titatively on the amount of thiamin added. In some of the experiments the fact is brought out that a mixture of the intermediates from which thiamin is made artificially will serve as well as thiamin itself for many plants. This indicates that the power to effect the final step of synthesis is often present in organisms or parts of organisms which have never acquired or have lost the power to effect the entire synthesis. It also suggests strongly that nature's method of synthesis is identical as to the last step with that whereby we made the vitamin in the laboratory. Some plants show a more conspicuous need of the thiazole part, some of the pyrimidine part, presumably because they differ with respect to their synthetic capacities for each part. Some plants, like all animals, must have the fully formed vitamin and can not effect even the final step of synthesis.

What does it mean with respect to the realm of nature as a whole? Its presence in seeds in large amounts seems to me highly significant, especially in view of the fact that seeds are often also repositories of carbohydrate dedicated to the nourishment of the seedling during the process of germination until the young leaves turn their green surfaces to the sun. More and more it seems that man commits a crime against nature when he eats the starch from the seed and throws away the mechanism necessary for the metabolism of that starch by the plant. Since plants have synthetic powers which men lack, the latter have small prospect of successful utilization of the starch unaided by the plants' enzymic component.

In fact as one surveys the situation in philosophical mood it seems that nature's entire economy of thiamin is hand to mouth. Her synthetic powers are barely adequate to keep life as a whole moving forward. She has to resort to symbiosis, whereby the synthetic deficiencies of one organism are made good by the scant surplus of others. She utilizes the dead remains of some of her children that others may grow and propagate their kind. She transports the substance from favored parts to those which are deficient in their synthetic powers. Very widely is it true that a generous external supply of thiamin increases visibly the vigor of the life processes of plants and animals. Probably the chemical instability of thiamin contributes materially to the economy of want.

It would be misleading to suppose that thiamin is the only vitamin which possesses a universal or nearly universal function in living cells. Vitamin C, vitamin B_2 and nicotinamide all appear to play somewhat similar roles. Thiamin is merely the most conspicuous example. The lack of no other accessory substance leads to so early, so profound and so universal a disaster.

These considerations also serve to explain the hitherto baffling problem of thiamin economy in human beings. It is a striking fact that the physiological consequences of thiamin deficiency affect every tissue. Pathological changes in beriberi affect nearly all internal organs. Also in practical trials of thiamin in therapy, favorable responses have been reported in a wide diversity of disordered conditions. In vain have we endeavored to find *the* specific effect of a deficiency of the substance and yet it is credited with almost panacean properties.

The reason is, we believe, that carbohydrate metabolism can not go forward in any living cell without thiamin. One of the outstanding achievements of modern biochemistry is the production of evidence that all cells, no matter whether of tiny unicellular organism or those of highly specialized tissues, have common needs. The liver, pancreas, the brain and each other organ of higher animals performs a special function for the entire assembly of cells which make up the body. But just as each home in a human society subsists by exchange of goods and services with others yet maintains its own kitchen and its own hearth so every cell carries on metabolism and generates energy within itself.

Mankind often lacks an ample supply of thiamin because nature generally must ration it carefully and further because he refines his grains and cooks his food. So when he suffers from constitutional disease his weakest organ may often show a benefit from an artificial supply whether the weakness be due to heredity, to past damage or to present severe strain upon the body economy, as in maternity, hard physical labor or in infectious fever. The apparent want is probably rendered more wide-spread by the fact that in human society the physically unfit increasingly survive and propagate their kind through interruption of the process of natural selection by humanitarian effort.

THE FUTURE OF THE CRELLIN LABORATORY[1]

By Dr. LINUS PAULING

DIRECTOR OF THE GATES AND CRELLIN LABORATORIES OF THE CALIFORNIA INSTITUTE OF TECHNOLOGY

ABOUT twenty years ago, to house the division of chemistry and chemical engineering, which was beginning its rapid expansion under the direction of Professor Arthur A. Noyes, there was constructed the Gates Chemical Laboratory, the gift of Mr. Charles W. Gates and his brother, Mr. Peter G. Gates. This

[1] Address at the dedication of the Crellin Laboratory of Chemistry at the California Institute of Technology, May 16, 1938.

marked the beginning of the period of development of the California Institute of Technology as an advanced scientific school. The second unit of the Gates Laboratory was built ten years later. In view of the personal interests of Professor Noyes, who was the leader in the introduction of the new methods of physico-chemical research in America forty years ago and the founder of the Research Laboratory of Physical Chemistry at the Massachusetts Institute of Technology, it is not surprising that the men whom he gathered about him were primarily interested in the field of physical chemistry and that it was in this field that their principal contributions to knowledge were made.

Professor Noyes, however, recognized the great importance of organic chemistry, and especially of that branch of organic chemistry dealing with substances which are physiologically active, such as vitamins and hormones; and he made plans for the development of the work of the division in this new direction. In my file of letters from Professor Noyes there is one, written in 1929, which contains a detailed chart of the course on which the division is now embarking, nine years later.

It was the interest taken in the work in chemistry at the institute by Mr. and Mrs. E. W. Crellin, leading to the construction of the Crellin Laboratory, which made the initiation of this new program possible. The Rockefeller Foundation, recognizing the need for fostering research in America in the border-line field between chemistry and biology and the suitability of the California Institute for this work, then made a large grant of money to support the researches to be carried on in the Crellin Laboratory during the next six years.

Organic chemistry was developed into a great science during the nineteenth century, and it seems probable that all or nearly all its fundamental principles have now been formulated. There is, however, a related field of knowledge of transcendent significance to mankind which has barely begun its development. This field deals with the correlation between chemical structure and physiological activity of those substances, manufactured in the body or ingested in foodstuffs, which are essential for orderly growth and the maintenance of life, as well as of the many substances which are useful in the treatment of disease. These various physiologically active substances are often extremely complex. Their chemical investigation has been made possible only by the development in recent years of highly refined techniques, permitting the organic chemist to determine the molecular structure of a very complex substance, even though it may be available only in minute amounts. In his attack on a recalcitrant molecule he may find it necessary to strengthen his forces by calling on the physical chemist, who during the past quarter century has developed powerful methods of studying the structure of molecules.

There are many ways in which chemistry is contributing to physiology and medicine—by the development of new general anesthetics, such as ethylene, vinyl ether and cyclopropane, of local anesthetics and of pharmaceuticals of all kinds, including such substances as sulfanilamide, with its extraordinary efficacy in the treatment of streptococcal infections—and continued progress will be made in these fields in the coming years. Considering the great advances in the study of vitamins and hormones since the time a decade ago when the synthesis of not one vitamin had been achieved, we may predict that success will soon reward the men who are now carrying on the attack on vitamin E and that many important discoveries will be made.

These substances are complex—containing twenty, thirty or forty atoms in the molecule—but not so complex as to make the determination of their structure by existent methods impossible. There is, however, a class of substances of the most extreme importance of life, the proteins, whose molecules contain thousands or tens of thousands of atoms. The proteins occur everywhere and serve the most varied purposes. The class includes such varied substances as pepsin, hemoglobin, albumen, globulin, keratin and insulin. The organic chemist has not succeeded in determining the configuration of any protein molecule, and it is doubtful that his methods alone can be applied with success, because the forces which hold the molecule in its characteristic configuration are probably not the primary valence forces with which he is accustomed to deal. Although there has as yet been little indication of a method of attack which might be successful, I feel that the important steps in the solution of this great problem will be taken during the next ten years, through the cooperation of the organic chemist and his colleagues in associated sciences.

In the Crellin Laboratory the organic chemists occupy the second and third floors and the auxiliary rooms on the roof. Conveniently close, occupying the first floor, basement and sub-basement, are the physical chemists, with their appliances for the study of molecular structure by the methods of photochemistry, magnetochemistry, spectroscopy and x-ray and electron diffraction.

For twenty-five years Professor Howard J. Lucas alone has ably carried the burden of instruction in organic chemistry at the institute, and he and, more recently, Dr. J. B. Koepfli have worked effectively on a research program. During the present year there has been increased activity in this field. There was given in March and April a series of lectures on the chemistry of vitamins by Dr. Alexander R. Todd, of the Lister Institute for Medical Research in London, who came here as visiting lecturer, and throughout the year chemical studies on vitamins and hormones were carried on in association with Professor F. W. Went and his colleagues in the division of biology. Dr. Edwin R. Buchman, who was associated with R. R. Williams in the structural investigation and synthesis of vitamin B_1 and who has been carrying on his studies of analogues of this substance at the institute, has been given appointment as research associate in organic chemistry; and Dr. Carl Niemann, of the University of Wisconsin and the Rockefeller Institute for Medical Research, has been appointed assistant professor of organic chemistry. Dr. Niemann, whose investigations have dealt with the chemistry of proteins and carbohydrates, is at present studying at the University of London and will take up residence at the Institute in July.

For the satisfactory completion of the Crellin Laboratory credit is due to the architects, Mayers, Murray and Phillip, and their representative Mr. Wayne Soverns, to Professor Robert A. Millikan, Professor W. B. Munro, chairman of the building committee, and Professor R. R. Martel, of that committee, to Professors W. N. Lacey and A. O. Beckman, who represented the division during the preparation of the plans and the construction of the building, to Mr. William C. Crowell, the contractor, and his able assistants, to Mr. Wesley Hertenstein, supervising engineer, and Mr. L. G. Fenner, superintendent of electrical construction, and to many others who contributed to the work. To all these men, and especially to Mr. and Mrs. Crellin, I express the thanks of the division of chemistry and chemical engineering, and its promise to make effective use of the new laboratory.

THE DEVELOPMENT OF CHEMISTRY AT THE CALIFORNIA INSTITUTE OF TECHNOLOGY[1]

By Dr. ROBERT A. MILLIKAN

CHAIRMAN OF THE EXECUTIVE COUNCIL OF THE CALIFORNIA INSTITUTE OF TECHNOLOGY

IN the spring of 1916 all of us scientific ground squirrels, who all over the United States come up occasionally to sun ourselves at the tops of the holes in which we are burrowing, found the news spreading from hole to hole that a new laboratory of physical chemistry was being started at Pasadena, and that this laboratory was to be under the direction of Arthur A. Noyes, who henceforth expected to oscillate between Boston and Pasadena.

The prestige of Dr. Noyes's name was what gave this news particular interest and currency, for the Institute of Physical Chemistry which Dr. Noyes had founded and directed at the Massachusetts Institute of Technology had already become, through his own work and that of the group of brilliant young men who had come out of it, the most outstanding laboratory of its kind in the country. Indeed, Dr. Noyes himself was already regarded as the most influential of the founders and inspirers of physical chemistry in the United States.

Within a few months of this time Dr. Noyes, whom I had never met before, and his old-time M. I. T. friend, Dr. Hale, whom I had known well since 1896, came to my door in the Ryerson Laboratory of Physics at the University of Chicago saying they wanted to talk over plans and discuss possible personnel for the new "Gates Chemical Laboratory." I first saw this laboratory in January, 1917, when I stopped here for a week to give a few lectures in Throop Hall on my way back to Chicago from Berkeley, where I had been giving the so-called Hitchcock lectures. Let me describe what I saw then. Just two buildings on this campus, namely Throop Hall and the Gates Chemical Laboratory, the rest weeds and dead or dying orange trees. Thirty-seven students all told had up to that date, January, 1917, taken the bachelor's degree from this institution, which in 1908 had announced to the world that it proposed to cease to be essentially a manual training high school and become one of the outstanding scientific and engineering schools of the country.

I marvelled then and I marvel now at the intrepidity, as well as the faith and the vision of the men who, led by George Ellery Hale, took the responsibility of making such an announcement. There was not a hundred thousand dollars of endowment in sight when they made it. By 1917 there were a few of them who had stepped up and backed up their words with enough of their own funds to provide some small beginnings of advanced educational facilities. Mr. Arthur H. Fleming and his daughter, Marjorie, had bought the present campus, and with the aid of other public-spirited citizens had provided for the cost of Throop Hall, erected in 1910.

The first provision for advanced work in chemistry or any other science was made six years later in 1916, when the brothers Charles and Peter Gates came forward and built the first wing of the Gates Chemical

[1] Address at the dedication of the Crellin Laboratory of Chemistry at the California Institute of Technology, May 16, 1938.