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VINCENT DU VIGNEAUD

*1901—1978*

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*A Biographical Memoir by*  
KLAUS HOFMANN

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*Biographical Memoir*

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*W. W. Weyland*

## VINCENT DU VIGNEAUD

*May 18, 1901–December 11, 1978*

BY KLAUS HOFMANN

VINCENT DU VIGNEAUD was born in Chicago in 1901. He was of French ancestry, the son of Alfred du Vigneaud, an inventor and machine designer, and Mary Theresa du Vigneaud. He attended Carl Schurz High School in Chicago, from which he graduated in 1918. When he was a freshman in high school, two friends, who had a chemical laboratory at home, invited him to join them in chemical experimentation. They obtained chemicals from a pharmacist and conducted experiments that involved the fabrication of explosives containing sulfur. This was his first contact with science.

World War I was under way, and young people were needed on the farms. Seniors in high school were offered the opportunity of working on the farms in spring and receiving their diplomas in June. Young Vincent worked through spring and summer on a farm near Caledonia, Illinois. He was very proud of the fact that he could milk twenty cows by hand, and he decided to become a farmer. His older sister, Beatrice, changed his mind and suggested that he go to the University of Illinois at Urbana-Champaign to study chemistry. He followed her advice and registered in chemical engineering. He later recalled:

I found during the first year that it was chemistry rather than engineering that appealed to me most. I switched to a major in chemistry since I was deeply impressed by the senior student's work, especially in organic chemistry. I also found that I was most interested in those aspects of organic chemistry that had to do with medical substances and began to develop an interest in biochemistry.

Young du Vigneaud had no money and had to put himself through college and graduate school. Tearing down boilers, picking apples, working in the library, and jerking sodas were some of his occupations. But the job that helped most financially was that of headwaiter. The next most remunerative job turned out to be the teaching of cavalry tactics and equitation as a reserve second lieutenant in the cavalry.

One day, while working as a waiter, Vincent saw a pretty redhead and said to one of his colleagues, "That's the woman I am going to marry"—and he did. The young woman was Zella Zon Ford. She was an English major, but as she and Vincent became better acquainted he saw to it that she took classes in mathematics and chemistry. Although she graduated as an English major, she knew sufficient chemistry so that after their marriage on June 12, 1924, she was able to teach chemistry in high school.

One of the professors at Illinois who exerted a significant influence on young du Vigneaud was Carl Shipp Marvel, known as "Speed." Du Vigneaud was much impressed with Marvel's lectures and research program, and he decided to do his senior thesis with him. Later he selected Speed to become his master's degree adviser. As he progressed with his studies, he became more and more interested in the relations between biochemistry and organic chemistry. He took advanced courses in biochemistry from H. B. Lewis and the nutritionist W. C. Rose, whose studies on nutrition of the white rat later became role models for some of du Vigneaud's metabolic investigations. He was particularly taken with a lec-

ture by Professor Rose in which the work of Banting and Best on insulin was discussed.

Du Vigneaud earned his master's degree in February of 1924 and accepted a position with the Du Pont Company; he later worked for some time with Dr. Walter Karr at the Philadelphia General Hospital. Nevertheless, his mind was set on graduate study and the earning of a Ph.D. degree. Professor Marvel recalls the following episode:

When du Vigneaud received his master's degree he was offered a job with Walter Karr in Philadelphia, but he was too poor and had no money to pay his way to Philadelphia. To help him out I gave him an assignment to make 10 pounds of cupferron for our organic preparations laboratory and told him I would pay him, as a wage, whatever amount he could produce in material for under the price which we would sell it. He did not ask for any hourly work or time, but we generally agreed that way. In producing the 10 pounds, he'd accumulated enough money to get to his Philadelphia job.

In the spring of 1925 du Vigneaud received an invitation from Professor John R. Murlin to join the Department of Vital Economics at the University of Rochester, New York, to undertake graduate work on the chemistry of insulin. Professor Murlin was a physiologist and not a chemist, and du Vigneaud was eager to discuss his chemical problems with other chemists. In this connection, he became acquainted with Hans Clarke, who at the time was working for Eastman Kodak. Later, Clarke became professor and chairman of the Biochemistry Department at the College of Physicians and Surgeons in New York, and the two men struck up a lifelong friendship.

In 1927 du Vigneaud graduated with a Ph.D. degree; the thesis title was "The Sulfur in Insulin." During his last year in Rochester he was awarded a National Research Council Fellowship, which enabled him to pursue postdoctoral studies with John Jacob Abel, professor of pharmacology at the

Johns Hopkins University Medical School. Here, in collaboration with Oscar Wintersteiner and Hans Jensen, the insulin studies were continued. A second fellowship enabled the young du Vigneaud to do some traveling abroad. He became acquainted with the synthesis of peptides in the laboratory of Max Bergmann at the Kaiser Wilhelm Institut in Dresden and spent some time with Professor George Barger in Edinburgh, Scotland. Bergmann, a former student of Emil Fischer, was a pioneer in the peptide field who later became a member of the Rockefeller Institute for Medical Research (now Rockefeller University) in New York.

Broadly equipped to engage in independent scientific pursuits, du Vigneaud accepted a position in the Department of Physiological Chemistry at his alma mater in Illinois. Biochemistry had become his chosen field, and the opportunity presented itself to have graduate students. He spent three happy years in Illinois; at age thirty-one he became professor and chairman of biochemistry at George Washington University Medical School in Washington, D.C. He was saddened to leave the outstanding department at Urbana with such great professors as Adams, Marvel, Shriner, and Fuson in organic chemistry and Professor Rose in biochemistry, but the opportunity for greater independence was decisive.

He stayed at George Washington from 1932 to 1938, when he was invited to head the Department of Biochemistry at Cornell Medical College in New York City, a chair that had been occupied by Stanley R. Benedict. In connection with this move he stated:

When I came to Cornell Medical College, I brought along five members of my research group, Mildred Cohn, George W. Irving, Theodore Loring, Gail Miller, and John Wood. As in the transfer from Illinois to George Washington I thus had continuity, people with whom I had already been working. This I regard as very important when moving from one place to another. Just as in transplanting a tree with some soil around it, if possible it is well to move a man with some of his environment.

The awarding of the 1955 Nobel Prize in Chemistry constituted an unquestionable triumph for du Vigneaud, but he expressed definite opinions pertaining to the awarding of prizes for scientific achievement. He said to a reporter, "I am expecting to stay in the research field, in the academic world, but I want to tell you I will never work for any prize. I refuse to let my rewards rest in the hands of any committee."

In answer to a congratulatory note I sent him on the occasion of his award, he answered: "The real thrill of such an award is sharing the pleasure with one's friends, and particularly with those who have been associated with me on the trail."

The highly productive career at Cornell Medical College came to an end with his assumption of emeritus status in 1967. But a generous invitation from Professor Harold A. Scheraga, then head of the Chemistry Department at Cornell University in Ithaca, made it possible for du Vigneaud to continue his investigations as professor of chemistry. He was very happy and productive in Ithaca and enjoyed his new surroundings. He wrote to his former collaborators and students: "Those of you who know the Ithaca area will appreciate that I have a fantastic view from my office on the sixth floor of the Chemistry Research Building overlooking Cayuga Lake to the northwest and Beebe Lake, waterfalls and the Fall Creek gorge down below."

In addition to his outstanding contributions to science, du Vigneaud was a great teacher and lecturer. His lectures to students were interesting and well prepared. He emphasized the importance of teaching and his advice to the faculty was: "Remember your first obligation is teaching; when you are teaching it takes precedence over research." His presentations at home and abroad were masterpieces of staging. He would go over his slides with the projectionist in the greatest detail so that the presentation would proceed flawlessly. He was a showman, an artist in communicating research find-

ings. It was a genuine pleasure to listen to his presentations, which were as meticulously prepared and rehearsed as were his scientific papers.

Professor du Vigneaud's scientific career was abruptly terminated when he suffered a stroke in 1974. He died on December 11, 1978. His wife, Zella, had passed away one year earlier. Professor du Vigneaud is survived by a son, Vincent, Jr., and a daughter, Marilyn Renée Brown. Both are physicians.

If one views the totality of du Vigneaud's contributions to science, one recognizes a thread of continuity connecting sulfur-containing, biologically important compounds. This thread extends from insulin to cysteine, homocysteine, methionine, cystathionine, biotin, penicillin, oxytocin, and vasopressin. In the Messenger lectures, delivered at Cornell University in Ithaca in 1950, he likened his scientific work to a trail in research; he wrote:

An attempt was made to retrace the research trails originating from a study of insulin that I have had the pleasure of working out in association with various collaborators over a period of twenty-five years. I attempted to present not only the findings encountered, but also in many instances the stepwise evolution of these findings, including the accidents of fate that played a part.

Some of du Vigneaud's earliest researches dealt with the chemical nature of insulin. Abel crystallized insulin in 1926, and Jensen, Wintersteiner, and du Vigneaud investigated the composition of acid hydrolysates of the crystalline hormone. With the rather primitive methods available at the time, the presence in such hydrolysates of cystine and various other amino acids was established. Based on this evidence, it was concluded that insulin was a protein. Du Vigneaud commented later: "It may seem strange to speak of work establishing insulin as a protein because it is now a generally ac-

cepted fact that a hormone can be a protein or that a protein can be a hormone, yet at that time (1928) there was great reluctance in accepting this viewpoint." The thinking at that time was strongly influenced by the concepts of Willstätter regarding the chemical nature of enzymes that were assumed to be composed of a small functional coenzyme and a protein carrier. Insulin was believed to be a small molecule that was attached or absorbed to a high molecular weight carrier.

In 1930 du Vigneaud became acquainted with L. F. Audrieth, a faculty colleague at the University of Illinois, who was an expert in the liquid ammonia field. He was impressed with liquid ammonia as a solvent for insulin and the sparingly soluble cystine. Audrieth's use of metallic sodium as a reducing agent in liquid ammonia prompted du Vigneaud to apply this method to the conversion of cystine to cysteine. He devised the technique of S-benylation of cysteine by adding benzyl chloride to sodium in liquid ammonia-reduced cystine. The observation that the S-benzyl group was removed from S-benzylcysteine by reduction with sodium in liquid ammonia represented a significant contribution to peptide chemistry; it made possible the transient protection of the thiol group of cysteine during peptide syntheses.

In 1932 Bergmann and Zervas introduced the benzyloxy-carbonyl group (carbobenzoxy group) into amino acids and peptides, and with the discovery that this protecting group could be cleaved by catalytic hydrogenolysis they laid the groundwork for the development of modern peptide synthesis. Du Vigneaud became interested in this method and embarked on synthesizing carbobenzoxy derivatives of amino acids. The story has it that in his laboratory the carbobenzoxyamino acids failed to crystallize. One day, Max Bergmann came to visit the laboratory and, lo and behold, from that time on the carbobenzoxyamino acids crystallized beautifully. Did Bergmann carry seed crystals in his pockets? The

discovery that benzyloxycarbonyl groups can be removed from cysteine and cysteine-containing peptides by sodium in liquid ammonia broadened the scope of the carbobenzyoxy method and opened its applicability to peptides containing sulfur.

As we proceed with this discussion, it will become apparent that the techniques du Vigneaud developed early in his career provided answers to problems he encountered at a later time (oxytocin and vasopressin). Much of du Vigneaud's work in intermediary metabolism concerned the formation of cysteine in the animal organism and the metabolic relationships among methionine, cysteine, homocysteine, cystathionine, and choline. He called the underlying reactions "transulfuration" and "transmethylation." It was known that methionine could support growth of laboratory rats on a cysteine-free diet, and Rose had shown that methionine was an essential dietary constituent for the rat. In short, the rat is capable of synthesizing cysteine but not methionine. In 1931 du Vigneaud discovered a new sulfur-containing amino acid while exposing methionine to strong sulfuric acid. This compound was the next higher symmetrical homolog of cystine and he named it "homocystine." Later, he discovered that the reduced form of this amino acid, homocysteine, was a metabolically important compound. Du Vigneaud observed that homocysteine, like methionine, could support the growth of rats on diets deficient in cystine.

These observations pointed to a metabolic relationship between methionine and homocysteine and suggested that demethylation of methionine could be involved in cysteine biosynthesis. Du Vigneaud synthesized L-cystathionine, a thioether in which the carbon chains of cysteine and homocysteine are connected by a single sulfur atom, and found that this compound sustained growth of rats on a cysteine-deficient diet. This observation indicated that the rat was capable of cleaving the thioether linkage with formation of cys-

teine. It was observed further that cystathionine did not give rise to homocysteine, an observation that was supported by *in vitro* studies with liver slices. The addition to liver slices of a mixture of homocysteine and serine resulted in a 60 percent conversion of homocysteine sulfur into cysteine, providing strong evidence for the hypothesis that homocysteine was indeed an intermediate in the formation of cystathionine. The importance of serine as a precursor of cysteine had been demonstrated earlier by Dewitt Stetten.

Before continuing the discussion of du Vigneaud's work on the intermediary metabolism of sulfur compounds, it seems fitting to have a short synopsis of the status of biochemistry in the 1930s. At that time, the Biochemistry Department of the College of Physicians and Surgeons at Columbia University, under the leadership of Hans Clarke, had developed into one of the outstanding departments in the country and one that made scientific history. It was in this department that Rudolf Schönheimer and his colleagues performed the classical tracer experiments pointing to "the dynamic state of the body constituents." The application of isotopes to the solution of biochemical problems provided the key for these developments, which revolutionized biochemical thinking. Harold C. Urey, also of Columbia University, had developed the methodology for the preparation of deuterium oxide and other elements enriched with respect to stable isotopes, and the availability of these compounds opened far-reaching biochemical frontiers. Because growth experiments had severe limitations, du Vigneaud applied the new tracer techniques to the study of the conversion of methionine to cysteine. He synthesized *DL*-methionine labeled in the  $\beta$  and  $\gamma$  positions with  $^{13}\text{C}$  and containing  $^{34}\text{S}$  and fed this compound to rats. The rats were shaved at the beginning of the experiment and received another haircut after thirty-eight days in the experiment. The cystine isolated from the hair contained  $^{34}\text{S}$ , but no  $^{13}\text{C}$ . From the results of this ex-

periment it was concluded that only the sulfur, not the carbon chain of methionine, was utilized for cysteine biosynthesis. This provided final proof that, in the rat, cysteine synthesis from methionine involves demethylation with formation of homocysteine followed by condensation of the homocysteine with serine to form cystathionine. The latter is cleaved with formation of cysteine and  $\alpha$ -ketobutyric acid. In essence, the conversion of methionine to cysteine involves a transfer of the methionine sulfur to serine. This, according to du Vigneaud, became known as "transulfuration."

An interesting coincidence led to the discovery of the concept of transmethylation or methyl transfer. Here again the crucial evidence was derived from rat feeding experiments. Rose observed good growth of rats fed a methionine-cysteine-free diet that was supplemented with homocysteine. Similar experiments carried out in du Vigneaud's laboratory produced negative results; the rats failed to grow. The animals in both laboratories grew well when the diet was fortified with methionine. The difference in the results was traced to the vitamin supplements used. Du Vigneaud employed crystalline B complex vitamins, but Rose used rice bran extract (Tikitiki) as the vitamin source. Du Vigneaud noted that his rats developed fatty livers while on experiment. It was known from the work of Best that choline inhibited fatty infiltration of the liver, and Du Vigneaud reasoned that this pathology could be the result of a choline deficiency. He decided that the factor missing in his diet could be choline, and this proved to be correct. Accordingly, diets containing both homocysteine and choline were fed, and such a regimen supported growth as well as did methionine.

On the basis of these findings du Vigneaud speculated that choline, a compound rich in methyl groups, could act as a methyl donor for the conversion of homocysteine to methionine. These early findings led to the concept of transmethylation and that of "labile" methyl groups. The obser-

vation that rats grew well and failed to develop fatty livers on a choline-free diet supplemented with methionine suggested to du Vigneaud that the methionine could serve as a methyl source for choline synthesis. These concepts were amply confirmed by tracer experiments. Methionine in which the methyl group was enriched with respect to deuterium was fed to rats, and choline was isolated from the tissues. This choline contained deuterium in its methyl groups, demonstrating transmethylation from methionine. Conversely, choline containing deuterium was given to rats, and deuterium was present in the methyl group of methionine. Thus the hypothesis that methionine was biosynthesized from homocysteine by a methyl transfer from choline was substantiated. It was also observed that the transfer of methyl groups was a continuous process. In addition, du Vigneaud found that the methyl group of creatine was derived from the methyl group of methionine. The transfer of methyl groups from methionine to choline and from choline to methionine is a reversible process, but the methyl group of creatine does not serve as a methyl donor for the conversion of homocysteine to methionine. Based on these studies, du Vigneaud concluded:

From our study, we know only that the methyl group of methionine and choline can be transferred, but we do not know whether methionine or choline react directly or whether they are precursors of derivatives from which the methyl groups are released. Although methionine can be demethylated *in vitro*, the conditions required are drastic. Attention must therefore be directed to any possibility whereby the bond between the methyl group and the sulfur atom may be weakened. The formation of a sulfonium ion would be expected to effect such a labilization.

It remained for Cantoni to identify the methyl donor in biological systems as the sulfonium ion S-adenosylmethionine.

The work on biotin resulted from an invitation to du Vigneaud from Paul György to collaborate in establishing the chemical nature of the anti-egg-white injury factor in liver,

which György had designated as vitamin H. Rats receiving diets containing large proportions of raw egg white as the source of protein develop severe dermatitis and nervous disorders and die if the condition is not relieved. Certain foodstuffs, such as liver and yeast, contain a substance capable of preventing and curing this disorder. The curative factor was named vitamin H by György (H being derived from the German word *Haut*, meaning skin). Biotin, a yeast growth factor, had been isolated from egg yolks by Kögl and Tönnes. Du Vigneaud, György, and collaborators were able to cure egg-white injury with Kögl's pure biotin, demonstrating that vitamin H and biotin were one and the same compound. Biotin was isolated from liver extracts and milk in the Cornell laboratories, and the chemical structure of the compound was established. The structure worked out by du Vigneaud and collaborators was verified by chemical synthesis in the Merck laboratories. Biotin, first discovered as a yeast growth factor, turned out to be a mammalian vitamin.

The Second World War interrupted the operations of the laboratory, and du Vigneaud was invited by the wartime Committee on Medical Research, OSRD, to join the great effort being organized in this country and in England to work on the chemistry of penicillin. Many contributions to penicillin chemistry emanated from the Cornell laboratory. Perhaps the most outstanding were those dealing with the synthesis of minute quantities of the antibiotic and its identification with the natural compound.

One amusing sidelight to the penicillin story comes from Sofia Simmonds. During a discussion with Hans Clarke, she remarked that penicillin must contain sulfur. Hans Clarke, who was in charge of the U.S. part of the super-secret penicillin project, was shocked to hear this and he wanted to know how she'd found out. She said we all could tell; the labs on the second floor, where the work was being done, leaked ben-

zylmercaptan into the hallway—any V du V person knew what that meant.

Du Vigneaud's work on the posterior pituitary principles oxytocin and vasopressin was started in 1932 and continued until 1940, when it was interrupted by the Second World War. During this time, however, the emphasis of the laboratory was on the metabolic aspects, transulfuration and transmethylation, and du Vigneaud referred to his work with the posterior pituitary hormones as his hobby. Some progress had been made in purification of these principles, mainly by the use of precipitation and electrophoretic techniques, but of prime importance were some preliminary observations suggesting that oxytocin and vasopressin were derivatives of cystine. During the war, new techniques became available that had a critical effect on the progress of the posterior pituitary hormone project. Of immediate importance were the Craig countercurrent distribution published in 1944 and the starch column technique of Moore and Stein for the quantitative separation of mixtures of amino acids in acid hydrolysates of proteins on a micro scale.

Du Vigneaud returned to the study of the posterior pituitary principles in 1947. A concentrate he had received from Parke-Davis in 1940 that was stored during the war years was reassayed in 1947 and had retained 50 percent of its original oxytocic potency. Homogeneous oxytocin exhibiting a high level of biological activity was isolated from this material by the Craig countercurrent technique. The amino acid composition of an acid hydrolysate of this material, determined by the Moore-Stein technique, showed the presence of cystine, glutamic acid, aspartic acid, glycine, isoleucine, leucine, proline, and tyrosine in molar ratios of 1:1. In addition to these amino acid residues, the hydrolysate contained three moles of ammonia. The amino acid residues plus ammonia accounted for 97 percent of the hydrolyzed

material. Molecular weight determinations were in agreement with a monomer. Oxytocin was oxidized with performic acid, and the amino acid composition of the oxidized material was determined. The composition was identical to that of the unoxidized material, except that in lieu of cystine two molecules of cysteic acid were present.

It followed from this and other results that oxytocin was a cyclic peptide. Using the dinitrofluorobenzene technique of Sanger, it was shown that oxytocin contained a free amino group that was derived from one of the two cysteine residues; a free carboxyl group was not present. By a combination of the Edman technique and analysis of partial acid hydrolysates, the amino acid sequence of oxytocin was established as H-Cys-Tyr-Ile-Glu-Asp-Cys-Pro-Leu-Gly-OH. The final, as yet unanswered, question related to the sources of the three ammonia molecules. These were shown to be asparagine, glutamine, and glycnamide. Thus the structure of oxytocin was established as H-Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gly-NH<sub>2</sub>. In his characteristically cautious approach, du Vigneaud commented as follows: "It is obvious that, in spite of the fact that this was the only structure we could arrive at through the realization of the results from our degradative work, synthetic proof of structure was mandatory."

The crucial steps in du Vigneaud's oxytocin synthesis were based on reactions in liquid ammonia he had investigated many years earlier. When subjected to reduction with sodium in liquid ammonia, oxytocin was converted to the open-chain oxytoceine, and this on air oxidation reconstituted biologically active oxytocin. This behavior of oxytocin was the key for its successful synthesis. Another model study, using the natural hormone, was performed that suggested the strategy for a successful synthesis. Oxytocin was reduced to the open-chain oxytoceine, and benzyl chloride was added to the reaction mixture, affording S,S'-dibenzoyloxytoceine. Deben-

ylation of this material with sodium in liquid ammonia followed by air oxidation regenerated biologically active oxytocin.

The facile ring closure to the 20-membered ring structure of oxytocin from the open-chain peptide oxytoceine indicated that the open-chain structure had a preferred conformation in which the two SH groups are located in close proximity for cyclization to occur. This appears to constitute the first example of the now well-established principle that the amino acid sequence of a protein endows it with the thermodynamic information necessary for folding into a specific conformation. Based on these model reactions, du Vigneaud synthesized N-benzyloxycarbonyl-S,S'-dibenzyloxytoceine and converted the synthetic material into active oxytocin in the manner discussed above. The synthetic oxytocin was identical with the natural hormone. The first oxytocin synthesis was communicated to the *Journal of the American Chemical Society* on July 13, 1953. The paper concluded with the following statement:

If the synthetic product truly represents oxytocin, which it does so far as we are concerned, this would constitute the first synthesis of a polypeptide hormone. What effect slight changes in the structure of a compound of such complexity might have on chemical, physical, and biological properties must be investigated.

While the work on oxytocin was under way, the structure of vasopressin was also determined. With a wealth of data based on degradation studies, paralleling those outlined for oxytocin, a structure for arginine vasopressin was arrived at that was very similar to that of oxytocin. This hormone embodies the same ring structure as oxytocin but contains two amino acid exchanges. Isoleucine is replaced by phenylalanine and leucine is substituted by arginine. Lysine vasopressin contains lysine in lieu of arginine.

A synthesis of lysine vasopressin was completed in 1960. The observation by du Vigneaud that certain combinations of amino acids into peptides can result in compounds exhibiting potent physiological activities opened a vast field of biological and chemical research. He stated, "It is a little startling to think that the amino acids when put together in a certain way, in a particular architecture, can lead to such an array of compounds exhibiting such a variety of physiological and pharmacological properties."

Du Vigneaud's findings with oxytocin and vasopressin were of great fundamental importance: They demonstrated for the first time that replacement of certain amino acid residues in the sequence of a physiologically active peptide can bring about significant changes in biological action. The exchange in oxytocin of isoleucine for phenylalanine and of leucine for arginine (or lysine) alters the physiological activity of the molecule from one of mainly oxytocic to one with mainly vasopressor potency. These discoveries have stimulated much research into the relations between peptide structure and physiological function. Hundreds of analogs of the posterior pituitary hormones have been prepared as a consequence of du Vigneaud's work, and his pioneering studies have spawned the recent explosive activity in the peptide field.

Thus far we have been concerned with the story of du Vigneaud's life and with his many scientific accomplishments. We may now ask: Who was this man and what was the atmosphere in his laboratory that promoted such a wealth of fundamental work? His laboratory was extremely well organized. Since he was a very busy man who was not always available for consultations, he initiated a system of colored slips for communicating with him. There was a pink slip for suggesting new ideas and new research approaches, there

was a green slip for reporting research results, and, finally, a white slip for requesting microanalytical services. The "greens" were du Vigneaud's favorite. He wanted them at least weekly from every researcher in the group, and he read them with extreme care. To those who were reluctant to write up half-finished experiments, he insisted that that was the fun of the research to him. He couldn't remember (he said) the results presented to him in a neat package at the end nearly as well as if he had been in on them as they developed day by day. Many a collaborator was awed by his memory for details in someone else's research reports, from months or years gone by, which he could bring to bear on the problem at hand. The potential aid thus available, once appreciated, did a lot to lighten the task of grinding out the green slips! But, besides all of this red tape, there was ample opportunity to have a private audience with the chief.

The laboratory was a busy place indeed, and hard work was the order of the day. Graduate students were expected to spend several evenings a week in the laboratory, as well as part of Saturday, and papers were frequently written late into the night. Professor du Vigneaud lived in the suburbs of New York, but he maintained a beautifully furnished room in the department where he spent many a night during the week. These were the evenings when he came to visit with his collaborators. Smoking a White Owl cigar, which he gracefully waved poised between his strong fingers, he shared a cold soft drink with us and discussed the latest research results. Speaking quietly and easily, he used such words as "exciting," "surprising," "intriguing"—all suggesting great pleasure in the stepwise evolution of the research. He was always highly interested in the day's results and was truly devoted to his scientific work. He felt very secure and loved his work. To a reporter he said:

I have had the privilege and the thrill of following those researches that I've always wanted to do. I've always had the privilege of working on what I've wanted to work on. I have been accompanied in the various stages of these exploratory researches by a group of fine and loyal associates. I've also been fortunate throughout the years in the generous research support I've received from various sources.

He had a highly critical attitude toward laboratory results and this permeates his writings. Every possible angle of a project was discussed at great length, and new approaches and ideas that could clarify an issue were explored in depth. Papers were written in collaboration with those who did the work; a secretary was present, and while discussions went on she was typing the latest version of a draft. A great many versions were hammered out before the chief was satisfied.

Unquestionably, du Vigneaud was in command, and he was highly respected by his collaborators. He had a jovial manner with people, and every year he invited his entire crew to his home in Scarsdale for a picnic with softball and other entertainment. "Dee," as he was known by his colleagues over the years, associated with a great number of graduate students, postdoctoral fellows, and visiting professors. All the people who ever worked in Dee's laboratory belonged automatically to the V du V Club. He kept in constant touch with us, and every year during the Federation meetings we all got together for beer and pretzels to share time with former colleagues, the chief, and his charming wife, Zella.

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## HONORS AND DISTINCTIONS

## DEGREES

B.S., University of Illinois, 1923

M.S., University of Illinois, 1924

Ph.D. (Biochemistry), University of Rochester, 1927

## HONORARY DEGREES

D.Sc., New York University, 1955

D.Sc., Yale University, 1955

D.Sc., University of Illinois, 1960

D.Sc., University of Rochester and St. Louis University, 1965

## UNIVERSITY APPOINTMENTS

National Research Council Fellow, Johns Hopkins University, 1927–28

National Research Council Fellow, Kaiser Wilhelm Institute, Dresden, Germany, and University of Edinburgh Medical School, 1928–29

Associate, University of Illinois, 1927–30

Professor and Head of Department of Biochemistry, School of Medicine, George Washington University, 1932–38

Professor and Head of Department of Biochemistry, Cornell University Medical College, 1938–64

Professor Emeritus of Chemistry, Department of Chemistry, Cornell University, 1964–74.

## MEMBERSHIPS

National Academy of Sciences, 1944

American Philosophical Society, 1944

Royal Society of Sciences of Uppsala, 1950

Honorary Fellow of the Royal Society of Edinburgh, 1954

Honorary Fellow, Royal Institute of London, 1959

## AWARDS AND LECTURESHIPS

Hillebrand Award, Washington Chemical Society, 1936

Foster Lecturer, University of Buffalo, 1939

Harvey Society Lecturer, 1942

- Meade-Johnson Vitamin B Complex Award, American Institute of Nutrition, 1942
- Hitchcock Lecturer, University of California, 1944
- Nichols Medal, New York Section, American Chemical Society, 1945
- Borden Award, Association of American Medical Colleges, 1947
- Visiting Lecturer, American Swiss Foundation for Scientific Exchange, Switzerland, 1947
- Award of Merit for War Research, United States Government, 1948
- Lasker Award, American Public Health Association, 1948
- Stieglitz Memorial Lecturer, University of Chicago, 1948
- Eastman Lecturer, University of Rochester, 1949
- Liversidge Lecturer, University of Cambridge, 1949
- Special Lecturer, University of London, 1949
- Messenger Lecturer, Cornell University, 1950
- Herter Lecturer, New York University, 1952
- Edsel B. Ford Lecture, Henry Ford Hospital, 1954
- Goldforb Lecturer, 1954
- Harvey Society Lecturer, 1954
- Osborne and Mendel Award, 1954
- John Scott Award, Philadelphia, 1954
- Remsen Memorial Lecturer, Johns Hopkins University, 1954
- Scientific Award, American Pharmaceutical Manufacturers' Association, 1954
- Chandler Award, Columbia University, 1955
- Annual Hanna Lecturer, Western Reserve University, 1955
- Nobel Prize in Chemistry, Nobel Foundation, 1955
- Passano Award, Passano Foundation, 1955
- Dakin Memorial Lecturer, Adelphi College, 1956
- Willard Gibbs Medal, Chicago Section, American Chemical Society, 1956
- Nieuwland Lecturer, University of Notre Dame, 1956
- Edgar Fahs Smith Lecturer, University of Pennsylvania, 1958
- Alumni Achievement Award, University of Illinois, 1959
- Martland Memorial Lecturer, 1959
- Nutrition Foundation's 20th Anniversary Award, 1961
- Pirquet Society of Clinical Medicine Medalist, 1964
- American College of Physicians Award, 1965
- The Eli Lilly Lecture Award, Endocrine Society, 1967

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