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STANLEY, WENDELL MEREDITH (b. Ridgeville, Indiana, 16 August 1904; d. Salamanca, Spain, 15 June 1971) chemist, virologist, educator.

In 1935 Wendell Stanley crystallized tobacco mosaic virus, an achievement which was awarded a Nobel Prize in 1946. This and subsequent findings demonstrated that an infectious agent could have the properties of a chemical molecule and posed the biochemical problems of the mechanisms of inheritable duplicability. The initial observations were soon confirmed in England by F.C. Bawden and N.W. Pirie, who showed also that this and other plant viruses contained ribose nucleic acid (RNA). Their result, in its turn, set the problem of the structural and functional roles of the nucleic acids in viruses. The almost simultaneous discovery by M. Schlesinger of deoxyribonucleic acid (DNA) in some bacterial viruses extended this finding. Thus, in the years 1935 and 1936, the biologists were startled to learn that some of the smallest organisms, in the group known as "filterable viruses," were isolable by methods designed for proteins and were amenable to rigorous chemical and physical characterization. The results at that time indicated that the viruses contained both protein and a distinctive but little studied substance, a nucleic acid. Early commentators on these findings called attention to the similar reproductive capabilities of viruses and genes, and in 1937 E. Wollman added "La possibilité d'"inoculer" des genes à des cellules ne nous semble pas pouvoir être exclue a priori."

By 1944, these events culminated in the demonstration by O.T. Avery, C.M. Macleod and M. McCarty that the Pneumococcal transforming agent was a biologically specific DNA. Thus within the period of 1935 to 1944, the fundamental problems of the nature of the gene, its duplication and mode of action had been transferred to model systems of virology and microbiology. The analysis of these systems over the next thirty years determined the course of

biological science by facilitating the dissection of the mechanisms of inheritance, and by leading to the integrative development of numerous disciplines, i.e., biochemistry, genetics and structural chemistry, as "molecular biology."

Wendell Stanley, the initiator of this modern era of biology, was the son of James G. and Claire (Plessinger) Stanley. His parents published the local newspaper, and as a boy, Stanley helped to collect news, to set type and to deliver the final product. He attended public schools in the little town of Ridgeville, completed the last two years of high school in Richmond, Indiana, and entered Earlham College in Richmond, Indiana, in 1922. In addition to academic majors in chemistry and mathematics and an active social life, Stanley played football for all four of his collegiate years and captained a winning team in his senior year. In a state known for several outstanding sports-oriented colleges, the relatively slight Stanley was selected as end of the All-Indiana State team. Nevertheless, Earlham College, which began as a Quaker school, prided itself on the quality of its liberal arts education, stressing the examination of values and moral commitments, as well as of "facts." Several events in Stanley's later career suggest that the choice of Earlham and his life there contributed significantly to his bearing and attitudes.

On graduation in 1926, Stanley aspired to be a football coach and in the spring of that year visited the campus of the University of Illinois with this future in mind. While there he met Roger Adams, a doyen of organic chemistry. He learned of graduate work in chemistry and armed with his baccalaureate from Earlham, entered the University of Illinois. As a graduate student with Adams, he worked on two types of problem, one on the stereochemistry of biphenyls and the other on the synthesis and properties of compounds potentially bactericidal for Mycobacterium leprae. He published eleven papers on these subjects with

Adams between 1927 and 1933, obtaining an M.S. in 1927 and a Ph.D. in 1929. Among these, Stanley and Adams synthesized hydnocarpylacetic acid and showed it to be identical with natural chaulmoogric acid. Also all the bactericidal aliphatic sodium salts were found to be marked depressants of surface tension.

A paper in this area was published in 1929 with Adams and another graduate student, Marian S. Jay, who married Stanley in that year. The couple had a son and three daughters, of whom the son, Wendell, Jr., is known for his work in molecular biology. It may be relevant to Stanley's later success that the single joint paper of Stanley, Jay and Adams in the Journal of the American Chemical Society follows an early paper by J.B. Sumner and D.B. Hand on the isoelectric point of crystalline urease, determined as the point of minimum solubility. This is a method used by Stanley in his later crystallization of tobacco mosaic virus.

Stanley was an Instructor at Illinois in 1930, and won a National Research Council Fellowship in Chemistry, which he took in 1930-1931 with Heinrich Wieland in Munich, Germany. His work with Wieland was on the characterization of the sterols of yeast.

The Stanleys returned to the United States during the Depression; he was appointed to a position with W.J.V. Osterhout at the Rockefeller Institute in New York. Osterhout, who had been studying the transport and concentration of ions in plant cells, such as Valonia, had asked Stanley to develop a model system to transport ions selectively across a membrane. Stanley, quite unfamiliar with problems of this type, read extensively in the field and in 1931 helped to devise systems for the selective accumulation of potassium and sodium. A non-aqueous medium representing the protoplasmic surface was interposed between alkaline and acidic aqueous phases. An accumulation of the cations occurs in the more acid phase, followed by an increase of osmotic

pressure and of water entry. The entire system simulated accumulation in Valonia very well, permitting a comparison in model and Valonia of the factors modifying uptake. The work with Osterhout undoubtedly sharpened Stanley's understanding of the biophysical chemistry of the time, and probably introduced him to some current problems of plant physiology.

In 1932 he moved to the Department of Animal and Plant Pathology of the Institute, established at Princeton, New Jersey, since 1916. This branch arose in response to the principle that the Institute could not limit itself to the study of human disease and to the proposal in 1914 to establish a Department of Plant Pathology. The distinguished American microbiologist and comparative pathologist, Theobald Smith, became Director. Laboratories were built on farm land on the outskirts of Princeton. Smith and the groups he assembled became active in the study of various protozoan, bacterial and virus diseases of veterinary importance. In 1926, a branch of General Physiology, comprised of John Northrop and Moses Kunitz, became part of Smith's administrative domain, as had numerous other groups representing insect physiology, parasitology, genetics and nutrition. By 1926, the size and diversity of the enterprise became excessive for Smith, who was eventually replaced by Carl Ten Broek, an early collaborator knowledgeable in virus infections. Under Ten Broek, who helped to sustain the work of virologists such as Richard Shope and Otto Glaser, a Division of Plant Pathology was established in 1931 with Louis O. Kunkel as its Head. He moved to Princeton in 1932 and brought Stanley there shortly thereafter.

Kunkel had come from the Boyce Thompson Institute for Plant Research and had been associated with C.G. Vinson and A.W. Petre, who had obtained promising results in the chemical separation of tobacco mosaic virus. Kunkel asked his entire group to focus on mosaic diseases, principally that of the tobacco

mosaic disease. In 1892, the Russian, D. Ivanovski, had shown that this disease could be transmitted by the sap of an infected plant after filtration through porcelain. M. Beijerinck in Delft had made similar observations in 1898 and had postulated the existence of a pathogen smaller than bacteria, i.e., a "filterable virus." Among several virologists in Kunkel's group, Francis Holmes had developed a method of estimating infectious virus particles by counting the localized lesions arising after inoculating the leaves of selected plants. Philip White was growing virus-susceptible tomato roots aseptically in tissue cultures in order to dilute out possible secondary invaders. Kunkel himself discovered related viruses and compared their host ranges with that of tobacco mosaic virus. He is also known for the "heat-cure" of plants, including trees, thought to be infected by viruses. Some of these infectious agents are known to be mycoplasmas and not to be viruses.

Beginning with the work of H.A. Allard in 1916, various investigators had concentrated and purified the virus. Between 1925 and 1935, Vinson and Petre had used lead acetate to precipitate the virus. The fact that the virus might be handled as a chemical precipitable by protein precipitants led Stanley to explore the possibility that this virus was a protein. In 1933 and 1934, Stanley worked furiously to test the infectivity of fresh or partially purified extracts exposed to more than a hundred reagents, including some proteolytic enzymes. Such enzymes, including trypsin, had been isolated and crystallized just a few years earlier by Northrop and Kunitz at the Institute in Princeton. The successes and methods of this group were a continuing source of encouragement in this early period. Stanley found that trypsin inactivated the virus but that the latter could be reactivated. The enzyme affected the plant more than the virus, and Stanley concluded that trypsin did not degrade the virus proteolytically. On the other hand, a slow inactivation by pepsin in the

range of hydrogen-ion concentration (pH) in which pepsin was proteolytic was consistent with the idea that the virus was a protein. In general, infectivity was lost at extreme pHs, or in the presence of oxidizing agents, or of protein precipitants. Pursuing the results of Vinson and Petre, it was possible to use a low concentration of lead acetate at high pH to eliminate colored materials without reducing infectivity, and he introduced such a step in his initial successful purification. During purification steps, the pH was adjusted at non-inactivating levels, which facilitated solubilization or precipitation, and which he had established earlier.

In this early work, published in 1935, large batches of frozen infected plants, ground in the frozen state, were thawed in a buffer containing sodium phosphate (high pH) and the filtrate was precipitated at lower pH with a high concentration of ammonium sulfate. This precipitate contained virus which was extracted and reprecipitated. Lead acetate at high pH was used to remove colored material and an asbestos powder adsorbed the virus at low pH. The virus was eluted at high pH and the virus was crystallized from this solution as small "needles" by the addition of acetic acid to a defined low pH in the presence of 20% saturated ammonium sulfate.

The initial report in 1935 described a product containing 20% nitrogen but the first complete paper in 1936 (accepted in November 1935) reported nitrogen contents by two methods of 16.1-16.6%, values consistent with those of proteins and most nucleoproteins. However, Stanley did not find phosphorus or sulfur in the virus. The protein was recognized to be very large since it did not pass through membranes that did not retain smaller proteins, such as egg albumin. Resolution and recrystallization of the protein some ten times did not affect the dilution of the virus used to produce local lesions. The extracts of single lesions gave rise, in subsequent infections, to very much larger amounts

of the infectious protein, indicating its multiplication, as befits a virus. Antisera against the virus were prepared in guinea pigs and rabbits, and these reacted specifically against purified virus preparations, as well as against the juice of infected plants. Uninfected plants did not contain proteins capable of reacting with these antisera. In a later study it was shown that tobacco mosaic virus multiplied as such in tomato plants. Further, a distinctly different strain of the virus, the aucuba mosaic virus, multiplied as such in aucuba-infected tobacco.

In interpreting his results, Stanley was influenced by the results of Northrop and Kunitz, who had described the existence of pancreatic proenzymes, such as proteolytically inactive trypsinogen. This substance was converted by proteolysis to active trypsin by adding a trace of the active proteolytic enzyme. Could a plant contain a serologically inert pro-virus that would be converted "autocatalytically" by the active virus to a serologically active virus? It was shown very soon that significant amounts of comparable large molecules capable of serving as pro-virus were not present in the juice of normal plants, although various modifications of the precursor hypothesis were not excluded. It was not until the late 1940s, in work with bacteriophage systems, that it was shown that virus multiplication required extensive de novo synthesis of proteins and nucleic acids, and very much later in the 1960s that the processes of synthesis of nucleic acids and proteins were comprised of far more complex metabolic and synthetic events than that described for the conversion of trypsinogen to trypsin. In 1935 Stanley stated that "Tobacco-mosaic virus is regarded as an autocatalytic protein which, for the present, may be assumed to require the presence of living cells for multiplication." It was shown a decade later, in 1946 and 1947, in studies with bacterial viruses, that the host cells continued to supply the energy, as

well as an extensive metabolic apparatus, for the multiplication of these viruses. These conclusions are applicable similarly to plant and animal viruses multiplying in their respective hosts.

In discussing the extraordinary result that an organism capable of inheritable duplication could be defined as a relatively simple substance capable of forming crystalline arrays, Stanley entered the morass of wondering if the virus were "alive." His conclusion that this virus was not "alive" elicited much discussion of the meaning of the term and, in particular, we can note the important essay in 1937 by N.W. Pirie entitled "The Meaninglessness of the Terms Life and Living." After a useful discussion of the attributes of the many properties of organisms and substances, Pirie noted the lack of agreement on the meaning of the word "living." He suggested that "it seems prudent to avoid the use of the word 'life' in any discussion about border-line systems," and indeed his essay squelched further discussion for about twenty-five years. However, in later years, with the development of space programs, many individuals, including Pirie, have then had to attempt to define just which characteristics ought to be sought in the samples to be collected on Mars or elsewhere.

The first group to confirm Stanley's discovery included F.C. Bawden and N.W. Pirie, who in earlier studies of the potato X virus had concluded that this virus was comprised of proteinase-sensitive proteins. However, this flexuous virus did not easily form crystalline arrays. Turning to tobacco mosaic virus, they were able to isolate the "needles" observed by Stanley, but with the aid of the X-ray crystallographers, J.D. Bernal and I. Fankuchen, it became clear that the "needles" did not possess three-dimensional regularity. The purified virus particles were relatively stiff rods of constant diameter, which were aligned during flow, and packed in hexagonal arrays to form

needle-like "liquid" or "para" crystals. This occurred on precipitation by salts at a pH of minimum solubility, i.e., at the isoelectric point as determined by Sumner and Hand in 1929, or by steric exclusion and the abstraction of water to large foreign hydrophilic molecules. Bernal and Fankuchen, in later detailed studies of the virus "paracrystals," described the open-ended needles as "tactoids." Bawden and Pirie also showed that a further purification of virus particles in concentrated suspension permitted a separation into two phases, of which the bottom phase was spontaneously birefringent in polarized light, i.e., the virus had crystallized in the arrays represented by the smaller "tactoids." The top phase was now more dilute and showed anisotropy of flow, becoming birefringent in polarized light in regions of flow aligning the particles. Cycles of differential centrifugation effected this degree of purification from both soluble contaminants and insoluble cell fragments.

Although Bawden and Pirie have each questioned the identity of Stanley's initial product, it should be noted that the high nitrogen content was corrected by the end of 1935, before the first paper by the English group (submitted on 17 November 1936 and published on 19 December 1936). Furthermore, Stanley's material was analyzed by an American crystallographic group, and the data published in November 1936 was described by the English group as follows in a note added on 3 December 1936: "Wyckoff and Corey have published an X-ray study of the ammonium sulphate crystals of tobacco mosaic and aucuba protein. Their measurements of the intramolecular spacings obtained with unorientated material agree with ours, notably the lines they record at 11.0, 7.44, 5.44 and 3.7 A correspond to our measurement of the planes (0006, 9, 12, 18) respectively." Thus the material obtained by the English workers was identical to an early preparation of the virus obtained by Stanley, i.e.,

made before any publication by the former group.

In addition to the British clarification of the degree of order found in isolated viral arrays, their earliest paper records their discovery of the presence of 5% RNA in this virus, a result they soon extended to related viruses. Higher percentages of RNA were discovered later by this group in some spherical viruses, such as the tomato bushy stunt virus and the tobacco necrosis viruses. At first Stanley was unwilling to accept this result, which had been communicated to him by Pirie early in 1936. Stanley considered the RNA to be a disposable contaminant and disregarded the unusual ultraviolet absorption spectrum of the virus, now known to relate to the presence of nucleic acid. However, H.S. Loring, a collaborator of Stanley, found phosphorus and RNA in organic combination with protein in several viruses, and in 1938 Loring and Stanley corrected their earlier variable and confusing values. Their report was extended in 1939 by F.A. Ross and Stanley to include the presence of sulfur in the virus, exposed as sulfhydryl groups in side chains of cysteine in the native protein.

The discovery of the presence of RNA in the virus and its solubilization after denaturation of the virus protein by heat, detergents, alkali or acid facilitated the characterization of this material. It had been suggested by P.A. Levene that RNA was comprised of four different nucleotides to form a tetranucleotide. The RNA of the virus contained the four classical nucleotides but diffused more slowly than a tetranucleotide might. In 1942 the nucleic acid, isolated after heat denaturation of the virus, was shown by S.S. Cohen and Stanley, using measurements of diffusion, sedimentation and viscosity, to be much larger, indeed, having an average molecular weight of 300,000. The product was highly asymmetric and spontaneously birefringent, although it slowly depolymerized on standing. The size and shape of this material

suggested a lengthwise orientation within the virus, which also contained linearly assembled smaller subunits of protein. The packaging of the protein around the nucleic acid presumably rendered the latter insusceptible to degradative enzymes. Although the largest weight of the product isolated at this time was only an eighth of the total RNA of a virus particle, less drastic methods have yielded RNA molecules of greater than two million daltons. Such molecules of RNA are infectious themselves, and indeed some of this size were probably among the mixture of molecules isolated in 1942, since some fifteen years later infectious RNA has been prepared after heat denaturation.

As indicated above, the criticism of Stanley's early studies had been severe. Nevertheless Stanley did not respond in kind. The dialogue, criticism and competition led in many instances to stimulated efforts and new results. Before 1937, Stanley had obtained collaborative assistance from physical chemists in New York, R.W.G. Wyckoff, J. Biscoe and G.I. Lavin. In the period of 1937 to 1942, the work of Stanley's laboratory multiplied with the assistance of numerous younger chemists, H.S. Loring, Frank A. Ross, M. Lauffer, G.L. Miller, C.A. Knight and S.S. Cohen. The physical biochemist, Max Lauffer, was particularly important in formulating approaches to defining the molecularity of tobacco mosaic virus and of tomato bushy stunt virus, and in characterizing macromolecules generally. The English group asked early on if the crystalline preparations of infectious protein contained only the distinctive rod-like particles, and both groups used physical and chemical methods in developing the affirmative answer. Was the infectivity a function of a singularly-sized rod? Lengthwise aggregation occurred under many biological and chemical conditions, but careful sedimentation studies by Lauffer revealed that monomeric rods were the infectious entity. Rods of shorter length were seen in electron microscopy of infectious samples, but

these are now known to be derived from longer rods broken in the preparation of the sample for microscopy. How homogeneous was a population of virus particles? Lauffer, analyzing the spreading of a sedimenting boundary of tomato busy stunt virus, concluded that the diameters of the particles could deviate from the mean by no more than 1%. In an exuberant moment, Lauffer referred to "living molecules."

Nevertheless, it is of considerable interest that neither group tested the infectivity of viral RNA before 1956. Despite the availability of appropriate viral RNA after 1936 and inactivating crystalline ribonuclease in 1940, despite the demonstration of DNA as Pneumococcal transforming agent in 1944 and the apparent infectivity of phage DNA, accepted by the community of phage workers in 1953 following the discovery of the Watson-Crick model, the thought that the viral RNA might be the genetic element of this virus was not tested before 1956.

In 1940 E. Pfankuch et al. had studied X-ray induced mutations of the virus and had attributed differences in the phosphorus contents of the parent and mutant strains to irradiation-induced alterations in the nucleic acid part of the virus. These data were not considered convincing in 1941 by C.A. Knight and Stanley who had found differences in the amino acid compositions of various strains. They had concluded that "the chemical differences between strains probably lies not in the nucleic acid but rather in the protein part of the virus molecule." They apparently did not consider the possibility that the nucleic acid might determine the composition of the protein. Following this line of thought, Miller and Stanley modified amino acid residues with a variety of reagents but found that, although many groups could be modified without loss of biological activity, the virus propagated was normal virus. At this point in the work, early in the entrance of the United States into World War II, the

work of the laboratory was diverted to the isolation of influenza virus and the production of an influenza vaccine.

Nor is the record of Bawden and Pirie more enlightening on this question. Only after the startling reports of Gierer and Schramm and of Fraenkel-Conrat in 1956 did these workers undertake to test the infectivity of RNA preparations. Finding low levels of such activity in an inefficient assay by their RNA samples, they were suspicious initially of the meaning of their results. However, as the mechanisms of virus multiplication and of the roles of the nucleic acids were clarified, they eventually accepted the concept that the RNA or DNA of a particular virus can constitute its genetic element.

Although Stanley had defined the reproductive process as one requiring the participation of cells, his approach to the problems of virus multiplication, as well as that of Bawden and Pirie, focused on the nature and structure of the virus particle. This approach provided unique materials for the development of electron microscopy, and for some years the well-defined tobacco mosaic virus served as the yardstick for the standardization of the magnification in the microscope. Neither group ever attempted to analyze the multiplication of a virus in its cellular site, because it appeared too difficult to obtain tissue in which a high percentage of cells were infected. This had led a few workers to begin to reexplore the long-known bacteriophage systems, in which it was possible to time the initiation of infection, the duration of the multiplication process and the yield of virus per infected cell. Furthermore, it was possible to infect all the bacteria of a population simultaneously to provide a system for the study of chemical events during bacteriophage multiplication. This type of chemical study of virus multiplication began in 1946, was extended to animal cells infected in tissue culture in 1953, and finally to infection of separated plant protoplasts in 1967. It is now known

that certain virus infections of plants permit the growth of virus-infected cells, which can be isolated in high yield and with which processes of virus multiplication can be studied. In retrospect it can be seen that this late development could have been sought in the late 1930s.

In any case the exigencies of World War II altered the priorities of Stanley's laboratory, and with the participation of Miller, Lauffer and Knight, Stanley developed an inactivated vaccine for viral influenza. A Sharples Super-centrifuge, found to be useful in sedimenting various types of particles, was applied to the study of the concentration of influenza virus grown in the allantois of the embryonated chick. The large capacity and efficiency of this equipment made this the method of choice for a large-scale preparation of virus. The size, stability and chemical inactivation of the virus were studied, as well as its immunizing potency. The general procedure has proved to be useful in the development of several commercial vaccines. Stanley became a consultant to the Secretary of War and a member of the U.S. Army Commission on influenza. In 1948 he received a Presidential Certificate of Merit for his work in vaccine development.

The many exciting and important results of Stanley and his early collaborators led to his election to the American Philosophical Society and National Academy of Sciences in 1940 and 1941 respectively. He had won many prizes and academic honors, including honorary degrees from Earlham, Harvard and Yale before the beginning of the War. At the end of the War, a new round of awards began in 1946, including the Nichols Medal of the American Chemical Society and the Nobel Prize, shared with J.B. Sumner and John H. Northrop, for their crystallization of enzymes, and Stanley also received an honorary degree from the University of California. Early in 1947, the Trustees of the Rockefeller Institute decided to close the Princeton Laboratory, announcing

this in the press without the prior knowledge of the Director, Carl Ten Broek, and senior Members including Stanley and Northrop at the Princeton branch. Individuals were offered the opportunity to renew their work in New York. Although this was acceptable to Kunkel who kept his home in New Jersey and Kunitz who moved to New York, many others, including Stanley and Northrop, left the Institute.

In 1948 both Nobelists accepted positions at the University of California in Berkeley, California. Stanley joined the Faculty as the founder of the Virus Laboratory-to-be and the Chairman of a new Department of Biochemistry. He moved at the peak of his career to a University which, as a matter of policy, had frequently recruited the most eminent professorial stars to build new areas or Institutes in the University complex. The move occurred at the end of a strenuous War, in which scientists of the Berkeley campus had contributed in an outstanding way to the magical thunderclaps that had precipitated the final collapse of the Japanese. Penicillin, which produced miraculous cures of many bacterial diseases, had also become a major product in the course of the War. Science was perceived as an enormous force in the future of the planet, and, although the development of penicillin had not solved the problem of virus infection, it was well known that knowledge was power and the development of similarly wonderful drugs for the cure of virus disease was only a step away. The soldiers were going to return to college and to the University, the fruits of the baby boom were to appear at its doors only ten years after that, and growth of the University was essential, particularly in areas of science, to prepare for the glorious future. Stanley began his second career as an educational administrator, in an optimistic University.

From 1948 to 1953, he recruited able young scientists for both Departments, and in 1953 resigned as Chairman of the Department of

Biochemistry, as that developing unit was increasingly productive and independent. In a period in which the enzymological basis of intermediary metabolism was being explored increasingly in microbial systems, members of that Department, such as W.Z. Hassid and H.A. Barker, were recognized as leaders in such studies. After his resignation as Chairman of Biochemistry, Stanley focused on the tasks for which he had been recruited. The Virus Laboratory became an assembly of leaders in disciplines crucial to the development of virology. C.A. Knight had come with Stanley and had reestablished study of plant viruses. H.K. Schachman, a physical chemist who had worked for years with Lauffer at Princeton, had organized the laboratory concerned with the physical characterization of macromolecules. Schachman was to become Director of the Virus Laboratory after Stanley's death. R.C. Williams, a distinguished electron microscopist, had been recruited, as had the protein chemist, H. Fraenkel-Conrat, and G. Stent, a phage worker, who had studied with M. Delbruck. H. Rubin began a study of tumor viruses, and several animal virologists, F.L. Schaffer and C.E. Schwerdt, concerned with the isolation of the virus of poliomyelitis, crystallized the virus in 1955. In that year also, Fraenkel-Conrat and Williams had reassembled the RNA and protein subunits of tobacco mosaic virus to form an infectious product, and in the following year the former showed that the RNA alone was active and had been protected by its protein coat. In 1960 Stanley participated in a group which had determined the complete sequence of the amino acids in the protein subunit.

He urged the University to create a Department of Virology, which he chaired from 1958 until 1964. In this period Stanley wrote many reviews and participated in many symposia related to viruses. In 1959 he and F.M. Burnet edited a three-volume compendium entitled "The Viruses." Before and during this period he had become increasingly active in the affairs of national

science, as Chairman of the Editorial Board of the Proceedings of the National Academy of Sciences, as a Director of the American Cancer Society, and as a member of the Board of Scientific Counselors of the National Cancer Institute.

He was also deeply and consistently occupied in campus life, as an officer of the Faculty Club and in the Faculty Senate. In the period of a developing Cold War, the influence of McCarthyism had led to an imposition of loyalty oaths on the Faculties of many Universities, including that at Berkeley. Stanley served as Chairman of the University Senate Committee on Academic Freedom. He signed the California oath himself, but publicly defended the rights of others who refused to sign oaths as a matter of conscience. He vigorously opposed this imposition as a condition of employment and participated in the work of groups of academics in resisting oaths and in bringing the legal issues to the courts. A court decision eventually declared the unconstitutionality of the oath.

Stanley was convinced of the need to communicate current advances and perspectives of science to lay and medical groups. He helped to organize a television series on viruses. His efforts in addressing the public led to his election as an honorary member of the National Association of Science Writers.

After 1964, when the Department of Virology was enlarged to become the Department of Molecular Biology, Stanley was relieved of some administrative duties and shifted his interests even more extensively to the national scene. In this period of the growth of the National Institutes of Health, he served as a member of the Advisory Committees to the director, James A. Shannon, and to the Secretary of the Department of Health, Education and Welfare. In the 1960s also, the work on avian and mammalian tumor viruses had increasingly created the sense that such viruses might be etiological agents of human cancer, and the feeling grew that Stanley's contributions might relate to the control of

this disease as well. In addition to awards by the American Cancer Society, he was selected as President of the Tenth International Cancer Congress in 1970. The hypothesis that tumor viruses, responsible for human cancer, might be isolated and used in the development of immunizing vaccines, was one perspective leading to the passage of the National Cancer Act in 1971. The expanded national effort, which attempted to document the concept, discovered in the next five years that this idea was much too oversimplified, but in its turn discovered new facts concerning the genetic relations of tumor viruses which have led to new rounds of excitement and hope.

Stanley suffered several severe illnesses in his later years but continued to live a full and vigorous life, which included extensive travel. He died of a heart attack in Spain where he had attended a scientific conference and had discussed tumor viruses. He is buried in California. The laboratory which he built at the University of California is named the Wendell M. Stanley Hall.

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A list of Stanley's publications until 1948 is obtainable from the Archives of the Rockefeller University. A more complete list until 1970 is available in the Archives of the University of California at Berkeley. Key publications to which reference has been made include: The Isolation and Properties of Crystalline Tobacco Mosaic Virus, p. 196 in Les Prix Nobel en 1947 (Published Rung. Boktryckeriet, P.A. Norstedt and Souer, Stockholm, 1949); (With R. Adams) The synthesis of chaulmoogric acid from hydnocarpic acid, J. Am. Chem. Soc. 51:1515 (1929); (With M.S. Jay and R. Adams) The preparation of certain octadecanoic acids and their bactericidal action toward B. leprae, XV, J. Am. Chem. Soc. 51:1261 (1929); (With H. Wieland) Zur kenntnis der sterine

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