

such direct application to the work of the anesthetist that the point need not be especially illustrated. It may be said, however, that many agents and methods contributed by chemists and physicists are first applied by the physiologist and pharmacologist to determine the use to which the new agents or methods can be put before they are applied clinically. While the first agents to be introduced may have come into use without such preliminary investigation, those that are introduced to-day are subjected to thorough tests. The interest of the physician anesthetist in the effects produced by anesthetic substances and other drugs which he uses is evident in the work of Searles,¹¹ who studied the effect of ether and sodium amytal anesthesia on the blood. Such investigation emphasizes the importance of collaboration of clinician and scientist for, if possible, the separate effect of the anesthetic and of any other drug that may be used must always be determined. It is in this field that the study of psychology becomes important, for it must never be forgotten that the psychologic processes of the animal differ from those of the human being. Therefore, it is not always possible to apply the information obtained from animal experimentation to clinical application of the agent.

The study of languages requires the attention of the anesthetist. Obviously, in scientific writing, many of the same words are adopted by users of different languages, but it is of great importance to the reader of scientific articles that the author should have had at his command a sufficient choice of words that his meaning may be exactly expressed and that, if his

article is translated into another tongue, it will not suffer thereby.

By mathematicians many fundamental contributions had been made, usually through physics; however, the mathematician is indispensable in the correlation of data that are gathered not only in the course of experimentation but also in clinical application of anesthetic preparations. It is not easy for those of us who are not mathematicians to assemble statistics derived from our work and properly to interpret their value.

I hope that these illustrations of the indispensable value of the fundamental sciences in the establishment of anesthesiology, a new specialty in medicine, will interest you sufficiently so that your continued assistance may be anticipated. Unfortunately, those of us who are interested in the development of this new specialty and those who will follow us in the field of endeavor are not sufficiently well equipped from your point of view. In the absence of an individual genius, then, development of the new medical specialty will, in all probability, take place in institutions where scientists and clinicians can work together and where facilities exist whereby investigation can be carried on, new facts established and new agents and methods developed; these factors, together, will permit further reduction of pain among human beings. In the future, I hope that animal experimentation, made painless by anesthesia, will be accepted by those who have condemned it in the past when their attention is called to the fact that needless pain caused by disease will be spared both animals and man.

OBITUARY

PHOEBUS AARON THEODOR LEVENE 1869-1940

PHOEBUS AARON THEODOR LEVENE, member emeritus of the Rockefeller Institute for Medical Research, died at his home in New York City on September 6, 1940. He had returned from a vacation in Montana but a short time before, and was about to resume his insistent quest for the knowledge of life processes.

Dr. Levene was born in Sagor, Russia, on February 25, 1869. When he was about two years old, the family moved to St. Petersburg.

The young Levene entered the Classical Gymnasium, and from this school he enrolled in the Imperial Military Medical Academy in St. Petersburg. He was one of the five Jewish students allowed to enter his class. At that time Borodin was the professor of chemistry. It was Borodin's son-in-law, Professor Dianin, who allowed Levene to carry on work at will in the chemical laboratory.

¹¹ P. W. Searles, *Am. Jour. Surg.*, 41: 399-404, 1938.

During the year 1891, because of the growing anti-Semitism in Russia, and the resulting need for education of the younger members of the family, the Levenes migrated to the United States, arriving July 4, 1891. After a few months, Levene returned to St. Petersburg to finish his examinations for his medical degree. He was graduated in the autumn of 1891. He returned to New York in March, 1892, and soon took his examinations for the practice of medicine and practiced on the lower East Side until 1896.

Because of his conviction of the importance of chemistry to the advancement of medical science, he enrolled at Columbia as a special student in the Department of Chemistry in the School of Mines. At the same time Professor J. J. Curtis kindly gave him a place to work in his laboratory at the College of Physicians and Surgeons. In later years he supplemented this training by periods spent in Berne under Professor Drechsel, in Marburg under Professor Kos-

sel, in Berlin under Professor Emil Fischer and in Munich in the Technische Hochschule.

Levene's strong bent toward research on the chemical nature of biological materials was but partly satisfied in the limited time permitted by his medical practice. To the good fortune of biochemistry, the way was opened for him to devote all his efforts to these studies by his appointment in 1896 as associate in chemistry at the State Pathological Institute of New York.

In November of the year 1896 he developed tuberculosis and went to Saranac Lake as a patient of Dr. Baldwin. He then went to Davos for a year. All this time Professor von Giesen held the post in the State Pathological Institute open for him. When he returned from Switzerland, though far from well, he at once went to work. During the years 1900-1902 he worked at the Saranac Laboratory for the Study of Tuberculosis because the State Pathological Institute was undergoing reorganization. In 1902 he returned to work there under Dr. Adolf Meyer.

In January, 1905, came his great opportunity when at the invitation of Dr. Simon Flexner he joined the small group who formed the laboratory staff of The Rockefeller Institute for Medical Research, where in July, 1907, he was advanced to the rank of member.

The Rockefeller Institute provided the ideal environment for the flowering of his genius. The stimulus of an inspiring atmosphere, the unexcelled laboratory facilities and the opportunity for choice of problems without regard to their difficulty and length afforded a widened horizon of scientific endeavor to which he devoted his abilities for thirty-five years. Under his sympathetic guidance several distinguished biochemists laid the foundations of their important careers. In July, 1939, he retired and became a member emeritus of the institute but still continued his researches with unabated energy.

Dr. Levene's eminence in his chosen field was recognized by the award to him of the Willard Gibbs Medal of the Chicago Section of the American Chemical Society in 1931, and of the William H. Nichols Medal of the New York Section in 1938. He was a member of the National Academy of Sciences, American Philosophical Society, Bayerische Akademie der Wissenschaften, Royal Society of Science (Upsala, Sweden), Halle Akademie der Naturforscher, Société Royale des Sciences Medicales et Naturelles de Bruxelles and many professional societies.

Dr. Levene married Anna M. Erickson, of Lewistown, Montana, in 1920. Through their congenial tastes there grew a home of spiritual and artistic harmony, the center for a wide circle of devoted friends from many fields.

In such fortunate circumstances Dr. Levene dis-

played an extraordinary capacity for hard work. He read voraciously in several languages on many subjects. In addition to directing the researches of a number of coworkers, he carried on with his own hands a large volume of experimental work of great delicacy. In the laboratory and in his private library at home, chemistry and its medical significance were a supreme passion; in the midst of his friends, he gave full play to his varied interests in classical and modern art.

To discuss the wide scope of Levene's scientific activities in the space of a few paragraphs is not easy. Fortunately for the reviewer, however, although these researches relate to almost all fields of biochemistry, they present a logical and coordinated pattern. He wrote a number of comprehensive summaries and two monographs, in the preparation of one of which it was the privilege of the writer to collaborate.

Dr. Levene began his career of independent research with an investigation of the transformation of proteins into carbohydrates by the animal organism. This undertaking was an intuitive expression of his lifelong interest in these two important types of biological materials. Two of his early studies were of outstanding significance to protein chemistry: improved analytical methods, developed in collaboration with Dr. D. D. Van Slyke, and the isolation of one of the first crystalline intermediate products of protein hydrolysis, in cooperation with Dr. George B. Wallace.

Of all tissue components, the proteins have offered the supreme challenge to the skill and ingenuity of the chemist. At the beginning of this century the work of Emil Fischer had resulted in his enunciation of the polypeptide theory of structure, based on the isolation of various amino acids from the hydrolytic products of these complex molecules. During the nineteen-twenties this theory was challenged, particularly by a hypothesis in which the molecule was regarded as being made up of diketopiperazine rings—condensed amino acid cycles—joined by auxiliary valence forces. Levene had previously noted the great ease with which a substance of this latter type, isolated by him in 1906, lost its optical activity. A systematic study, extending over several years, of the racemization of a series of synthetic diketopiperazines and peptides revealed the difference in behavior of the two groups of compounds. When this technic was applied to the proteins themselves, they were found to resemble more closely the chain structures than the cyclic compounds, thus supporting Fischer's theory.

The major emphasis in Levene's protein studies, however, was on his brilliant investigations of the characteristic non-protein constituents of the nucleoproteins and of the glycoproteins, namely, the nucleic acids and the nitrogenous sugars, of which brief mention will be made later. It should be noted that both

these types of substances are substituted sugars, thus forming a logical connecting link between his broad interests in proteins and the carbohydrates.

As in the case of proteins, two conflicting theories have been advanced for the structure of the polysaccharides, one claiming a union of the individual components in chain form by chemical valency, the other assuming cohesion of ring forms through subsidiary valency. Levene's approach to this problem was through the study of the natural tendency toward condensation of the simple sugars under mild conditions. In practically every case the product was found to be a chain structure. The results have therefore supported the chemical valence theory of union between parts of the polysaccharide molecule, a view now generally accepted.

Two other important aspects of sugar structure received illumination through Levene's researches—the evolution of a method to determine the point of linkage in substituted carbohydrates and the elucidation of ring structures of sugars and their derivatives. Both techniques were essential in unraveling the complicated formulas of the nucleic acids.

At the beginning of this century, knowledge of the structure of the nucleic acids, which are essential constituents of the chromosomes, was in a rudimentary state. It had been shown only that they were composed of phosphoric acid combined with nitrogenous and non-nitrogenous substances. There was no information regarding the nature of the non-nitrogenous compounds, the quantitative relationships between the different components or their mode of union.

Throughout four decades these substances were under persistent investigation by Levene, with the result that their structures are now known in detail. The identification of the sugar in the so-called animal nucleic acid, which had baffled all investigators, was finally achieved in 1929 through his genius. He showed that the nucleic acids are tetranucleotides, each of the latter being composed of phosphoric acid, sugar and a nitrogenous compound. The sequence of the union of the constituents and the positions of the substituents on the sugars were then established. The sugars—ribose in plant nucleic acid and deoxyribose in animal nucleic acid—had not previously been known to occur in nature. As a result of Levene's work we have an exact concept of the structures of these huge molecules, probably the most complex biological materials whose architectural picture has been reconstructed.

At an early stage in his work Levene became interested in the unique group of substances known as glycoproteins, which contain high percentages of carbohydrate. These complex compounds were revealed by him to be derivatives of nitrogenous sugars.

The nitrogen-containing sugars in themselves con-

stituted an extremely difficult problem. Whereas in simple sugars the position in space of every substituent had been determined, that of the nitrogen atom could not be assigned by the methods of classical organic chemistry. New, indirect procedures had to be discovered. For this purpose Levene undertook an exhaustive synthetic study of the nitrogenous and the corresponding non-nitrogenous hexoses and their derivatives. From the data the allocation of the nitrogen was deduced. This investigation marked the beginning of his fundamental studies on the correlation of chemical structure with optical activity.

Another group of compounds of complicated formulas, the lipoids, was brought into orderly classification through Levene's researches. The literature was in a sadly confused state, with as many substances described and separately christened as there were authors. By evolving methods for the preparation of these materials in pure state, however, he was able to create scientific order out of chaos in this domain. He showed that three main groups of substances exist among lipoids, two phosphorus-containing and the third phosphorus-free. Closer study demonstrated the fact that two contained a sugar in their molecules, thus cementing their relationship to his studies on other types of carbohydrates.

Through Levene's investigations on optically active materials, particularly among the sugars and proteins, he came to realize the basic significance of optical rotation both as a tool for the elucidation of structures of naturally occurring substances and as a subject of great theoretical import. The problem of configurational relationships—in preparation for which he had, at the height of his career, to renew and broaden his knowledge of advanced mathematics and physics—was to him in later years the most enthralling subject among his varied researches. In these studies, and in fact throughout all his work, he was outstandingly successful in applying the methods and theories of physical chemistry in the province of biology.

As an example of the broad perspective of his scientific philosophy, his analysis of the biological significance of the chemical individuality of tissue elements may be cited. In the first classification he placed those compounds—such as nucleic acids, lipoids and conjugated sulfuric acids—which, though indispensable to life, exhibit no individuality, no specificity; they are found in all tissues, in all organs of all species, are invariable in their structures and occur wherever life is present. Typical of the second classification—the members of which may be present or absent in one or more organs, in one or another species, but preserve their chemical individuality in various species—are the hormones and enzymes. Finally, in the proteins we encounter a group of substances whose complex rela-

tions are still further complicated by the fact that they appear to show differences in chemical structure with variation of species.

To future generations of inquirers into the complexities of living matter, Dr. Levene extended this message of hope and confidence, which is quoted from the concluding lines of his acceptance address at the Willard Gibbs Medal presentation in 1931: "Step by step, one mystery of life after another is being revealed. Whether the human mind will ever attain complete and absolute knowledge of and complete

mastery of life is not essential. It is certain, however, that the revolt of the biochemist against the idea of a restriction to human curiosity will continue. New discoveries in physics, in mathematics, in theoretical chemistry furnish new tools to biochemistry, new tools for the solution of old problems and for the creation of new ones. So long as life continues, the human mind will create mysteries and biochemistry will play a part in their solution."

LAWRENCE W. BASS

MELLON INSTITUTE

SCIENTIFIC EVENTS

ENGINEERING EDUCATION AT THE RENSSELAER POLYTECHNIC INSTITUTE

A NEW plan in engineering education will be put into practice at Rensselaer Polytechnic Institute this year. Through the cooperation of the General Electric Company, a large group of carefully selected students will attend for three consecutive months on the plants of the company.

This plan differs from other cooperative arrangements with industries for the education and employment training of engineering students in the fact that it permits graduation of the students within the regular four-year period, instead of making necessary an extra year in college.

The chief objection of the general cooperative plan—the extra year with its cost to the student in time and money—has been finally overcome. This will be accomplished mainly by including a classroom program to run currently in the plants with the practical experience program, and by arranging summer courses at the institute during which the students will make up what they missed in their absence. Another important feature contributing to the feasibility of this four-year plan is the fact that the outside courses will be concentrated in three consecutive months in the junior year alone rather than being split into alternating periods of several weeks each over several years.

The students selected will be juniors in the departments of mechanical engineering and electrical engineering. The courses will begin on April 1 and continue to July 1, when the students will return to the institute for the summer courses specially designed for them. Thus they will begin their senior year with three months of practical training behind them and at a time when they will be beginning to think most seriously of obtaining jobs after graduation. Much of the work of their last year can thus be interpreted in terms of what they have observed in practical experience. Also they will have had three months to demonstrate and measure their abilities under the observa-

tion and counsel of prospective employers; the work of their senior year also can be interpreted and developed in terms of their discoveries in these respects. Naturally, the General Electric Company entered the plan with the hope that it would help make available men for permanent employment, but there is no employment obligation on the part of either the company or of the students. However, it is pointed out that the experience obviously would be valued by any employer.

In common with other cooperative "earn as you learn" plans, the student will receive wages while in training, thus enabling him to help pay his way through his last year. It is estimated he should save from \$75 to \$125 over living expenses.

EXTENSION COURSES IN AERONAUTICAL ENGINEERING OF CORNELL UNIVERSITY

IN cooperation with the Federal Government's program for national defense, Cornell University opened in Buffalo on October 7 an extension center giving advanced training in aeronautical engineering to employees of the aircraft industry. Unlike some programs set up by other institutions, under which employees must leave their jobs for a time to attend school, the Cornell plan will bring the faculty to the industries and give courses after working hours, so that production will not be curtailed at this critical time. These courses are the first ever given away from the university by the College of Engineering.

A staff from the college, under the direct supervision of Dean S. C. Hollister, will hold classes in Burgard Vocational High School, where facilities have been made available by the Buffalo Board of Education. The entire program will be financed without Federal or state funds.

Instruction will be offered especially for qualified employees of the Curtiss-Wright Corporation and the Bell Aircraft Corporation, where there has been for some time an acute shortage of aeronautical engineers. The immediate plan is to convert mechan-