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Obituary Notice

DAVID KEILIN, 1887–1963

The sudden death on 27 February 1963 of David Keilin deprived the scientific world of a biologist the span of whose scientific activities is unlikely to be equalled, much less excelled, in the future. These activities extended from descriptive morphology of protists, fungi and insects to the biochemistry of respiratory enzymes and metallo-protein compounds. It is, consequently, not possible for one person to deal adequately with all aspects of his work and in this appreciation of the man and his scientific achievements the main emphasis will be on his biological work. That bearing on parasitology will be considered in some detail, whereas the later, more biochemical, work will be considered briefly as fuller accounts of it have already been given by E. F. Hartree (*Biochem. J.* **89**, 1–5), T. R. R. Mann (*Biogr. Mem. Fellows R. Soc.* **10**, 185–207) and E. C. Slater (*Enzymologia*, **26**, 313–20). In the brief survey of his biochemical work I have made much use of summaries and reports written by Keilin himself and I have often given the essence of lines of work summed up in his own words which express his conclusions with the elegance, lucidity and brevity characteristic of his style. As I was closely associated with David Keilin and in almost daily contact with him for just on forty years, it is natural that the following account will to some extent reflect my own interests and those aspects of his personality which became manifested during long and intimate contact both in private life and collaboration in scientific and administrative work.

For details of his early life and career before he came to Cambridge I am indebted to his widow, Dr Anna Keilin and his daughter, Dr Joan Keilin. I am fortunate also in having a number of mutual friends of long standing, both in the Molteno Institute and in other Departments of the University, with whom discussion has shown the great influence of his work and of his personality upon his friends and colleagues.

Before considering his scientific contributions in detail, a brief account of the salient stages in his life and career will be given.

Although his parents were of Polish nationality, David Keilin, the fourth child of a family of seven, was born on 21 March 1887 in Moscow where his parents were then residing. The family soon returned to Warsaw. His father, a business man and small landowner, and his mother, a wise and energetic woman, were devoted to their children and anxious to give them a good education. David was not a robust child, probably already suffering from the asthma which was to handicap him throughout life, and until the age of ten he was taught at home by a governess. He then attended the Górski School, a well-known private school, where for seven years he was an average pupil in most subjects but showed an aptitude for literature, mathematics and languages, studying Polish, Russian, French and German. This knowledge of languages was later a great help in his career making much literature accessible to him and favouring the close personal contacts he cherished with a great number of workers from all over the world. He began his university studies in Belgium where, in 1904, he went to the University of Liège and read Natural Sciences, including the elements of logic and philosophy and where one of his teachers was Edward van Beneden. He completed a two-year course in one year and obtained the 'Diplôme de la Candidature des Sciences Naturelles'. He was deterred from pursuing the study of medicine by his liability to asthma and in July 1905 he moved to Paris where he spent some of his time reading at the Bibliothèque St Genevieve, visiting art galleries and attending the lectures on philosophy of Professor Henri Bergson at the Collège de France. His ultimate field of study was determined by a chance occurrence. He took shelter from a heavy rain storm in a building and entered the lecture room of the Laboratoire d'Evolution des Êtres Organisés where Professor Maurice Caullery was lecturing. He was so much impressed with the lecture that he continued to attend the course three times weekly and, during the questions and discussions after the lectures, he established personal contact and started a life-long friendship with Caullery. Caullery discerned Keilin's potentialities and invited him to start some research at the laboratory under his direction. Keilin willingly accepted this offer and was thus launched on his career in biology. Acting on Caullery's advice, he entered the Sorbonne and read zoology under Professor Alfred Giard, geology under Professor E. Haug, and also botany and embryology. During the vacations he worked at the Marine Stations at Wimereux, Roscoff and Banyuls, and he also collected assiduously in the neighbourhood of Paris. The visits to the marine stations and the collecting expeditions must have given him great pleasure, both scientifically and in the personal relationships, because in later years he loved to recount tales of happy incidents and minor mishaps which occurred during them; and, although he himself became more and more restricted to 'bench work' he never failed to urge young workers to go out into the field and collect. To him the 'living' animal or plant was the important thing and should be foremost in the mind of all biologists and, indeed, biochemists.

Caullery believed that the best training for a young worker was to study in depth a problem in which his results could be compared and checked with those of previous workers. He therefore set Keilin to work on the protozoa parasitic in earthworms of which ample material was readily available and, while much was already known about them, much more remained to be worked out and there was a need for a comprehensive treatment of this group bringing old and new knowledge together. While collecting for this study, Keilin came across many other free-living and parasitic organisms. He became especially interested in Diptera and was intrigued by the problems of their life-cycle and adaptations to special habitats, especially those correlated with the adaptation of the immature stages to the parasitic mode of life. He was occupied in these studies, which formed the basis of a thesis which he presented for the D.Sc. Degree in the Sorbonne in 1915, until he left Paris and came to Cambridge in February 1915. He was invited to Cambridge by G. H. F. Nuttall, then Quick Professor of Biology, at the instigation of Stanley

When he arrived in Cambridge he joined Nuttall in the Quick Laboratory and was given a Research Studentship in Medical Entomology, and later (1916) he was appointed Assistant to the Quick Professor. He joined Magdalene College and entered the University as an advanced student obtaining the B.A. Degree by research and, in due course, taking the M.A. Degree. In those days the Quick Laboratory was housed in a single large room in the old Department of Pathology occupying a corner position at the junction of Downing Street and Corn Exchange Street. In this single room, over-burdened with furniture and apparatus, over-crowded with workers, ill-heated and badly ventilated, Keilin began his work in Cambridge. However, in spite of the discomfort and lack of facilities, the laboratory was an active centre of research and their difficulties did not daunt the members. Many were the stories, related by Nuttall and Keilin in later years, of mishaps, sometimes amusing but often frustrating which the unstable floor, damp walls and vagaries of the 'plenum' system of ventilation brought about.

In 1921, Nuttall and other members of the Department moved to the newly founded and newly built Molteno Institute for Research in Parasitology where they had pleasant and convenient accommodation and, at that time, delightful and restful surroundings and better, albeit still inadequate, equipment.

Here Keilin continued to work until the end, as Nuttal had done. To both the end came suddenly and peacefully while they were still active mentally and physically, to Nuttall in 1937 at the age of 75 and to Keilin in 1963 also at the age of 75.

During these early years in Cambridge, Keilin was very insecure financially and was dependent on various grants. He held Beit Memorial Fellowships, first Junior and then Senior, from 1920 to 1927. In 1925 he was appointed University lecturer in Parasitology, the stipend of which even in those days would not by itself provide a competence, but it was supplemented by grants from the Medical Research Council. This was a very prolific period scientifically and papers on insects and protozoa appeared in rapid succession. He continued to hold this lectureship until 1931 when he succeeded Professor G. H. F. Nuttall as Quick Professor of Biology, the subject of study of the Professor now being changed from 'Parasitology' to the 'Study of the Biology of the Cell'. On his election to the Quick Professorship in 1931, Keilin also became Head of the Department of Parasitology and Director of the Molteno Institute and he held these three posts until he retired on reaching the age limit in 1952. Retirement from office did not mean retirement from active work in the laboratory and he continued full-time work with unabated zeal in the Molteno Institute until the end of his life.

When he became Quick Professor, Keilin was elected to a Professorial Fellowship in Magdalene College. In the College he found a congenial atmosphere and he very much enjoyed the friendly social and rich intellectual life and the contacts not only with distinguished workers in all fields of study but, more especially, with the younger members of the College whom he met there. A notable feature of both his social and scientific life was his interest in young workers in the throes of establishing themselves in their careers. Such people found in him a patient listener of their hopes, fears, achievements and difficulties and a ready store of sage advice and, also, a good humoured, teasing treatment which relieved tension and made problems assume a less formidable aspect. One of his constant admonitions to his more senior co-workers was always to keep in close and friendly association with young workers, not only to help them, but also to benefit from their critical attitude and fresh ideas. One of his outstanding traits was that of 'approachability' and during his long days in the laboratory, usually from 9 a.m. until 7 p.m. or later, even after his official retirement, anyone could walk into his room and be sure of receiving a sympathetic hearing, whether it was to announce a success or discuss a problem! It is true that at times he continued absentmindedly to shake the test-tube which was almost invariably in his hand and to glance wistfully at his idle spectroscope; but no one was ever denied a hearing or rebuffed. Consequently, it is not surprising that his own writing was mostly done early in the morning or late in the evening or when at rather rare intervals he stayed at home for a few days to devote his whole time to writing and from which almost penitential incarceration he thankfully returned to his laboratory to, as he expressed it, 'have a rest working at the bench'!

It is a curious coincidence that the year in which he was appointed University Lecturer in Parasitology is the year in which his work changed direction, from the previous mainly morphological studies of protists and insects, to more biochemical work or, as he preferred to term it, cellular biology, his special field of interest being respiratory carriers and respiratory catalysts in relation to cellular metabolism. The landmark in this divergence of effort is the publication in 1925 of the paper entitled 'Cytochrome, a respiratory pigment common to bacteria, yeast, higher plants and animals'.

In discussing Keilin's scientific achievements it will be convenient to consider first his purely biological work on protists and insects and later to deal with the cellular biology studies, although the two themes merge into one another and overlap to some degree.

PARIS 1909–15

Research on insects and protozoa

His first scientific publication was a short note describing the parasitism of the larval stages of the cluster fly (*Pollenia rudis*) in an earthworm, and it is interesting to note that the work on *Pollenia*, which was to provide the orientating theme for all his later studies, arose incidentally from his investigations on the protozoa of earthworms. After he had spent several years of intensive work on the subject, the appearance of Hesse's monograph in 1909, 'Contribution à l'étude des monocystidées des oligochètes' (*Arch. Zool. exp. gen.* **43**, 27–301), brought to Keilin the bitter realization that his work had been in vain and was forestalled by this fine monograph. To counter the natural disappointment at this setback, Keilin set to work to salvage the 'lost' effort by completing work on insects which he had come across incidentally while collecting material for his work on protozoa. Among them he had come across and bred out dipterous larvae parasitic in the earthworm *Allolobophora chlorotica*. The adults bred from these parasitic larvae proved to be

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great masses in autumn, but of which the life-cycle was completely unknown. He found that the mature female deposits eggs in soil in late August or early September where they hatch in 4–6 days. The young larvae burrow into the ground and enter the vesicula seminalis of the earthworm through the male genital pore. When the larva reaches the lumen of the genital segments, it enters a period of diapause which lasts throughout the winter until the following spring. Towards the end of April or beginning of May the larva becomes active, leaves the vesicula seminalis and migrates through the general body cavity to the anterior end of the worm. While traversing the anterior segments of the host, the larva has its posterior end directed forwards and when it reaches the prostomium, its posterior end ruptures the wall of the prostomium and thus puts the post-abdominal spiracles in contact with the air. The larva, once it has access to air, begins to grow rapidly, feeding on the worm which no longer eats or burrows. About 6 days later the larva moults to the second instar and about 9 days later the larva undergoes a second moult and enters the third instar. The larva has now become much larger, it feeds voraciously on all tissues of the worm and gradually becomes free from the body of the host. Finally, 9–10 days later, only the anterior two or three segments of the larva are attached to the remaining few posterior segments of the worm the rest of which has been eaten by the rapidly growing larva. The larva then becomes detached, buries itself deeper in the soil and pupates. The pupal stage lasts 35–45 days and then the adult fly emerges. There is apparently only one generation in the year; but possibly the flies which have overwintered may lay in the spring and give rise to a cycle similar to that arising from the reactivated diapausing larva. In any case, the larval winter diapause of the first-stage larva is controlled by the low temperature and at any point the larva may be reactivated and the cycle set in motion by putting the infected earthworm at a temperature of 19–21° C. In the laboratory flies emerged as early as January. This was a very exciting discovery and aroused great interest and, at first some disbelief, among entomologists both in Europe and America. It was also important in another respect as it focused Keilin's attention on two main themes which were to guide his future work. These were, first, adaptation of dipterous larvae to the parasitic mode of life and, secondly, the overriding importance of respiratory requirements in controlling the life-cycle of parasitic and free-living insects. Thus rapid growth is dependent on an ample supply of oxygen and, for example, the larva of *Pollenia* does not grow during the period of quiescence in the genital organs or during its migration to the prostomium when the supply of oxygen is limited but as soon as the spiracles are put in communication with the air, rapid growth begins. In much of his other work on Diptera the morphology of the tracheo-spiracular system was examined in relation to adaptation to respiratory needs and this work was drawn together in an outstanding paper on 'Respiratory systems and respiratory adaptations in larvae and pupae of Diptera' published in 1944. This morphological investigation was intended to be preliminary to later investigations on the physiological and biochemical aspects of insect respiration. However, when at an early stage of the physiological work, the discovery of 'cytochrome' aroused his interest in the more

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gradually reduced as the wider field of intracellular respiration became the main subject of research. Thus to the loss of entomologists, the plans for a second series of papers on the physiological and biochemical aspects of insect respiration were never realized.

Although the outline of the life-cycle of *Pollenia rudis* was published in 1909, the full and detailed study of this organism, and of the comparative biology of dipterous larvae, was not published until 1915 when it was presented as a Thesis for the Degree of 'Docteur ès Sciences Naturelles' in the Sorbonne and was published in the *Bulletin Scientifique de la France et de la Belgique.*

In the meantime a number of papers had been published, including a detailed study of the morphology of the larval stages of the genus *Phora* in which it is concluded that all larval and pupal characters of the Phoridae are typical of the Diptera Cyclorrhapha. Among many short papers are some pregnant with general ideas such as the importance of the ventral pharyngeal ridges in distinguishing between saprophagous and, as he termed them, 'biontophagous' larvae which feed on living organisms and another paper in which the adaptations of the larval stages of Anthomyidae are described, especially in relation to the carnivorous mode of life. Another paper in this period is a comparative account of the genus *Trichocera* in which it is shown that the larva is a true Eucephala and consequently the *Trichocera* should be removed from the Tipulidae and placed in the Eucephala, probably near the Rhyphidae (Anisopodidae). Another interesting note describes the larva of *Trichomyia urbica* which differs from larvae of other Psychodidae by living in the trunks of fallen trees in which it bores galleries and is xylophagous, whereas all the other genera have aquatic larvae.

In the major paper published in 1915, a number of interesting conclusions were drawn from the work on *Pollenia* and other dipterous larvae. The immune reaction of the earthworm to infection with the larva was described and it was emphasized that the young larva became surrounded by a phagocytic cyst formed by the worm and that, whereas the normal uninjured larva could pass the winter months within the cyst and break free in the spring, if a larva had been injured, by the mouthparts of another larva or otherwise, it might be destroyed by the phagocytes. Other general points discussed are the almost universal occurrence of three larval instars in cyclorrhaphous Diptera and the close correlation of the morphology of the larvae with the mode of life, especially as regards the cephalo-pharyngeal armature, so that it is often possible to determine the mode of life, biontophagous, predaceous, saprophagous or phytophagous, from an examination of the mouthparts. A very interesting discovery was of the occurrence on the ventral surface of the thoracic segments of dipterous larvae of three pairs of groups of three or four sensory hairs which were always associated with the openings of the stalks of the imaginal buds of the legs of the imago. This led Keilin to suggest that all organs, locomotory or otherwise, have, in addition to their obvious function, a primary sensory one and that when through parasitic or other adaptation the organs are lost, vestiges of them remain in the form of sensory structures, such as setae or papillae. The lack of external appendages and the very simple sensory organs found in cyclorrhaphous larvae and other structural features led him to put forward the suggestion that all

Cyclorrhapha have, in the course of their phylogeny, had parasitic larvae in which adaptation had resulted in the loss of external appendages and mouth parts and great reduction in the sense organs; and that the existing free-living dipterous larvae have become so by secondary adaptation. This secondary adaptation to the free-living mode of life by the acquisition of new methods of locomotion and new, cuticular, mouthparts and so on, he regarded as verification of 'Dollo's law of the irreversibility of evolution'.

This was the culmination of his work in Paris, which was almost entirely devoted to insects. The rich variety of forms dealt with and of new life-cycles described he attributed not to 'luck', as some other workers believed, but to the fact that his collecting was largely done in the small garden of the laboratory situated in the shadow of the Panthéon and surrounded by the large built-up area of the Quartier Latin. This little garden was thus a kind of biological oasis in which a concentrated fauna and flora developed and in which the close proximity of the various organisms arising from continual breeding in a limited area gave the maximum opportunity for infection and, also, for the collector to obtain all stages of the organisms easily. In less restricted areas dispersal would very much reduce the chances of so readily obtaining different stages of the life-cycles of either free-living or parasitic forms.

CAMBRIDGE 1915–25

Research on insects and protists

His early years in Cambridge were spent in similar work and during them he described the morphology and life-cycles of many hitherto unknown or incompletely known dipterous larvae and also of a number of very interesting protists most of which occurred as parasites of dipterous larvae. In this period, also, he attributed his success to the exploitation of natural, limited habitats, notably rot-holes and slime fluxes of trees, which, as he said, formed veritable 'cultures' in which the different organisms pullulated in close proximity so that there was every opportunity for transmission of parasites. Thus all stages of both hosts and parasites occurred in a small area and could be collected relatively easily.

The number of new organisms and new life-cycles he described led one of his entomological friends to remark that Keilin found more new species within a few minutes walk of the laboratory than had been done by some expeditions to distant lands! Keilin himself deprecated the view sometimes expressed by others that he had been very 'lucky' to find so many new organisms and he attributed his success to the selection of suitable habitats and an intensive investigation of the fauna and microflora occurring therein. Indeed, he always advised young workers to base their research whenever possible on material which was readily available, preferably in the living state, and to avoid problems where difficulties of obtaining supplies limited the work. He also believed that workers should study intensively their field of research until, as he expressed it, 'they dominated the subject'.

The ten years after his arrival in Cambridge were very productive ones and only a few of the more important of them can be mentioned here. It was during this period that he completed all his practical work on entomology, although some of his results were not published until much later or were extended by co-workers and published jointly.

The main publications tended to be biological and comparative morphological studies of dipterous larvae, although a number of papers dealt with protists and some with nematodes. A paper of much interest was 'Recherches sur les Anthomyides à larves carnivores' comprising comparative studies of the biology and morphology of the early stages of the genera *Melanochelia*, *Graphomyia*, *Allognota*, *Phaonia*, *Myospila*, *Mydaea*, *Hydrotaea* and *Muscina*. The general conclusion is that although many Anthomyia larvae live in the most varied decomposing materials, in fact the larval stages are often not saprophagous but are carnivorous and feed by predation on other animals living saprophagously in the same medium, most commonly on dipterous larvae. He showed how morphological characters, especially of the bucco-pharyngeal armature, are correlated with the mode of life and allow the habits of the larvae to be deduced from study of their structure.

It was also shown that some of the genera, *Hydrotaea* and *Muscina*, differ from the truly carnivorous forms. They show characters intermediate between carnivorous and saprophagous forms and may feed both saprophagously and carnivorously. These larvae he termed 'semi-carnivorous'. Other genera with larvae belonging to this group were described later (with P. T.), including *Ophyra*, *Polietes* and *Mesembrina*. Other papers on Diptera include a comparative account of the larvae of *Trichomyia*, *Psychoda* and *Phlebotomus*; and of the early stages of the families Trichoceridae and Anisopodidae (both with P. T.). During the First World War Keilin joined in work of military importance being carried out under Nuttall in the Quick Laboratory and these studies led to the publication, with Nuttall, of a paper on 'Hermaphroditism and other abnormalities in *Pediculus humanus*' based on a detailed examination of 155 hermaphrodites, of which some were found in 'wild' populations of lice, some in lice bred in the Quick Laboratory and 123 in material comprising the progeny from crosses of *P. corporis* and *P. capitis* received from A. Bacot. The conclusions arrived at were that a complete gradation could be recognized in the hermaphrodites from the male type passing through types with co-existing characters of both sexes in a varying degree to the female type. All the hermaphrodites could be classified as belonging to Friese's 'Mixed Gynandromorphs'. It was notable that the state of development of the gonads in the hermaphrodites did not accord with that of the secondary sexual organs. As Nuttall and Keilin found that in 'wild' lice the hermaphrodites formed only 0·2–8 % of the lots in which they occurred, whereas in the crosses between *P. corporis* and *P. capitis* in some families over 20 % were hermaphrodites, they concluded that the hermaphrodites occasionally found among 'wild' populations are derived from fortuitous crosses between *corporis* and *capitis*.

Nuttall and Keilin had planned to produce a large monographical study on *Pediculus humanus* and much work had been done on the subject but other interests diverted both authors and, finally, the incomplete work was published in 1930 as

'Iconographic studies of *Pediculus humanus*' in which the beautiful and exact illustrations, many of them drawn by Keilin, reach the highest standard of scientific illustration.

Towards the end of this period his interest was turning towards the more physiological and biochemical aspects of insect respiration and he had begun to concentrate on experimental work on the subject; but to clear the ground, so to speak, he had been preparing a major work on the morphological and biological results of his studies on Diptera. This work was first written in French and remained unpublished for many years owing to the increasing effort devoted to the cellular biology studies. It was not until 1944 that this paper 'Respiratory systems and respiratory adaptations in larvae and pupae of Diptera' appeared in print. It is an indication of Keilin's capacity for work and absorption in scientific pursuits that the revision of the manuscript, translating it from French to English and bringing the literature up to date, was done as a pastime to relieve the tedium when illness kept him away from the laboratory.

This paper, besides containing much original work and new ideas and generalizations, summarized in a brief and cogent form all the important previous work on the subject, so that it is an important vantage point for all later workers in this field. It would occupy too much space to attempt to summarize this paper but a few of the outstanding conclusions may be mentioned. It is divided into two parts, 'Part 1. Respiratory systems in dipterous larvae', and 'Part 2. Respiratory adaptations of larvae and pupae of Diptera'. Some of the generalizations arising from the survey of the respiratory systems in Diptera are that from the time the larva hatches all the tracheo-spiracular metameres are present, arising from either functional or non-functional spiracles and that in all stages the total number of tracheo-spiracular metameres is ten pairs.

Spiracles which become functional after a moult are always formed from pre-existing spiracles which may have been functional or non-functional. The metathoracic spiracles of dipterous larvae, except in the Bibionidae, are non-functional in all stages of the larva, but become functional in the imago. The mesothoracic spiracles and their tracheal metameres are absent in all larval stages. In dipterous larvae the metapneustic system appears as the first stage of development in all respiratory systems except the apneustic. It is notable that there are no transition stages between the oligopneustic and polypneustic systems during larval development. The seven pairs of abdominal spiracles are either all functional or all closed. The development of the hemipneustic systems differs from that of other polypneustic systems by passing through a propneustic stage. In the course of development of different respiratory systems, the functional spiracles appear in the order of their morphological and physiological importance.

To explain the occurrence of 10 pairs of spiracles in dipterous larvae composed of 11 metameres and the absence of spiracles from the mesothorax, Keilin postulated that the spiracles were primarily intersegmental, as 11 segments would provide only 10 intersegmental spaces. If during evolution the spiracles moved from their primary position by migrating on to the segments, one segment would be left without spiracles and, if the first pair of spiracles moved anteriorly on to the first thoracic segment and the remaining nine pairs posteriorly to the third thoracic and eight abdominal segments, the full polypneustic system would be formed with a *pair of spiracles on the prothoracic, metathoracic and eight abdominal segments*, and the mesothorax would be devoid of spiracles. Thus, the basic pattern for the tracheo-spiracular systems of dipterous larvae would arise and from it the various other systems could evolve by reduction in the number of functional spiracles during the various stages of development. It is true that this interesting suggestion has not received general acceptance but it was a very stimulating idea and can still serve as a basis for further work on the problem of the origin of the tracheo-spiracular system.

In 'Part 2. Respiratory adaptations of larvae and pupae of Diptera' the adaptations of dipterous larvae to the aquatic and parasitic modes of life (including parasitism in earthworms, snails, terrestial and aquatic arthropods, Amphibia, reptiles, birds and mammals) are discussed and so also are the adaptations of larvae in viviparous Diptera and the adaptations of pupae of Diptera. He points out that the great majority of species with parasitic larvae belong to the Cyclorrhapha, whereas among the Orthorrhapha larvae with a truly parasitic habit are very uncommon.

In the parasitic dipterous larvae the dominating factor in the respiratory adaptation is 'that usually they cannot feed and grow actively without bringing their highly developed tracheo-spiracular system into communication with air. This is reflected in certain structural features of these larvae, their behaviour within the host and their life histories'. This is contrasted with what is found in Hymenoptera in which 'on the whole the respiratory requirements of parasitic hymenopterous larvae, unlike those of dipterous larvae, affect very little their inter-relationships with the host or their life history'. This difference may be explained by the facts that as hymenopterous larvae are not very active, they have comparatively low respiratory requirements which are easily satisfied by the amount of oxygen dissolved in the surrounding medium, and the thin cuticle of the body facilitates gas exchange.

Finally, he considers some exceptions to the generally accepted view that 'the polypneustic or more primitive respiratory systems characterize the terrestrial mode of life, while the oligo- or apneustic systems which derive from it mark a subsequent adaptation of these insects to a submerged life in a fluid or semifluid medium'. He decides that these exceptional cases can be explained by re-adaptation of aquatic forms to a terrestial life and that in this process they evolve new adaptations and do not revert to the more primitive respiratory systems, thus conforming with Dollo's generalization on the irreversibility of evolution.

Consideration of the problem of the origin of nematodes led Keilin to suggest that existing free-living Nematoda are not primitive but are derived from parasitic forms by a secondary re-adaptation to the free mode of life. Thus the Nematoda 'would be derived from a group of free-living organisms which have gradually adapted themselves to parasitism. In consequence of parasitic adaptation the whole structure of these animals has undergone a very marked modification which may be termed "parasitic specialisation". Subsequently, for an unknown reason, some of these parasitic forms have gradually reverted to the free mode of life, in other words, have become free-living by a secondary readaptation. They have not, however, reacquired the characters of the primitive free-living group to which they at first belonged, but have readapted themselves to the old mode of life with the means afforded by their specialised new morphology.' In the same paper he discussed the view advanced by some authors that the Nematoda are derived from Arthropoda and concluded: 'Though it appears to me that we cannot accept the view of the Arthropod origin of Nematodes, I do not propose to advance any other phylogenetic hypothesis which will be more acceptable.'

'All we can say at present is that the systematic position of Nematodes still offers a problem for further investigation. The assumption that the actually free-living Nematodes are derived from parasitic forms, and that the primitive free-living stock of organisms from which the latter have originated has completely disappeared, merely emphasizes the difficulty in connecting the Nematodes with any known group of Invertebrates.' His interest in this problem was stimulated by his own work on an interesting nematode, *Aproctonema entomophagum*, which he described as a parasite of larvae of the mycetophilid fly *Sciara pullula*.

Keilin's work on Protista was mainly incidental to his studies on dipterous larvae and was accomplished between 1914 and 1923. It is remarkable that in the eleven papers published during this period he described no less than eight new genera and twelve new species of protists, all of which occurred as parasites of insect larvae. These papers display a mastery of microscopical technique, powers of acute observation and fine draughtsmanship together with an exceptionally wide knowledge of biology and a readiness to tackle problems in fields far from his main subject. This breadth of outlook may be seen from a list of species described:

Fungi *Monosporella unicuspidata* gen.nov., sp.nov.
Coelomomyces stegomyiae gen.nov., sp.nov.
Helicosporidium parasiticum gen.nov., sp.nov.

Protozoa
Amoebaea. *Entamoeba mesnili* sp.nov.
Gregarinomorpha. *Leidyana tinei* sp.nov.
Dendrorhynchus systeni gen.nov., sp.nov.
Caulleryella aphiochaetae gen.nov., sp.nov.
Allantocystis dasyhelei gen.nov., sp.nov.
Schizocystis legeri sp.nov.
Lipotropha macrospora gen.nov., sp.nov.
Lipotropha microspora sp.nov.
Ciliata. *Lambornella stegomyiae* gen.nov., sp.nov.

The advantage of exploiting restricted habitats is emphasized by the fact that five of the new genera and seven of the new species were found in larvae living in slime fluxes from wounds in two trees. Special mention must be made of two of these organisms. *Helicosporidium parasiticum* differs markedly from all known protists and Keilin considered that it formed a new type of organism which could be temporarily included in the Sporozoa but now it is considered to be a fungus allied to *Monosporella* (Weiser, personal communication). The elucidation of the morphology of this organism and especially of the structure of the spore, was a most exacting task in microscopy. Thus, Keilin showed that the spore which when mature is only 5–6 μ in longest diameter contains three disk-shaped central cells (sporozoites) surrounded by a spirally coiled filament measuring $60 \times 1\,\mu$ when unrolled and has a fine, transparent surrounding membrane (sporocyst). He believed that the central cells are the infective stage of the parasite and that the function of the spiral filament is to rupture the outer membrane during dehiscence of the spore. The sporozoites are ingested by the host larvae, probably reach the body cavity by penetrating the wall of the gut and there enter on the schizogonic cycle which precedes spore formation.

The other organism of special interest is *Coelomomyces stegomyiae* which Keilin described from a single larva collected by W. A. Lamborn in Malaya and sent to Keilin as the larva of *Stegomyia scutellaris* Walker. Keilin considered that it was a fungus, probably belonging to the Phycomycetes but showing some resemblance to the Chytridinae. Since Keilin's original description as many as twenty-three named species have been described, and it is placed among the aquatic fungi belonging to the order Blastocladiales. All species so far known are parasitic in mosquitoes, with three exceptions, one in the hemipteran *Notonecta* and two in larvae of the flies *Simulium metallicum* and *Chironomus paraplumosus*. The mosquito hosts belong to forty-six genera, but twenty-five of the host species belong to the genus *Anopheles*. The parasite is widely distributed and has been recorded from all continents except South America. The possibility of using it as a means of biological control of mosquitoes has aroused much interest and experiments with this end in view have been carried out in various parts of the world. Unfortunately, the failure so far to cultivate the organism and the difficulty of obtaining infection of mosquitoes under laboratory conditions have made the results inconclusive.

Although he made no claim to be expert in systematics, his perspicacity in classifying the newly described protists is shown by the fact that all but two of the new generic and specific names he proposed are still valid; *Entamoeba mesnili* has been placed in a new genus, *Dobellina*, and *Lambornella* in the genus *Tetrahymena*.

In the early years of the decade 1921–30, his interest began to be more directed to experimental work and he published papers on the nephrocytes in larvae and pupae of the fly *Lonchaea chorea*, on the absence of paedogenetic multiplication in the blow-fly (*Calliphora erythrocephala*) and on the appearance of gas in the tracheae of insects. At this time he was intrigued by the respiratory adaptations of the larvae of the horse bot-fly (*Gasterophilus intestinalis*) which, after a long migration involving the tongue and pharynx of the host, settles in the stomach as a young second-stage larva and there becomes fixed to the wall by its mouthparts, grows, undergoes a second moult and develops into a mature third-stage larva increasing in weight from about 10 to 450 mg or more. In early summer the mature larvae are passed out in the faeces, they burrow into the soil, pupate and the adult flies emerge after 4–5 weeks. Eggs are laid attached to hairs on the legs of horses and hatch when the horse licks the area. The first-stage larva burrows into the tongue,

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migrates to the pharynx and from thence to the stomach, which it reaches about September. For the 7 months or more which the larvae spend in the stomach they are dependent for oxygen on the bubbles of air which the host swallows with its food and the posterior spiracles are adapted to enable them to open in contact with air but to close tightly when submerged in liquid. The larva is also provided with special tracheal cells which contain haemoglobin which enables the larva to store oxygen in a form available for use when the larva has no contact with air bubbles.

CAMBRIDGE 1925–63

Research on cellular biology

The life-cycle of *Gasterophilus* has been described in some detail because it was the study of the respiratory requirements of the larvae in the stomach of the horse that led Keilin to the discovery of cytochrome and set him on the road to his future important biochemical work in the field of cellular biology and, more especially, problems of intracellular respiration and the role therein of metallo-protein compounds. These problems are fundamental ones common to all living matter and success in studying them depends to a large extent upon the selection of suitable material for experimental work. It is therefore understandable that from now onwards Keilin did not restrict his work to insects or parasitic organisms but utilized biological material which was readily available in quantity and was suitable for spectroscopic and manometric techniques. Such material he found largely in yeast, bacteria, heart-muscle tissue and preparations from various plants as well as haemoglobin from blood and other cells of various organisms. Nevertheless, whenever possible the results obtained were checked by direct observation on the intact living organism. He had a great respect for yeast as a tool in biochemical research and was insistent that almost all vital processes could be found in the intact yeast cell.

This phase of his work occupied him for the next 40 years until his death after a morning spent at his bench in the laboratory. During this period he attracted many co-workers from all over the world, some for short visits and some for a number of years, whilst Dr E. F. Hartree who joined him in 1934 collaborated with him for the next 30 years, Dr H. Laser joined the laboratory in the same year and Dr T. R. R. Mann in 1935. In Cambridge he established close relationships with Dr M. Dixon and Dr R. Hill of the Department of Biochemistry, both of whom collaborated with him on certain aspects of the work. As well over 200 papers were published from the laboratory by Keilin and his co-workers in this period, it would be impossible to summarize all the work and only some of the most outstanding contributions in which Keilin himself was actively engaged will be mentioned here.

The importance of this work on cellular biology was generally acknowledged and it was generously supported financially by the Rockefeller Foundation and, in later years, by the Nuffield Foundation, the Wellcome Trust and an anonymous donor in the U.S.A. Special additional grants were obtained at times from the Medical Research Council, the Agricultural Research Council, and the Royal Society.

As has already been mentioned, Keilin's entry into the field of intracellular respiration resulted from his study of the respiratory system of the larva of the horse bot-fly (*Gasterophilus intestinalis*). He was trying to determine spectroscopically whether the haemoglobin which is present in the tracheal cells of this larva is synthesized by the larva or is derived from the haemoglobin of the horse within which the larva lives. He noticed that another substance was present which showed a spectrum with strong absorption bands which were visible spectroscopically under reducing conditions, whereas under these conditions the characteristic spectrum of haemoglobin would be almost imperceptible. On the contrary, the strong, characteristic absorption bands of the new substance almost disappeared on oxidation, that is, under conditions in which the absorption bands of oxy-haemoglobin would be plainly shown. He soon found that this new substance was present in animal tissues, in bacteria, in yeast and in plants. As the change from the oxidized to the reduced state could be followed spectroscopically, it was possible to see its oxidation and reduction in living cells. Not only could these changes be seen in suspensions of cells but Keilin could demonstrate directly under the micro-spectroscope the oxidation and reduction of this substance in the wing muscles of the wax moth (*Galleria mellonella*) during periods of rest and activity of these muscles.

He named this substance cytochrome because it is a pigment which occurs almost universally in cells of aerobic organisms. He described cytochrome as comprising three components (*a*, *b* and *c*). Each component is an iron–porphyrin–protein compound and each differs from the others in the porphyrin and in the protein parts. This very important discovery was published in 1925 in a paper entitled 'Cytochrome, a respiratory pigment common to bacteria, yeast, higher plants and animals'.

Studies of the reactions of cytochrome led Keilin to conclude: 'Thus the cytochrome system of aerobic cells provides the main natural pathway for hydrogen or electron transfer from molecules of substrate to oxygen.' This reconciled the rival theories of cellular respiration then current, that of hydrogen activation (Wieland–Thunberg), and that of oxygen activation (Warburg), since it demonstrated that they were really two portions of the same respiratory system. Later another component, a_3 which, unlike components *a*, *b* and *c*, is autoxidisable, was described (with E. F. Hartree) and strong support was adduced for its identity with cytochrome oxidase or Warburg's oxygen-transporting enzyme.

This work on cytochrome was so fundamental that it may be said to have started a new era in the development of our knowledge of cellular respiration. Not only did his research on haemo-proteins set in train a vast amount of work on respiratory mechanisms but it also stimulated much work in other fields of biochemistry.

The component *c* of cytochrome is easily extractable from tissues and methods for its isolation and purification, first from bakers' yeast (with R. Hill) and later from heart muscle (with E. F. Hartree) were devised and it was possible to study in detail its catalytic activities and other biochemical properties. The 'first demonstration of direct rapid oxido-reduction reactions between iron atoms forming part of different haem-protein molecules' was given (with E. F. Hartree) when it was shown that when reduced cytochrome *c*, which is not autoxidizable, was added to colloidal suspensions of tissue preparations it immediately becomes oxidized. It was further shown that the oxidation of aromatic amines, giving the '*indophenol reaction*' with 'Nadi' reagent, which had hitherto been attributed to the so-called *indophenol oxidase*, is brought about by the cytochrome system, especially its components a_3 and *c*. It was found that the haemoglobin-free heart muscle preparation contains a complete dehydrogenase-cytochrome system but is devoid of substrate and, consequently, cytochrome is in the fully oxidized state. On the addition of succinic acid, as substrate, cytochrome rapidly becomes reduced but reoxidizes on shaking in air. He concludes that 'the succinic dehydrogenase-cytochrome system of the heart muscle preparation behaves in every respect like a cellular respiratory system'. Later (with Tsoo E. King) the results on dehydrogenase were extended by studies on the reconstitution of the succinic oxidase system from soluble succinic dehydrogenase and a particulate cytochrome system preparation and on the effect of inhibitors on the reconstituted system.

Studies on intracellular respiratory catalysts were helped greatly by Keilin's investigation on carbon monoxide as an inhibitor of respiration and of the activity of certain metallo-enzymes which often makes it possible to determine the specific property of one of several metallo-proteins involved in cellular metabolism.

In the study of other intracellular catalysts it was shown that peroxidase is a haematin-protein compound very closely resembling methaemoglobin (oxidized haemoglobin) and that it forms compounds with the substrate hydrogen peroxide which are spectroscopically identifiable and this provided a direct visual demonstration of union between an enzyme and its substrate (with T. Mann). Catalase, another widely distributed enzyme was also studied (with E. F. Hartree), and it was shown that contrary to the general view, the function of catalase is not the decomposition of hydrogen peroxide, which occurs only in the presence of comparatively high concentrations of hydrogen peroxide, but that under normal physiological conditions, when hydrogen peroxide is generated slowly, the reaction of catalase serves to utilize it for the peroxidatic oxidation of certain substances such as the lower alcohols. A detailed comparative study of catalase, peroxidase and methaemoglobin was published later; and also a study of catalase, peroxidase and metmyoglobin as catalysts of coupled peroxidatic reactions (with E. F. Hartree).

Work was also directed to non-haematin containing enzymes and (with T. Mann) carbonic anhydrase, the nature of which had hitherto been unknown, was isolated in a pure state from red blood corpuscles of mammals and shown to be a zinc-protein compound. Although the presence of zinc in organisms had been known for many years, the demonstration of its presence in carbonic anhydrase was the first indication of its biological significance and established at least one function of this metal in organisms. Another interesting finding was that sulphanilamide acts as a very powerful, highly specific and perfectly reversible inhibitor of carbonic anhydrase (with T. Mann). The blackening of crushed or cut tissues of some plants, or of the latex of some plants and the blood of some invertebrates when exposed to air, is due to the oxidation of some phenolic substances present in tissues, latex or blood by enzymes known as phenol oxidases. Pure polyphenol oxidase was isolated from cultivated mushrooms and it was shown to be a copper-protein compound, as had previously been shown by Kubowitz for the polyphenol oxidase of potatoes. A similar study (also with T. Mann) of the enzyme laccase from the latex of Japanese and Indo-Chinese lacquer trees proved, in spite of the difficulty in handling the latex which rapidly induces sensitivity and acute dermatitis unless great precautions are taken, that the metal of the active group of the enzyme is not manganese as had been believed by Bertrand, but is copper. Another copper-protein compound was isolated from red blood-corpuscles and described under the name haemocuprein (with T. Mann).

Meantime, interest in haemoglobin had not abated and, in fact, haemoglobin, its derivatives and reactions, served as a 'model' upon which to base work on the other metallo-protein compounds. The haemoglobin from *Gasterophilus* larvae was purified and its properties determined (with Y. L. Wang). Its molecular weight was found to be about 34 000; it contains only two haem nuclei per molecule, it has a very high affinity for oxygen and a very low affinity for carbon monoxide. Thus it differs greatly from horse haemoglobin and must be a product of the larva. Similarly, the haemoglobin occurring in some protozoa was studied (with J. F. Ryley) and its properties defined. Another problem studied was the red pigment in root nodules of leguminous plants which Kubo had shown to be a haemoprotein resembling haemoglobin. The pigment was extracted from root nodules of soya beans and purified and it was found to be a true haemoglobin combining reversibility with oxygen for which it has a very great affinity.

The wide but discontinuous distribution of haemoglobin in nature and the occurrence of other pigments with similar properties was reviewed in a paper entitled 'Distribution and diversity of haemoglobin'. Conclusions of general biological interest arrived at in this review are that 'the term haemoglobin can be adopted for all haemoproteins with protohaem as their prosthetic group and capable of combining reversibly with molecular oxygen'. The sporadic distribution of haemoglobin outside the vertebrates is interpreted as showing that haemoglobin could arise in nature independently in different organisms. This is not surprising because every aerobic organism and even some anaerobic organisms are to some extent potential producers of haemoglobin since all these organisms contain cytochrome components which are haemoproteins closely related to haemoglobin. Thus 'the fact that haemoglobin is not universally present is mainly due to the comparatively limited distribution of the highly specific proteins which, when united with haem, impart to its iron the remarkable property of combining reversibly with molecular oxygen'.

Advantage was taken of the chance availability of sealed ampoules of blood taken aseptically 24–45 years before (in connexion with Nuttall's work on blood immunity and blood relationship) to study (also with Wang) the stability of haemoglobin and of certain enzymes in blood. This investigation revealed that the oxygen capacity and oxygen dissociation curves of haemoglobin in such samples were the same as in fresh blood; that from a sample of guinea-pig blood 44 years old oxyhaemoglobin crystallized in the characteristic tetrahedral form; and, even more interesting, that the endo-erythrocytic enzymes such as catalase, carbonic anhydrase, glyoxalase and choline esterase had retained up to 85 % of their original activity. This problem of the stability of proteins and its implications to problems of resistance and quiescence of spores or other resistant forms of organisms greatly interested Keilin and he incorporated his ideas on the subject in his Leeuwenhoek Lecture of the Royal Society (1959) entitled 'The problem of anabiosis or latent life: history and current concept' in which he introduced the term *cryptobiosis* 'for the state of an organism when it shows no visible signs of life and when its metabolic activity becomes hardly measurable or comes reversibly to a standstill'.

The application of low temperatures to the study of absorption spectra was an important innovation. At the temperature of liquid air there is marked sharpening of absorption bands in the visible region of the spectrum. Thus when biological material was dissolved or suspended in aqueous glycerol, cooled rapidly in liquid air to a solid glass-like structure and then allowed to devitrify by warming to a microcrystalline mass, recooled to stabilize this and examined spectroscopically, the absorption bands become greatly sharpened and are intensified more than twenty times. By using this method it was possible

'(i) To detect and estimate cytochrome in cells of low respiratory activity such as spores of certain bacteria and tissues of parasitic helminths.

'(ii) To reveal the presence of a new, widely distributed, component (*e*) [now c_1] of cytochrome.

'(iii) To observe directly catalase in perfused haemoglobin-free liver and peroxidase in strips of horse-radish roots.

'(iv) To establish certain important features of methaemoglobin, catalase, and peroxidase.'

Keilin's ability to recognize the possibilities of an advance in one line of work being used as a tool for unravelling other problems is also shown by the extensive study of the enzyme 'notatin' or glucose oxidase (with E. F. Hartree). It was found that of the fifty sugars tested only glucose was rapidly oxidized, the reaction consisting of the quantitative oxidation of glucose to gluconic acid by oxygen which is reduced to hydrogen peroxide. This property was utilized not only as providing a rapid manometric method for the estimation of glucose directly in biological fluids containing other carbohydrates and proteins, but as a means of producing hydrogen peroxide for studying the reactions catalysed by catalase, especially the peroxidatic properties of catalase (with E. F. Hartree) and the reactions of this enzyme with hydrogen peroxide and hydrogen donors (with P. Nicholls).

Perhaps appropriately, Keilin's last communication published during his life was on cytochrome, and comprised a study (with W. D. Butt) on the absorption spectra and some other properties of cytochrome *c* and of its compounds with ligands.

For some years before his death Keilin had been writing a book surveying the origin and development of knowledge of respiration. The manuscript of this book has been edited and prepared for publication by his daughter, Dr Joan Keilin, and it will soon be published by the Cambridge University Press under the title *The History of Cell Respiration and Cytochrome*.

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CAMBRIDGE 1915–63

General activities

In addition to the wide range of work in which Keilin personally participated and published under his own name or as joint author, he stimulated and initiated and often supervised, a great volume of research on very diverse topics. In entomology among research students who worked under his supervision were L. G. Saunders, on Ceratopogoninae; J. M. Puri, on Simuliidae; S. Madwar, on Mycetophilidae; S. Sharif, on Pulicidae; G. W. Otter, on Cecidomyidae; M. L. Bhatia, on Syrphidae and L. Levenbook, on insect biochemistry. He also organized, for the Medical Research Council, work on the chemotherapy of malaria, at first, from 1928–37, with Mary Vincent and P. Tate. Later, in 1937, this work was taken over by Ann Bishop who had joined the Molteno Institute in 1929 to study Protozoa.

It would be impossible to detail the work of those associated with him on the biochemical side but special mention may be made of E. F. Hartree, H. Laser, T. Mann, E. C. Slater, for many years in the Molteno Institute, and P. George, F. A. Holton, P. Nicholls, W. D. Butt and M. H. Smith who worked in the Institute for periods of two or more years. R. Hill and M. Dixon, from the Department of Biochemistry, collaborated with him on some problems and were always in close contact along their lines of mutual interest. Visitors from overseas were numerous, especially in the post-war years and while some of them stayed for only short periods, others remained for a number of years. They included F. J. Stare, F. B. Straub, E. L. Smith, A. Lwoff, H. I. Kohn, W. P. Rogers, Y. L. Wang, J. Ettori, J. W. Legge, A. J. Rosenberg, D. I. Arnon, Britton Chance, A. Tissières, C. L. Tsou, D. B. Morell, C. Liébecq, H. Borei, W. D. Bonner, F. B. Finkle, C. H. Chin, W. E. Knox, E. Margoliash, P. B. Scutt, H. A. Bern, T. P. and E. K. Singer, E. Leone, R. H. Burris, E. Lucile Smith, D. G. Shappirio, Tsoo E. King, R. W. Estabrook, M. Morrison and A M. Clark.

Keilin's interests ranged far beyond his own immediate lines of work and he was always ready to encourage and help in the development of new lines of approach to biological problems. Thus, the Agricultural Research Council's Virus Research Unit owes much to the encouragement and help it received in the Molteno Institute in its early years when Kenneth Smith and Roy Markham found there accommodation and facilities for biochemical and biophysical investigations which were not available to them elsewhere. Similarly, M. F. Perutz and J. C. Kendrew worked in the Molteno Institute for some time during the early stages of their work on molecular biology and were greatly helped by the facilities available and by the encouragement and support they received from Keilin who was, naturally, intensely interested in their work on haemoglobin. He also greatly helped in the development of the research on the biochemistry and physiology of reproduction carried out by T. R. R. Mann and C. Lutwak-Mann on behalf of the Agricultural Research Council.

In spite of his love of 'bench-work' in the laboratory, Keilin always took a very active part in teaching and he valued the contact with young and enthusiastic students which lecturing and demonstrating ensured. He lectured on parasitology to candidates for the Cambridge Diploma in Tropical Medicine and Hygiene until 1931 when this Diploma was discontinued as well as giving short courses for the Natural Sciences Tripos Part II for candidates reading pathology and zoology and, indeed, he continued these lectures until 1936. In 1937 he began a series on 'Respiration and respiratory carriers' which soon grew to a course of sixteen lectures with demonstrations and was extremely popular not only with undergraduates but with research workers from many departments. These lectures were illustrated with striking and meticulously prepared demonstrations which were greatly appreciated by the large audiences who attended this course. The demonstrations were prepared in conjunction with E. F. Hartree and in later years some of the lectures were given by E. F. Hartree, E. C. Slater, R. Hill and P. Nicholls. Although his lectures were models of lucidity and careful preparation, perhaps Keilin was at his best after the lecture when spontaneous discussion developed with a small number of those especially interested in the subject. Then, the passage of time was forgotten and the discussion ranged far and never failed to clarify the problems and provide a stimulus to further experiments. This course continued until 1958. In spite of preoccupation with cellular biology, he maintained his interest in parasitology and, having assisted Nuttall for many years, he became editor of *Parasitology* in 1934 and continued this onerous task until the end.

Keilin was really in his element when engaged in actual work at the laboratory bench, either in the preparatory work or manipulating instruments such as manometers, more especially standing at his microspectroscope, his spectacles pushed up on his forehead, and shaking a reaction mixture in a test-tube! He claimed that his best ideas came to him while actually manipulating instruments. He always tended to use the simplest possible instruments and techniques available and had great faith in the value of the human eye and the direct vision spectroscope; in fact, he attributed much of his success to his use of the microspectroscope for all his preliminary work as in a high dispersion instrument the bands would be too diffuse to be easily seen. He was a very neat and tidy worker and however late he worked, his bench was cleared and left ready for work the next day. He was small in stature but compactly built, quick in movement and had noticeably delicate hands capable of the finest manipulations with neatness and dexterity. In all his work he set himself the highest standards and he was the sternest critic of his own results, foreseeing and testing every possible objection to the experiments and reasoning. Likewise, in the writing of manuscripts no time or trouble was spared to produce the characteristically clear and concise, yet elegant, phraseology of his published work. He always wrote the early drafts in pencil with the liberal use of an eraser, so that sentences and paragraphs could be written and rewritten time after time until they expressed his precise meaning. Frequently, manuscripts were laid aside for long periods before final revision and publication. He expected, sometimes vainly, that others would set themselves the same high standards as he did and this was soon appreciated by those who worked with him. With careless or badly presented work he had no sympathy and little patience; but he would go to endless trouble to help the willing worker to raise the standard of his experimental work and to present the results to the best advantage.

Among his outstanding characteristics were a persistent optimism, a deep devotion to science which made a bond between himself and all with the same devotion, a prodigous memory and a complete absence of any trace of pomposity or self-importance. Those in difficulties found it easy to confide in him and he had the gift of restoring confidence and imparting some of his own never failing enthusiasm to others. All ages and all ranks received the same patient and sympathetic hearing, sound advice and encouragement. He had a great capacity for disentangling complex problems and for suggesting new lines of approach and crucial experiments which would throw fresh light on the most difficult problems. This tolerant and sympathetic attitude pervaded the whole Institute and fostered the close and enduring ties of affection and loyalty which those who worked in the Institute, even for only short periods, felt thereafter towards Keilin and the Molteno Institute.

His liability to asthma reduced his capacity for outdoor activities and he travelled little, but he never let this disability curtail his research or, indeed, his academic responsibilities and he took a full share in the work of numerous University Boards and Committees and also took great pleasure in sharing in the social life of Magdalene College of which he was made an Honorary Fellow in 1957, an honour which greatly pleased him. His knowledge of languages enabled him to read widely in French, Polish and Russian literature as well as English. Much of his reading was done at night during the long hours when asthma kept him awake. He was appreciative of natural beauty and got much pleasure from short walks in the country; but he probably got most satisfaction, and even aesthetic pleasure, from a 'good experiment' and from discussion with a few close scientific friends.

The acclaim of his scientific achievements was international and was expressed by honours bestowed on him both at home and abroad. He was elected a Fellow of the Royal Society in 1928, was Croonian Lecturer in 1934, received the Royal Medal in 1939, the Copley Medal in 1952 and was Leeuwenhock Lecturer in 1958. He was elected an Honorary Member of the Society for General Microbiology in 1958. In 1947 he was made Membre Correspondant and, in 1955, Membre Associé Etranger of the Académie des Sciences, Paris. In 1959 he was elected a Foreign Honorary Member of the American Academy of Arts and Sciences and also a Member of the Polish Academy of Sciences, Warsaw. Honorary degrees conferred upon him included, D.Sc. Brussels, 1946; D.Sc. Bordeaux, 1947; M.D. Liège, 1951 and M.D. Utrecht, 1957.

No account of David Keilin's life would be complete without some reference to his singularly happy home life. He is survived by his widow Dr Anna Keilin and his daughter Dr Joan Keilin. Dr Anna Keilin, who had been a contemporary of his at the Sorbonne, where she studied medicine, was for many years a much respected medical practitioner in Cambridge. She always took a great interest in everybody associated with his work and was ever mindful of their welfare, especially of the young or those new to Cambridge. Her kindness and the warm hospitality of their home added greatly to the happiness of workers in the Molteno Institute and of the numerous visitors who passed through Cambridge. Also, her artistic skill provided beautiful illustrations for a number of his scientific publications and for wall charts. It was a source of much satisfaction to him that his daughter, although she qualified in medicine, chose to follow a career in research in biochemistry on lines of work cognate to his own special interests.

Keilin often expressed his personal views that any scientist's fame rested, not on office attained, or honours, academic or otherwise, received, but on his own achievements as shown in his published work. The appended list of Keilin's publications is as complete as possible and its perusal shows the extraordinary wide range of his scientific interests and the number of diverse fields in which he can justly be acclaimed to have been a pioneer. In the history of science he is assured of a high place amongst the leading scientists of his generation. His friends and colleagues deplore the loss of a staunch friend, an inspiring teacher and a sagacious and stimulating colleague.

P. TATE

LIST OF SCIENTIFIC PUBLICATIONS BY DAVID KEILIN

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