to endure during the last years of illness, when in addition to renewed brain surgery, he had to submit to a series of other operations, was an almost inhuman challenge to him and his family. The bravery and determination he showed, even when he was fully aware that his illness was terminal, was admirable. Letters he received during this period from colleagues and old friends who expressed their feelings of debt and gratitude for the guidance they had received from him when they were beginners in mycoplasmology were a source of consolation and pleasure to him. Very characteristically, such letters did not remain unanswered. The foreword he completed in early 1978 for the first volume of *The Mycoplasmas* (Academic Press, 1979) testifies to the active interest he maintained in mycoplasmology even at a very advanced stage of his illness. However, when during our last encounter, a few months before he died, I tried to bring up once again the subject of our former mutual love, his only comment was: "I have lost interest." He will be well remembered for the devotion to mycoplasmology that he did maintain until shortly before that sad moment.

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