MARJORY STEPHENSON

# Obituary Notice

## MARJORY STEPHENSON, 1885–1948

Marjory Stephenson disliked intensely the rituals connected with illness and death; it is felt that the only tribute to her memory which she would have appreciated would be one which might be of help to others. It is to this end that her contribution to research in chemical microbiology will be described in detail, for it covers almost the whole of the period during which the techniques of modern biochemistry have been applied to micro-organisms. She was one of the pioneers, and her philosophy of research contains much which must be of inspiration to those about to set foot in these fascinating fields.

Marjory Stephenson was born on 24 January 1885 at Burwell, near Cambridge. Except for the period during and immediately before the 1914–18 war she spent the whole of her life in Cambridge and the immediate neighbourhood. At Newnham she read Natural Sciences (Chemistry, Physiology, and Zoology); she always maintained a close link with her College and became a member of the Governing Body in 1931 and of the Council in 1944. After graduating, lack of funds prevented her taking up Medicine as she wished, and the period 1906–11 was spent in the study, and later the teaching, of domestic science at Gloucester County Training College and King's College of Household Science, London. She did not much enjoy this type of teaching and rarely spoke of this phase of her career.

In 1911 came the opportunity (for which she was deeply grateful) to enter biochemical research with R. H. A. Plimmer at University College, London. Here she worked successively on the lactase of intestinal mucosa, the synthesis of palmitic acid esters, and finally on experimental diabetes with E. H. Starling. The tenure of her Beit Memorial Fellowship (awarded in 1913) was however interrupted by the war. She joined the Red Cross and served with distinction in France and at Salonika, being made an Associate of the Royal Red Cross and awarded the M.B.E.

In 1919 she returned to Cambridge to join the enthusiastic group of workers that F. G. Hopkins was gathering, and who, under his leadership, were to make Cambridge the centre of biochemical thought in Britain for a generation. She found this lively environment very much to her taste and indeed helped to make it. Her own admiration and regard for 'Hoppy' is best seen in the obituary notice she wrote in 1948; it was to be unfortunately her last full contribution to this *Journal*. This feeling was reciprocated and her firm common sense was, especially during the 'thirties, a great standby to Hopkins in the running of his department, in which she had by then become a leading personality. With his encouragement she soon turned her attention to micro-organisms, and from then on they were to be the dominating influence in her scientific life. Her genius was for experiment rather than theory, and perhaps this explains their unique fascination for her; in 1930, when considering the place of bacteria in the universe, she wrote in the preface to the first edition of *Bacterial Metabolism*:

> Perhaps bacteria may tentatively be regarded as biochemical experimenters; owing to their relatively small size and rapid growth, variations must arise very much more frequently than in more differentiated forms of life, and they can in addition afford to occupy more precarious positions in natural economy than larger organisms with more exacting requirements.

Her work brought an international reputation, and finally (1945) the signal honour of being (with Dr K. Lonsdale) one of the first two women to be elected to Fellowship of the Royal Society. She was also one of the first women to receive the Sc.D. of Cambridge University, then titular only. It gave her a great deal of fun, when women were finally admitted to full rights of the degree, to observe the reactions of some of the older males when she appeared in her full regalia.

From the time that her Beit Fellowship expired Marjory Stephenson was supported by the Medical Research Council, first by annual grants and after 1929 as a member of their scientific staff. She was highly appreciative of the broad-minded attitude of this body, and served as secretary of their Committee on Chemical Microbiology from its inception until her death. She was an early member of the Biochemical Society (1914) and was a member of the Committee from 1928 to 1932.

Marjory Stephenson always had a deep interest in the biological side of her subject and this broadened as the years passed. She felt indeed that biochemistry owed a debt to biology which was not always recognized. This found expression in her desire that all types of microbiologists should have a closer liaison for their mutual advantage; to this end she was a leading spirit in the formation of the Society for General Microbiology in 1945, and she became its second President in 1947.

Marjory Stephenson (M.S., as she was known to her colleagues) had a vivid and arresting personality;

her feelings—and the expression of them—about people and affairs were always positive. She was intolerant of all forms of pretentiousness, whether scientific or personal. Her independence of judgement did not permit her to adhere consistently to any 'party-line', but her sympathies, and often her active support, were always to be found on the side of progressive movements. She was especially active in the interests of those European scientists whom the fascist regime had forced out of their own countries. In these and many other ways she found an outlet for the personal generosity which was so marked a feature of her human relationships.

She always worked very hard herself and expected the same degree of activity in others. For relaxation she turned, in later life in particular, to her garden, which was a source of great pride and pleasure to her and which she attacked with the same high technical efficiency that characterized her laboratory work. In the last years she became particularly interested in the finer arts of the cultivation of fruit trees.

Marjory Stephenson did not permit the penultimate stage of her illness, with its painful treatment, to affect her scientific activity or her general work for chemical microbiology. She carried on with so much of her usual vigour and essential gaiety that few knew the state of her health. The last stages fortunately passed rapidly; she died on 12 December 1948.

*Teaching and direction of research*

The teaching of advanced biochemistry in Cambridge is traditionally carried out by the leading workers in various fields whether or not they are members of the University staff. Marjory Stephenson took her full share in this from 1925 onwards. She did not much enjoy formal lecturing; lectures provided the facts, but it was in the informal chat during the practical class that she got in real touch with the student. Her success may be measured by the steady flow of recruits from the Part II Class to her research team.

It was in the guidance of the young research worker that Marjory Stephenson had her greatest influence. Her concern was to see that the novice gained the maximum advantage from his first years of work; she was not interested in an impressive flow of publications from her group. Though always ready with sound and practical advice, she never 'spoon-fed', and was content to allow her young people to test their own mettle, even though she might need to extricate them in the end. She encouraged persistence and insisted on the degree of thoroughness characteristic of her own work. Of Marjory Stephenson it may truly be said that 'infection not instruction is the secret of education'. Visits from the 'great' from other lands were always shared with her research workers, usually by delightful informal entertainment in her own home, where initial shyness or diffidence was so easily dispelled.

She believed firmly that research and teaching were complementary in the sense that each was likely to prove less fruitful unless the other was being actively pursued by the instructor. With the increasing development and interest in chemical microbiology and microbiology in general she worked hard for the establishment of a special Part II Biochemistry (Microbiological) in Cambridge. This was started in 1947, and in the same year the University recognized her long service to teaching by creating her its first Reader in Chemical Microbiology.

*Research in chemical microbiology*

Marjory Stephenson worked in this field for nearly thirty years (1920–48); during this time she published, either alone or in collaboration, some twenty-two original papers. Each of these was a substantial contribution to the subject; indeed it was characteristic that she did not publish until the work had been thoroughly established and had reached a certain degree of completeness. It is noteworthy that her publications do not include a single 'letter to the Editors'. Another characteristic was that her name never appeared on a paper unless she had been responsible for a full share of the actual work at the bench. It is therefore difficult to assess completely her direct influence in the development of this subject by reference to her own papers alone; much more work published independently by younger members of her team was suggested by her and its successful prosecution made possible by her counsel and aid. The high reputation of Britain in the establishment of this field was largely due to the parallel development of bacterial metabolism under her leadership and that of bacterial nutrition by a team of workers (also supported by the Medical Research Council) under Fildes. As both workers always recognized that they would, these two lines have now converged and the confluence is leading to some of the most important modern developments.

In an address given at the first meeting of the Society for General Microbiology in February, 1945, M.S. defined five levels at which research in microbiology could be undertaken. These were: (1) mixed cultures of organisms growing in natural environments, (2) pure growing cultures in complex media, (3) pure growing cultures in highly purified media (chemically defined), (4) non-proliferating cells in pure culture on chemically defined substrates, and (5) cell-free enzymes and coenzymes on pure substrates. These levels she considered represented only different methods of technical approach and that none should be considered higher or lower than another, although the solution of problems connected with (1) was perhaps the ultimate objective.

The main point was that research should be done concurrently or alternately at different levels, results obtained at one often providing the clue for solving outstanding problems at another. Although she did not formally state this philosophy until almost the end of her research career, it is obvious from her publications, as well as from personal contact, that it had guided her for many years, and had contributed largely to the sense of realism that was so marked a feature of her work. M.S.'s work was mostly at levels (4) and (5), but almost always undertaken as the best method of elucidating some problem connected with the whole growing organism.

When Marjory Stephenson went to F. G. Hopkins's laboratory she joined first in the work on the fat-soluble vitamins (Stephenson & Clark, 1920; Stephenson, 1920). A desire for a deeper understanding of fat metabolism in general led her (with M. D. Whetham) to her first work with bacteria.

> Studies in fat metabolism have hitherto been chiefly carried out on highly specialised vertebrate tissue. By making investigations on a unicellular organism, more susceptible of laboratory control,...

This was probably the only occasion on which bacteria were chosen deliberately as a tool for biochemical research; after that the fascination of the micro-organism itself exerted an ever-increasing grip.

In two papers (Stephenson & Whetham, 1922, 1923) on the fat metabolism of the Timothy grass bacillus (*Mycobacterium phlei*) careful 'balance-sheet' experiments were made with the growing organism. Perhaps the most important observations were, first, that growth could go on even after glucose had been exhausted, and secondly that while acetate alone would not support growth it could be metabolized in the presence of glucose with resultant increase in lipid material. Even in this first work an attempt (unsuccessful) was made to simplify the analysis of a catabolic reaction by cutting out growth. The nitrogen source was omitted from the medium and a heavy inoculum was used; glucose was not, however, attacked under these conditions.

The 'balance-sheet' technique was next applied (Stephenson & Whetham, 1924) to growing cultures of *Escherichia coli*, and the results had a profound influence on her work for many years. With glucose as carbon source no oxygen was taken up for the first 24 hr. even when air was bubbled through the culture, although growth was good and glucose disappeared rapidly. This observation must have focused her attention on the anaerobic way of life, and this was one of her main interests for the rest of her life; it is reflected not only in her own work but also in that of other members of her group. This characteristic aspect of bacterial metabolism intrigued her greatly. Thus she wrote (Stephenson, 1947), in a review on hydrogen transfer:

> Moreover amongst heterotrophs it is as anaerobes that bacteria specially excel...in other words it is in the use of hydrogen acceptors that bacteria are especially developed as compared with animals and plants.

The work quoted above also led her to this field from another point of view; substances such as lactate and succinate would not support the anaerobic growth of *Esch. coli* (though they would do so aerobically), and it was not possible to envisage an exothermic anaerobic breakdown of such substances alone. She now joined forces with Quastel who had been led to similar considerations from his work with *Pseudomonas pyocyanea*. At this period the washed suspension technique (first used by Harden & Zilva, 1915), which was to prove so useful (level 4) for the study of bacterial reactions isolated from the additional complexities of growth, was undergoing rapid development in Cambridge by Quastel and his colleagues mainly with reference to the dehydrogenase enzymes of bacteria. M.S.'s own part in this development was the application of the technique to the problems of anaerobic growth (Quastel, Stephenson & Whetham, 1925; Quastel & Stephenson, 1925). It had been found by the methylene-blue technique that such suspensions activated many substances to act as H donators; it was now found that other substances (e.g. nitrate, fumarate) were activated as H acceptors, i.e. re-oxidized reduced dyestuff. Furthermore, the suspensions brought about oxido-reduction reactions between pairs of such donators and acceptors, e.g.

$$CH_3CHOH.COOH + KNO_3 \rightarrow CH_3CO.COOH + KNO_2 + H_2O.$$

These suggestive findings were immediately tested in growth experiments; under anaerobic conditions growth was usually, though not always, obtained with *Esch. coli* and other organisms, provided that both a donator and an acceptor were present in the medium. Thus while lactate alone would not support anaerobic growth, it would in the presence of either nitrate or fumarate. For growth to occur it was suggested that energy must be liberated by the oxido-reduction reaction, and that a product must be formed capable of entering into the synthetic reactions of the cell.

The next aspect of anaerobic growth tackled concerned the obligate rather than the facultative anaerobes (Quastel & Stephenson, 1926). Here, apart from the question of the nature of the energy-yielding reactions, a second problem presented itself—why was oxygen apparently toxic to the organism? The peroxide theory then current was considered unsatisfactory by the authors whose noses were struck by the fact that *Clostridium sporogenes* always produced sulphydryl compounds

during growth. Following up this hint they demonstrated that cultures or cell suspensions of the organism remained viable even after oxygenation or treatment with hydrogen peroxide (up to about 0·02 %), and grew rapidly on subcultivation into suitable media provided that a source of —SH (such as cysteine) was present; without this there was a prolonged lag. It was suggested that —SH is required to establish a limiting reduction potential essential for the actual growth of these organisms. Perhaps the success which attended this work led to her intolerance with those who complained when a good biological odour was perceptible in the laboratory.

At this stage Marjory Stephenson felt that research on bacterial oxidations with its emphasis on the utilization of dyestuffs, nitrate and so on as oxidizing agents had become in some cases somewhat artificial.

> It is obvious however that for any organisms growing aerobically the most important hydrogen acceptor is molecular oxygen and that consequently a study of aerobic oxidations is essential if a true picture of the normal life of the cell is to be obtained.

This she undertook (Cook & Stephenson, 1928) for the oxidation of glucose and its typical fermentation products, using mainly washed suspensions of *Esch. coli*. Two facts of prime importance emerged. First, such oxidations were found to be largely independent of the viability of the organism; even when this was deliberately reduced to about 0·1 % of the original by ultraviolet irradiation the $O_2$ uptake was only reduced to a half, and then only initially. Secondly, except in the case of formate, less than theoretical $O_2$ uptakes were always obtained and no products other than $CO_2$ could be detected. The explanation for this was not found; it is now known that some carbon is built into cell material (oxidative assimilation).

The last study in this particular phase of her work was her first contribution at level (5) (cell-free enzymes). Following up an observation that the lactic dehydrogenase of suspensions of *Esch. coli* finally increased in activity on storage after a preliminary fall (other dehydrogenases decreased constantly), she succeeded in obtaining a specific cell-free preparation of the enzyme by autolysis of heavy suspensions (Stephenson, 1928). The enzyme could not use $O_2$ unless a carrier such as methylene blue was present; a search for a source of the missing natural carrier was not successful. This was the first cell-free bacterial enzyme to be obtained, and Marjory Stephenson would certainly have liked to have continued work of this type. Two years later she wrote (in the preface of the first edition of *Bacterial Metabolism*, 1930):

> ...we have indeed much the same position as an observer trying to gain an idea of the life of a household by a careful scrutiny of the persons and material arriving or leaving the house; we keep accurate records of the foods and commodities left at the door and patiently examine the contents of the dust-bin and endeavour to deduce from such data the events occurring within the closed doors.

But the time was not yet ripe; except for the occasional sturdy enzyme which resisted such drastic processes as autolysis, methods were not then available for the extraction of bacterial enzymes. The situation changed in 1938 with the invention by Booth and Green in Cambridge of a wet-crushing mill for bacteria with which it was possible to obtain a number of other enzymes. M.S. and her colleagues at that time (E. F. Gale and J. L. Still) returned to the attack; her own contribution was a full study (Gale & Stephenson, 1939) of the L-malic dehydrogenase of *Esch. coli*. They were not content only to study the kinetics of the enzyme (which required coenzyme I and diaphorase and was reversible); they also demonstrated the presence in *Esch. coli* of substances with the properties and functions of cozymase and diaphorase.

The period 1930–7 represents another phase of Marjory Stephenson's research career. It was perhaps the most fruitful and finally settled her reputation as a world authority in this field. Even if the doors remained locked, her ingenuity of approach permitted her several revealing peeps through the window. It seems particularly appropriate that almost all her own work during this time, as well as much of that of her team, had its origin either directly or indirectly, from a field observation made in her own well loved fenland.

> The culture used by us was originally obtained from the River Ouse, which had been recently subjected to an influx of fermentable carbohydrate material from a beet sugar factory and has given a visible fermentation with evolution of gas in the river itself.

The mud proved a fruitful source of interesting organisms. A mixed culture derived from it reduced sulphate to sulphide and produced methane from formic acid as well as from $H_2$ and $CO_2$ (Stephenson & Stickland, 1931*a*). The culture would grow on inorganic salts plus formate; during the first unsuccessful attempts to isolate the methane-producer by enrichment culture, a coliform organism (possibly *Escherichia formica*) was obtained which had the property, in washed suspension, of reducing methylene blue in the presence of $H_2$. The enzyme had the properties typical of a dehydrogenase and was named hydrogenase. Once discovered, it proved, surprisingly enough, to have a wide distribution among well-known organisms including *Esch. coli*. In one of the rare excursions into hypothesis M.S. permitted herself, she suggested that the function of hydrogenase might be as an intracellular reducing agent,

since many enzymes in cell-free systems are known to lose activity on becoming oxidized (Stephenson, 1947). But the very next paragraph begins:

> But whatever may be the function of the hydrogen-hydrogenase system in the cell it is a remarkably useful tool in the hands of the bacterial chemist, for by its use bacterial reductions can be studied rapidly and quantitatively by manometric methods and the products of reduction obtained unmixed with the products of oxidation.

This was particularly the case with the other two organisms obtained from the Ouse mud, both of which had hydrogenase. The sulphate-reducer was soon isolated; it was a strict anaerobe, morphologically similar to *Desulphovibrio desulphuricans* but not identical with known strains (Stephenson & Stickland, 1931*b*). It grew on the usual salts plus sulphate with fructose, lactate or formate as carbon source. The details of sulphate reduction were studied manometrically with washed suspensions using $H_2$ itself as donator.

The methane-producing organism proved exceptionally difficult to isolate in pure culture, even after prolonged enrichment on formate medium. Finally it was obtained by the single-cell technique. The organism (which was never identified) grew well on the usual salts with ammonium as N source and formate as C source. Experiments with washed suspensions showed that the energy-yielding reaction was (Stephenson & Stickland, 1933*a*)

$$4H.COOH = CH_4 + 3CO_2 + 2H_2O + 39 \text{ kg. cal.}$$

In the presence of $H_2$, methane only was formed; $CO_2$ was also reduced to methane by $H_2$. It was therefore likely that formate was first split to $H_2$ and $CO_2$, part of the latter then being reduced by $H_2$; in support of this $H_2$ was found to be present in the early stages. This organism differed from the methane producers so far studied (mostly in mixed cultures) in that only compounds containing one carbon atom yielded methane; these included also CO, formaldehyde and methanol.

The transfer of attention from the utilization of molecular hydrogen to its formation by bacteria followed naturally from the above work, and M.S. and several members of her team turned to a full investigation by the new methods of the production of $H_2$ from formic acid, which was then regarded as the key intermediate in $H_2$ production during fermentation. Stickland (1929) had already found that suspensions of *Esch. coli* grown on agar contained formic dehydrogenase, but did not liberate $H_2$ from formate until they had been in contact with it for some hours and had indeed begun to grow. About this time Karström had introduced the concept of adaptive enzymes, i.e. enzymes found in the bacterial cell only after growth in the presence of the substrate. In the new work (Stephenson & Stickland, 1932, 1933*b*; Yudkin, 1932; Woods, 1936) the enzyme liberating $H_2$ and $CO_2$ from formic acid (formic hydrogenlyase) was shown to be present only in cells grown in the presence of formate or substances probably giving rise to formate; strongly aerobic conditions were also adverse for enzyme formation. Although washed suspensions did not become adapted unless a source of N (broth) was present, strong evidence was obtained that the process was not linked to growth, and resulted from a chemical response to the presence of the substrate rather than to natural selection operating on a few organisms already having the enzyme. It is still a matter of doubt as to whether formic hydrogenlyase is a separate enzyme or whether it results from the linkage of formic dehydrogenase and hydrogenase through some electron carrier:

$$HCOOH \rightleftharpoons 2H + CO_2 + 2e; \quad 2H + 2e \rightleftharpoons H_2.$$

At the time M.S. favoured the first view, mainly on evidence derived from the distribution studies of the three enzymes; more recent work by others favours the second possibility. In 1947, in the review quoted below, she considered the question still open.

The metabolism of $H_2$ is a process almost unique to bacteria and its study yielded high dividends. She regarded the hydrogenase and hydrogenlyase systems as complementary (Stephenson, 1947):

> The hydrogenase reaction permits an organism to reduce its substrate without using an organic hydrogen donator whilst the lyase reaction enables it to oxidize its substrate without a hydrogen acceptor.

The work with formic hydrogenlyase had stimulated M.S.'s interest in the mechanism of adaptation, and with J. Yudkin she undertook a re-investigation of the long-known adaptation of *Saccharomyces cerevisiae* to growth with galactose as source of energy (Stephenson & Yudkin, 1936). In this case full production of the galactozymase system was obtained by incubating starved washed cells in galactose and buffer only. There was no significant change in either the total or viable count. Further strong, though not conclusive, evidence that adaptation did not depend on cell division came from the observation that 20–50% adaptation would still be obtained with suspensions whose viable count had been reduced to 2–5% by irradation with ultraviolet light. Galactozymase was thus probably another case of 'chemical adaptation'. She next made a similar study with *Esch. coli* (Stephenson & Gale, 1937*a*) but with quite different results. The galactose-fermenting system was largely adaptive, but could not be dissociated from growth.

These experiences with adaptive enzymes made a deep impression on M.S., which was reflected by some changes in her general technique of investigation. Thereafter, nearly every piece of work contained its section on the effect on the age of the culture used.

When it is remembered that during the growth of cultures the medium itself is constantly changing, some constituents disappearing and others appearing, it is easy to see that the enzyme activity of growing and even non-growing cultures in the ferment vats must be changing continuously, reflecting as it were, the changing conditions which they themselves have brought about (Stephenson, 1937).

During the 'thirties a good deal of work on the amino-acid metabolism of bacteria had been carried out by several members of the team with her guidance and encouragement. She now entered this field herself with the immediate objective of bringing the full armament of the newer techniques to bear on the old problem of the nitrogen-sparing action of carbohydrate in bacterial growth, characterized by decreased $NH_3$ formation. In two studies (Stephenson & Gale, 1937*b*; Gale & Stephenson, 1938) the deamination of glycine, DL-alanine, L-glutamic acid and DL-serine was tested with washed suspensions of *Esch. coli* grown under various conditions. In every case the presence of glucose during growth almost totally suppressed enzyme production, whilst the activity of suspensions already containing the deaminases was affected by glucose to a comparatively minor extent. The work, however, was not confined to this limited objective and other important factors (notably degree of aeration and age of culture) were also studied. Strong evidence was also obtained that the serine deaminase required a coenzyme factor; loss of this factor could be prevented in some cases by minute amounts of adenylic acid, and if loss had occurred at low temperatures, activity could be restored in the presence of phosphate by reducing systems. It seems likely from recent work in the U.S.A. that this coenzyme is a biotin nucleotide derivative.

Meanwhile, Gale (1938) had found adenosine to have coenzyme activity for an aspartase enzyme of *Esch. coli*; these findings in her own field, and the increasing general knowledge of the importance of nucleic acid derivatives as components of coenzymes and growth factors, decided M.S. to undertake a general investigation of their function in bacterial metabolism. In characteristic manner she decided that the first task was to get a detailed knowledge of the catabolism, if any, of such substances as adenine, adenosine and adenylic acid. This she did (Stephenson & Trim, 1938); and evidence was obtained that the breakdown of adenosine was the key reaction in all cases. But this programme was interrupted by World War II and was not resumed until nearly ten years later when she extended it to the degradation of ribonucleic and deoxyribonucleic acids (Stephenson & Moyle, 1949).

During the war years she initiated (Davies & Stephenson, 1941) work on the production of solvents (acetone, butyl alcohol) by *Clostridium acetobutylicum*. It was thought that the more clear-cut analysis possible with the washed-suspension technique (previous studies had all been with the growing organism) should throw more light on the factors influencing production of these economically important substances. It proved exceptionally difficult to obtain active cell suspensions even from vigorously fermenting cultures. Age of culture again proved important and it was necessary to wash and resuspend the cells in a complex solution containing broth or yeast autolysate; even then loss of activity was rapid.

M.S. also took part in some of the co-operative trials of microbiological assay methods for vitamins organized during the war by the Medical Research Council.

During the fermentation of plant juices by lactobacilli acetylcholine is often produced; after the war she made a characteristic attack on this problem (Stephenson & Rowatt, 1947). An organism with this property was isolated from Sauerkraut and provisionally identified as *Lactobacillus plantarum*; a full study was made of its general biochemical behaviour. Synthesis of acetylcholine by washed cells was obtained in a simple system of buffer, glucose and choline, and the kinetics studied. Finally, following Lipmann's work on coenzyme A, it was shown that pantothenate-deficient cells showed much reduced synthesis, which was increased fivefold by addition of pantothenate, so that in bacteria also acetylation of choline requires a pantothenate derivative as coenzyme. This was Marjory Stephenson's last completed work and typified her final philosophy of research; a problem arising at level (1), its confirmation at level (2), and detailed investigation at levels (3) and (4). Level (5) was not reached on this occasion, as some attempts to obtain a cell preparation were unsuccessful.

A striking feature of the research as a whole was the wide variety of technical methods used, both biochemical and microbiological. She never shirked using a new method, however difficult technically, even if it were required only to establish some comparatively minor point or to corroborate some matter for which there was already weighty evidence; this was equally true towards the end of her career when she might well have been forgiven for becoming a little conservative. She took very little for granted; whenever possible the products of the reactions she studied were fully identified by proper chemical methods even if their nature was pretty certain and indicated by considerable indirect evidence. This admirable habit of her own generation of biochemists (by no means so common to-day) she maintained to the end.

Marjory Stephenson was essentially an experimentalist; it is really remarkable how few of her papers contained a section formally labelled 'Discussion'; when such did occur it was devoted

rather to practical matters, or to the relation of the work to other fields, than to hypothesis. She was content to let her experimental results speak for themselves, and to lead herself and others to more experiments.

Great as was her regard for bacteria, she did not regard them as creatures of purpose. She considered teleology of no help to the bacterial chemist, although willing to admit that other types of biochemist might be more fortunate; in 1937 she wrote,

> It seems now clear that a belief in the functional importance of all enzymes found in bacteria is possible only to those richly endowed with Faith.

Outside original papers her writing energies were devoted mainly to her book *Bacterial Metabolism*. She wrote comparatively few reviews and these were largely factual; among them were the articles concerning bacteria in the first four volumes of the (then) newly established *Annual Reviews of Biochemistry*. Her book has been the standard work on the subject since its first publication in 1930. Originally conceived as a monograph covering the whole field in detail, the very rapid advance of the subject made it necessary for her to regard the succeeding editions rather as advanced text-books. The lucid style, customary thoroughness, and obvious enthusiasm for the subject made them more than this. Some aspects of the history of science had a strong interest for her, and she had avowed her intention of writing lives of Pasteur and of Hopkins; unfortunately this was not to be.

The most recent developments of chemical microbiology appeared to Marjory Stephenson to bring the subject to its most important and exciting stage, not only for microbiology (in its broadest sense) but for biochemistry also. She had long believed that chemical microbiology had a contribution to make to biochemistry which might come from no other source. This was now happening. Referring *inter alia* to work on the metabolic function of growth factors, enzymic adaptation and biochemical mutants of micro-organisms, she wrote (*Bacterial Metabolism*, 3rd ed.):

> ...such studies are peculiar to microbiology though certainly of wider application; they owe their success to the use of biological material which is prone to biochemical variation and tolerant of interference with its normal biochemical habit.

She was particularly excited about the hopeful beginning in the analysis of anabolic reactions which was being made possible by the use of the microbe as experimental material. In this new phase of research we shall not have Marjory Stephenson with us to play an active part; but the work will certainly go forward the more surely for all that she has done to bring chemical microbiology to its present stage.

Grateful acknowledgement is made to the many friends of M.S. (in particular Dr M. Robertson, Dr D. M. Needham and Dr L. H. Stickland) who have provided information or given me their views on this notice.

D. D. WOODS

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